Department of Energy

Office of Science
Consolidated Service Center

9800 South Cass Avenue
Lemont, IL 60439

October 9, 2026

Lewis Kamb
U.S. Right to Know

Via E-mail: lewis@usrtk.org

SUBJECT: FREEDOM OF INFORMATION ACT (FOIA) REQUEST NUMBER CH-2025-03169-F

Dear Mr. Kamb:

I am the authorizing official responsible for making the determination required by Section 1004.5(b) of the U.S. Department of Energy (DOE) regulations found at 10 CFR Part 1004, implementing the federal FOIA, 5 U.S.C. 552. You originally submitted your request to the National FOIA portal. DOE Headquarters (HQ) transferred the request to the DOE Office of Science-Consolidated Service Center (SC-CSC), Oak Ridge location (ORO), because ORO has jurisdiction over responsive records potentially existing at Pacific Northwest National Laboratory (PNNL). This letter serves as a partial response to your subject FOIA request. The request involves numerous responsive documents. Accordingly, DOE is releasing a portion of the documents that we have reviewed thus far and will continue to release monthly partial responses until the request has been fully processed.

In your original request, submitted on May 15, 2025, you indicated the following as the description of records you are seeking:

"All email correspondence sent to or from Dr. Amy Sims, Senior Research Scientist assigned to the Department of Energy's Pacific Northwest National Laboratory, via the email address amy.sims@pnnl.gov (Including attachments, CC and BCC), with any of the following email addresses, email domains, individuals or organizations:

1. @ecohealthalliance.org OR "Ecohealth Alliance"
2. @whi.iov.cn OR "WIV" OR "Wuhan Institute of Virology"
3. @email.unc.edu OR "UNC" OR "University of North Carolina"
4. Peter Daszak OR daszak@ecohealthalliance.org
5. Shi Zheng-Li OR zlshi@wh.iov.cn OR zhengli.shi@virosin.org OR 544728460@qq.com
6. Linfa Wang OR linfa.wang@duke-nus.edu.sg
7. Ralph Baric OR rbaric@email.unc.edu OR rsbaric@gmail.com
8. Timothy Sheahan OR sheahan@email.unc.edu
9. Boyd Yount Jr. OR byount@email.unc.edu
10. Tonie Rocke OR trocke@usgs.gov
11. Jerome Unidad OR junidad@parc.com

The time range for this request is Dec. 1, 2019 to Dec. 31, 2021."

Based on the most likely location for responsive records of your request, DOE asked Battelle, the contractor that manages and operates PNNL for DOE, to conduct a search of its files for responsive records. Battelle responded that it located numerous responsive records. In this fourth partial response, DOE is releasing 275 responsive documents, totaling 778 pages. Ninety-six documents contain redactions for Exemption 4 – Privileged and Confidential Information, and fifty-five documents contain redactions for Exemption 6 – Personal Privacy. Attached is a table listing which documents have redactions.

FOIA Exemption (b)(4) – Privileged or Confidential Information

Certain information contained in the listed documents below is being withheld under FOIA Exemption 4, 5 U.S.C. § 552(b)(4). Exemption 4 protects trade secrets and commercial or financial information that is obtained from a person and privileged or confidential. 10 C.F.R. § 1004.10(b)(4). Information is deemed "commercial or financial" as long as the submitter has a "commercial interest" in them. *Pub. Citizen Health Research Group v. FDA,* 704 F.2d 1280, 1290 (D.C. Cir. 1983). The redacted information is considered commercial because it pertains to confidential financial information regarding research funding. The information was obtained from a person, because "person" covers a broad range of entities including corporations. *Nadler v. FDIC,* 92 F.3d 93, 95 (2d Cir. 1996).

Where commercial or financial information is both customarily and actually treated as private by its owner and provided to the government under an assurance of privacy, the information is "confidential" within the meaning of Exemption 4. *Food Marketing Institute v. Argus Leader Media*, 588 U.S. 427, 440 (2019). Battelle has asserted that the information, i.e., confidential financial information regarding research funding, is customarily treated as confidential and not generally available to the public. In addition, the Government has provided assurance to Battelle that it will not release information that is confidential financial information regarding research funding. Disclosure of such confidential financial information would impair DOE's ability in the future to enter contractual arrangements.

FOIA Exemption (b)(6) – Personal Privacy Information

Certain information—i.e., personal contact information contained in the responsive documents is exempt from disclosure under Exemption 6 of the FOIA, 5 U.S.C. § 552(b)(6). Exemption 6 protects "personnel and medical files and similar files the disclosure of which would constitute a clearly unwarranted invasion of personal privacy." 5 U.S.C.§ 552(b)(6); 10 C.F.R. § 1004.10(b)(6). A determination under Exemption 6 requires a balancing of an individual's right to privacy against any public interest in the requested information.

The first step in the Exemption 6 balancing process is determining whether disclosure of the information would violate a viable privacy interest of the subject of the information. *See Schell v. HHS*, 843 F.2d 933, 938 (6th Cir. 1988). Once it has been determined that a personal privacy interest is threatened by a release of information, the next step is to assess whether there is a public interest in disclosing the information. *See Department of Justice FOIA Guide, Exemption 6,* at 1- 2, August 19, 2022. The Supreme Court has held that a public interest exists if disclosure would contribute significantly to the "public understanding of the operations or activities of the government." *Department of Justice v. Reporters Committee for Freedom of the Press*, 489 U.S. 749, 775 (1989). Finally, the two competing interests

must be weighed against one another to determine whether the harm to personal privacy or benefit to the public is the greater result. *See Ripskis v. HUD,* 746 F.2d 1, 3 (D.C. Cir. 1984).

Here, individuals have a substantial privacy interest in the nondisclosure of personal contact information. Disclosing this information could subject these individuals to possible harassment/unwanted contact. Conversely, there is very little public interest in knowing the personal contact information of individuals as these details do not aid in the "public understanding of the operations or activities of the government." *DOJ v. Reporters Committee*, 489 U.S. at 775. Therefore, the Privacy Act balancing test clearly weighs on the side of withholding the personal contact information and this personal privacy information has been redacted from the responsive records.

The determination relating to this portion of your FOIA request may be appealed within 90 calendar days from your receipt of this letter pursuant to 10 C.F.R. § 1004.8. Appeals should be addressed to Director, Office of Hearings and Appeals, HG-1, L'Enfant Plaza, U.S. Department of Energy, 1000 Independence Avenue, S.W., Washington, D.C. 20585-1615. The written appeal, including the envelope, must clearly indicate that a FOIA appeal is being made. You may also submit your appeal to OHA.filings@hq.doe.gov, including the phrase "Freedom of Information Appeal" in the subject line. The appeal must contain all the elements required by 10 C.F.R. § 1004.8, including a copy of the determination letter. Thereafter, judicial review will be available to you in the Federal District Court either: 1) in the district where you reside; 2) where you have your principal place of business; 3) where DOE's records are situated; or 4) in the District of Columbia.

You may contact DOE's FOIA Public Liaison, Kim Donham, via e-mail at kim.donham@doe.gov for further assistance and to discuss any aspect of your request. Additionally, you may contact the Office of Government Information Services (OGIS) at the National Archives and Records Administration to inquire about the FOIA mediation services they offer. The contact information for OGIS is as follows: Office of Government Information Services, National Archives and Records Administration, 8601 Adelphi Road-OGIS, College Park, Maryland 20740-6001, e-mail at ogis@nara.gov; telephone at 202-741-5770; toll free at 1-877-684-6448; or facsimile at 202-741-5769.

If you have any questions about this response, please contact Michelle Galbert, FOIA/PA Officer, at michelle.galbert@doe.gov.

Sincerely,

Geoff deBeauclair
Manager
Office of Science
Consolidated Service Center

Enclosures:
As Stated

Pacific Northwest NATIONAL LABORATORY

Battelle *The Business of Innovation*

ADVANCE PAYMENT INVOICE

P.O. Box 84391
Seattle, WA 98124-5691
Tel (509) 375-2121
Fax (509) 371-7600

Federal Tax ID: 31-4379427

Date	1/29/2020
Invoice No.	0120018
Customer Order No.	
PNNL Contract No.	75881
Full Advance	
Total Amount Due	$(b) (4)

University of North Carolina, Chapel Hill
Attn: Accounts Receivable
Box 2200
Chapel Hill, NC 27599-2200

Description	Amount (U.S. Funds)
Advance Payment Invoice	$(b) (4)

Billing in Accordance with Terms of the agreement

Send check payable in U.S. funds to:
Battelle
Attn: CASHIER
PO BOX 84391
Seattle, WA 98124-5691

Wire Information:
US Bank, Richland, WA
ABA No. (b) (4)
Account No. (b) (4)
SWIFT Code: (b) (4)

Approved by: Lea Gonzalez for Barb Hays

PLEASE RETURN COPY OF INVOICE OR REFER TO INVOICE NUMBER WITH REMITTANCE.

Strategic Partnership Projects Agreement No. 75881

Between

BATTELLE MEMORIAL INSTITUTE, PACIFIC NORTHWEST DIVISION

Operating under Prime Contract No. DE-AC05-76RL01830
for the U.S. Department of Energy

and

UNIVERSITY OF NORTH CAROLINA CHAPEL HILL

The obligations of the above-identified DOE Contractor shall apply to any successor in interest to said Contractor continuing the operation of the DOE facility involved in this Strategic Partnership Projects Agreement.

GENERAL TERMS AND CONDITIONS

PREAMBLE

WHEREAS, University of North Carolina, Chapel Hill requires the unique services or materials of **Pacific Northwest National Laboratory** that are not available to them in the domestic private sector;

WHEREAS, the Department of Energy may authorize the Facility Operator of **Pacific Northwest National Laboratory** to provide services and/or materials that are not available in the domestic private sector, and when the Department of Energy approved Agreement, which may not incorporate flow-down provisions from a University's contract or Agreement with another entity, is used as the contractual document;

WHEREAS, the **Battelle Memorial Institute** of the Department of Energy's **Pacific Northwest National Laboratory** has determined that it can perform the work in accordance with Department of Energy requirements; and

WHEREAS, the Department of Energy has determined that the proposed work to be performed for the University will not place the Department of Energy facility and its contractor in competition with the domestic private sector;

NOW THEREFORE, the Department of Energy has authorized the **Battelle Memorial Institute** to perform the work identified in Appendix A, Statement of Work, of this Agreement in accordance with the terms and conditions of this Agreement.

ARTICLE I. PARTIES TO THE AGREEMENT

The U.S. Department of Energy Contractor, Battelle Memorial Institute, Pacific Northwest Division, hereinafter referred to as the "Contractor," has been requested by University of North Carolina, Chapel Hill, hereinafter referred to as the "University," to perform the work set forth in the Statement of Work, attached hereto as Appendix A. It is understood by the Parties that, except for the intellectual property provisions of this Agreement, the Contractor is obligated to comply with the terms and conditions of its M&O contract with the United States Government (hereinafter called the "Government") represented by the United States Department of Energy (hereinafter called the "Department" or "DOE") when providing goods, services, products, processes, materials, or information to the University under this Agreement. It is further understood that the Contractor must not allow this work to adversely impact execution of DOE assigned programs at the facility.

ARTICLE II. TERM OF THE AGREEMENT

The term of this Agreement shall be effective as of the latter date of (1) the date on which it is signed by the last of the Parties thereto or (2) the date on which the Contractor receives advance funding from the University, if required under Article IV. **The completion date is May 31, 2020.**

ARTICLE III. COSTS

A. The Contractor estimated cost for the work to be performed under this Agreement is $(b) (4)

B. The authorized funding is $(b) (4) . This amount shall constitute the maximum funding obligation of the University, unless amended by mutual Agreement of the Parties. The Contractor has no obligation to continue performance of the work at a cost in excess of the authorized funding.

C. The Contractor agrees to provide at least 30 days' notice to the University if the actual cost to complete performance will exceed the authorized funding or the estimated cost of the work.

ARTICLE IV. FUNDING AND PAYMENT

The Sponsor shall pay the Contractor as follows:

A. Advance Payment. The Sponsor shall **advance full funding in the amount of $**(b) (4) payable upon execution of the Agreement. Upon termination or completion, any excess funds shall be refunded by the Contractor to the Sponsor. Payments will be directed as follows:

Check Payment:
Battelle
For Project Number: 75881
P. O. Box 84391, ATTN: Cashier
Seattle, WA 98124-5691

Wire Transfer:
U.S. Bank
Richland, WA 99352
ABA No. (b) (4)
Account No. (b) (4)
SWIFT Code: (b) (4)

For check payments, include Project Number 75881 and all invoice numbers being paid on the check. For wire transfers, include contract number and invoice number on the receiver info-line and list all invoice numbers being paid on the sender info-line.

B. Applicable Currency. All payments due the Contractor under this Agreement, including cost estimates and obligations of funds, shall be in United States dollars (U.S.$).

ARTICLE V. SOURCE OF FUNDS

The University hereby warrants and represents that, if the funding it brings to this Agreement has been secured through other Agreements such other Agreements do not have any terms and conditions (including intellectual property) that conflict with the terms of this Agreement.

ARTICLE VI. PROPERTY

Property or equipment produced or acquired in conducting the work under this Agreement shall be owned by DOE. No Federal funds of the Contractor will be used to purchase property or equipment for this Agreement. Property or equipment produced or acquired as part of this Agreement will be accounted for and maintained during the term of the Agreement in the same manner as Department property or equipment.

ARTICLE VII. PUBLICATION MATTERS

The publishing Party shall provide the other Party a 30-day period in which to review and comment on proposed publications that disclose technical developments and/or research findings generated in the course of this Agreement. The publishing Party shall not publish or otherwise disclose Proprietary Information identified by the other Party, except as provided by law.

ARTICLE VIII. LEGAL NOTICE

The Parties agree that the following Legal Disclaimer Notice shall be affixed to each report furnished to the University under this Agreement and to any report resulting from this Agreement which may be distributed by the University:

DISCLAIMER

This report was prepared by Battelle Memorial Institute on behalf of the U.S. Department of Energy (DOE), as an account of work sponsored by University of North Carolina, Chapel Hill. Neither Battelle Memorial Institute, DOE, the United States Government nor any agency thereof, nor Battelle Memorial Institute, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or Battelle Memorial Institute. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

PACIFIC NORTHWEST NATIONAL LABORATORY
operated by
BATTELLE
for the
UNITED STATES DEPARTMENT OF ENERGY
under Contract DE-AC05-76RL01830

ARTICLE IX. DISCLAIMER

THE GOVERNMENT AND THE CONTRACTOR MAKE NO EXPRESS OR IMPLIED WARRANTY AS TO THE CONDITIONS OF THE RESEARCH OR ANY INTELLECTUAL PROPERTY, GENERATED INFORMATION, OR PRODUCT MADE OR DEVELOPED UNDER THIS STRATEGIC PARTNERSHIP PROJECTS AGREEMENT, OR THE OWNERSHIP, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE OF THE RESEARCH OR RESULTING PRODUCT; THAT THE GOODS, SERVICES, MATERIALS, PRODUCTS, PROCESSES, INFORMATION, OR DATA TO BE FURNISHED HEREUNDER WILL ACCOMPLISH INTENDED RESULTS OR ARE SAFE FOR ANY PURPOSE INCLUDING THE INTENDED PURPOSE; OR THAT ANY OF THE ABOVE WILL NOT INTERFERE WITH PRIVATELY OWNED RIGHTS OF OTHERS. NEITHER THE GOVERNMENT NOR THE CONTRACTOR SHALL BE LIABLE FOR SPECIAL, CONSEQUENTIAL, OR INCIDENTAL DAMAGES ATTRIBUTED TO SUCH RESEARCH OR RESULTING PRODUCT, INTELLECTUAL PROPERTY, GENERATED INFORMATION, OR PRODUCT MADE OR DELIVERED UNDER THIS STRATEGIC PARTNERSHIP PROJECTS AGREEMENT.

ARTICLE X. GENERAL INDEMNITY

To the extent permitted by law applicable to the University, the University agrees to indemnify and hold harmless the Government, the Department, the Contractor, and persons acting on their behalf from all liability, including costs and expenses incurred, to any person, including the University, for injury to or death of persons or other living things or injury to or destruction of property arising out of the performance of the Agreement by the Government, the Department, the Contractor, or persons acting on their behalf, or arising out of the use of the services performed, materials supplied, or information given hereunder by the University or persons acting upon behalf of the University, and not directly resulting from the fault or negligence of the Government, the Department, the Contractor, or persons acting on their behalf.

ARTICLE XI. PRODUCT LIABILITY INDEMNITY

Except for any liability resulting from any negligent acts or omissions of the Government or the Contractor, the University agrees to indemnify the Government and the Contractor for all damages, costs, and expenses, including attorney's fees, arising from personal injury or property damage occurring as a result of the making, using, or selling of a product, process, or service by or on behalf of the University, its assignees, or licensees, which was derived from the work performed under this Strategic Partnership Projects Agreement. In respect to this Article, neither the Government nor the Contractor shall be considered assignees or licensees of the University, as a result of reserved Government and Contractor rights. The indemnity set forth in this paragraph shall apply only if the University shall have been informed as soon and as completely as practical by the Contractor and/or the Government of the action alleging such claim and shall have been given an opportunity, to the maximum extent afforded by applicable laws, rules, or regulations, to participate in and control its defense, and the Contractor and/or Government shall have provided all reasonably available information and reasonable assistance requested by the University. No settlement for which the University would be responsible shall be made without the University's consent, unless required by final decree of a court of competent jurisdiction.

ARTICLE XII. INTELLECTUAL PROPERTY INDEMNITY - LIMITED

If and to the extent permitted by law applicable to the University, the University shall indemnify the Government and the Contractor and their officers, agents, and employees against liability, including costs, for infringement of any United States patent, copyright, or other intellectual property arising out of any acts required or directed by the University to be performed under this Agreement to the extent such acts are not already performed at the facility. Such indemnity shall not apply to a claimed infringement that is settled without the consent of the University unless required by a court of competent jurisdiction.

ARTICLE XIII. NOTICE AND ASSISTANCE REGARDING PATENT AND COPYRIGHT INFRINGEMENT

The University shall report to the Department and the Contractor, promptly and in reasonable written detail, each claim of patent or copyright infringement based on the performance of this Agreement of which the University has knowledge. The University shall furnish to the

Department and the Contractor, when requested by the Department or the Contractor, all evidence and information in the possession of the University pertaining to such claim.

ARTICLE XIV. PATENT RIGHTS CLASS WAIVER DECLINED NON-EXCLUSIVE LICENSE TO UNIVERSITY

1. Definitions.

   A. "Subject Invention" means any invention or discovery of the Contractor, or, to the extent the University is performing any work under this Agreement, of the University, conceived in the course of or under this Agreement, or, in the case of an invention previously conceived by the University, first actually reduced to practice in the course of or under this Agreement. "Subject Invention" includes any art, method, process, machine, manufacture, design or composition of matter, or any new and useful improvement thereof, or any variety of plant, whether patented under the patent laws of the United States of America or any foreign country, or unpatented.

   B. “Facility Contractor” means BATTELLE MEMORIAL INSTITUTE as operator of PACIFIC NORTHWEST NATIONAL LABORATORY operating under DOE Prime Contract No. DE-AC05-76RL01830 or any successor contractor thereof.

2. Any subject invention made by the Facility Contractor under this Agreement will be governed by the provisions of the Facility Prime Contract with the DOE. In the event that the Government patents a Facility Contractor Invention, University retains a non-exclusive license.

3. The University and Facility subcontractor(s) as applicable, may retain title to their own Subject Inventions, subject to, the Government retaining a non-exclusive, non-transferable, irrevocable, paid-up license to practice or have practiced by on or behalf of the United States the Subject Inventions throughout the world, a requirement to report their Subject Inventions to DOE within 6 months after conception or first actual reduction to practice, whichever occurs first, in the course of or under this Agreement, U.S. Preference (35 USC §204) and such other conditions consistent with DOE patent waiver policy.

4. Facility Contractor grants to University a non-exclusive, irrevocable, non-transferable royalty free-license to all of Facility Contractor’s inventions arising under this Agreement.

ARTICLE XV. RIGHTS IN TECHNICAL DATA — UNLIMITED RIGHTS NON-PROPRIETARY

1. The following definitions shall be used.

A. “Facility Contractor” means BATTELLE MEMORIAL INSTITUTE as operator of PACIFIC NORTHWEST NATIONAL LABORATORY operating under DOE Prime Contract No. DE-AC05-76RL01830 or any successor contractor thereof.

B. "Generated Information" means information produced in the performance of this Agreement.

C. "Proprietary Information" means information which is developed at private expense, is marked as Proprietary Information, and embodies (1) trade secrets or (2) commercial or financial information which is privileged or confidential under the Freedom of Information Act (5 U.S.C. 552 (b)(4)).

D. "Unlimited Rights" means the right to use, disclose, reproduce, prepare derivative works, distribute copies to the public, and perform publicly and display publicly, in any manner and for any purpose, and to have or permit others to do so.

2. For work performed at the DOE Facility, the University agrees to furnish to the Facility Contractor or leave at the facility that information, if any, which is (1) essential to the performance of work by the Facility Contractor personnel or (2) necessary for the health and safety of such personnel in the performance of the work. Any information furnished to the Facility Contractor shall be deemed to have been delivered with Unlimited Rights unless marked as Proprietary Information. The University agrees that it has the sole responsibility for appropriately identifying and marking all documents containing Proprietary Information, whether such documents are furnished by the University or produced under this Agreement and made available to the University for review.

3. The Government and Facility Contractor agree not to disclose properly marked Proprietary Information to anyone other than the University without written approval of the University, except to Government employees who are subject to the statutory provisions against disclosure of confidential information set forth in the Trade Secrets Act (18 U.S.C. 1905). The Government and Facility Contractor shall have the right, at reasonable times up to 3 years after the termination or completion of the Agreement, to inspect any information designated as Proprietary Information by the University, for the purpose of verifying that such information has been properly identified as Proprietary Information.

4. The University is solely responsible for the removal of all of its Proprietary Information from the facility by or before termination of this Agreement. The Government and Facility Contractor shall have Unlimited Rights in any information which is not removed from the facility by termination of this Agreement. The Government and Facility Contractor shall have Unlimited Rights in any Proprietary Information which is incorporated into the

facility or equipment under this Agreement to such extent that the facility or equipment is not restored to the condition existing prior to such incorporation.

5. The University agrees that the Facility Contractor will provide to the Department a nonproprietary description of the work performed under this Agreement.

6. The Government shall have Unlimited Rights in all Generated Information produced or information provided by the Parties under this Agreement, except for information which is disclosed in a Subject Invention disclosure being considered for patent protection, or which is marked as being Proprietary Information.

7. Copyrights. The University may assert copyright in any of its Generated Information, and may also require the Contractor, at the University's expense, to register copyright and assign copyright in any Generated Information produced by the Contractor which the University wishes to copyright. Subject to the other provisions of this article, and to the extent that copyright is asserted, the Government reserves for itself a royalty-free, worldwide, irrevocable, non-exclusive license for Governmental purposes to publish, disclose, distribute, translate, duplicate, exhibit, prepare derivative works, and perform any such copyrighted works.

8. The terms and conditions of this article shall survive the Agreement, in the event that the Agreement is terminated before completion of the Statement of Work.

ARTICLE XVI. ASSIGNMENT

Neither this Agreement nor any interest therein or claim thereunder shall be assigned or transferred by either Party, except as authorized in writing by the other Party to this Agreement, provided, the Contractor may transfer it to the Department, or its designee, with notice of such transfer to the University, and the Contractor shall have no further responsibilities except for the confidentiality, use, and/or non-disclosure obligations of this Agreement.

ARTICLE XVII. SIMILAR OR IDENTICAL SERVICES

The Government and/or Contractor shall have the right to perform similar or identical services in the Statement of Work for other Sponsors.

ARTICLE XVIII. EXPORT CONTROL

Each Party is responsible for its own compliance with laws and regulations governing export control.

ARTICLE XIX. DISPUTES

The Parties shall attempt to jointly resolve all disputes arising from this Agreement. In the event a dispute arises under this Agreement, the University is encouraged to contact Contractor's Ombudsperson in order to further resolve such dispute before pursuing third- party mediation or other remedies. If the Parties are unable to jointly resolve a dispute within a reasonable period of time, they agree to submit the dispute to a third-party mediation process that is mutually agreed upon by the Parties. To the extent that there is no applicable U.S. Federal law, this Agreement and performance thereunder shall be governed by the laws of the State of Washington, without reference to that state's conflict of laws provisions.

ARTICLE XX. TERMINATION

Performance of work under this Agreement may be terminated at any time by either Party, without liability, except as provided above, upon giving a 60-day written notice to the other Party. The Contractor shall terminate this Agreement only when the Contractor determines, after direction from DOE, that such termination is in the best interest of the Government, provided however, that the Contractor shall have the right to terminate unilaterally if the University shall have failed to advance the funds required by Article IV. In the event of termination, the University shall be responsible for the Contractor's costs (including closeout costs) through the effective date of termination, but in no event shall the University's cost responsibility exceed the total cost to the University as described in Article III, above.

It is agreed that any obligations of the Parties regarding intellectual property will remain in effect, despite early termination of the Agreement.

In witness whereof, the Parties hereto have executed this Agreement.

BATTELLE MEMORIAL INSTITUTE PACIFIC NORTHWEST DIVISION		**UNIVERSITY OF NORTH CAROLINA CHAPEL HILL**	
Name	Barb Hays	Name	
Title	Senior Contracts Specialist	Title	
Date	January 29, 2020	Date	

From: Hays, Barbara A[barb.hays@pnnl.gov]
Sent: Mon 3/2/2020 2:04:38 PM (UTC-08:00)
To: Van Buren, Eve[evevb@email.unc.edu]
Cc: Farrell, Ronda Lee[farrelrl@email.unc.edu]; Parrish, Kalyn[klparrish@unc.edu]; Hays, Barbara A[barb.hays@pnnl.gov]; Waters, Katrina M[Katrina.Waters@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]
Subject: RE: Subaward 5116540 Between UNC Chapel Hill and Battelle/PNNL
Attachment: 75881 SPP Agreement.pdf
Attachment: 75881 advance_payment_invoice_ 0120018.pdf
Attachment: Sponsor Registration Form (PNNL) 7_9_19.docx

Eve, we are willing to accept 5 U.S.C. § 552(b)(4) dvance payment. The attached revised Agreement and invoice reflect the change. It's important to note, however, that we are not allowed to use DOE funding to "finance" non-DOE work. Therefore, the 5 U.S.C. § 552(b)(4) will authorize PNNL to start work. At the end of each month, we will submit an invoice for actual costs that we expect to be reimbursed net 30. The advance funding and the invoice reimbursements will allow PNNL to continue working; if we run out of cash on-hand, we will have to stop work until invoice payments are reimbursed. With this revised agreement to reduce the amount of advance pay, it's important that invoices are reimbursed in a timely manner.
The attached revised Agreement explains the process in Article IV Funding and Payment.

Because of the urgency of getting this Agreement in place and PNNL starting work, I also revised Article III, Term, to change the effective date to be when the Agreement is fully signed/executed (instead of the date we receive the advance payment). With an executed Agreement, I will try to get approval to use Battelle funding to allow us to start work while we wait for the advance payment to arrive

If you approve, please counter-sign the Agreement and return to me as soon as possible.

Also, I'm not sure if I requested a sponsor registration form when we submitted our proposal. Can you please complete and sign the attached and return it to me as soon as possible. Thank you

Barb Hays
Senior Contracts Specialist
Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999
Richland, WA 99352 USA
Tel: 509-372-4008

barb.hays@pnnl.gov

From: Van Buren, Eve <evevb@email.unc.edu>
Sent: Monday, March 02, 2020 11:17 AM
To: Hays, Barbara A <barb.hays@pnnl.gov>
Cc: Farrell, Ronda Lee <farrelrl@email.unc.edu>; Parrish, Kalyn <klparrish@unc.edu>
Subject: Subaward 5116540 Between UNC Chapel Hill and Battelle/PNNL

Hello Barb,

I'm in UNC's Office of Sponsored Research and am working on the subaward referenced above.

I'm writing to see if you would be amenable to an advance payment of 5 U.S.C. § 552(b)(4) stead of the full amount. If so, we could execute this agreement without further delay. An advance payment of 100%, however, will require

additional upper level approvals.

Thank you,
Eve

Eve Van Buren
Subaward Specialist
Office of Sponsored Research
University of North Carolina at Chapel Hill
104 Airport Drive, Suite 2200
Campus Box 1350
Chapel Hill, NC 27599
evevb@email.unc.edu
(919) 962-3115



Strategic Partnership Projects Agreement No. 75881

Between

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Operating under Prime Contract No. DE-AC05-76RL01830
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UNIVERSITY OF NORTH CAROLINA CHAPEL HILL

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WHEREAS, the Department of Energy may authorize the Facility Operator of **Pacific Northwest National Laboratory** to provide services and/or materials that are not available in the domestic private sector, and when the Department of Energy approved Agreement, which may not incorporate flow-down provisions from a University's contract or Agreement with another entity, is used as the contractual document;

WHEREAS, the **Battelle Memorial Institute** of the Department of Energy's **Pacific Northwest National Laboratory** has determined that it can perform the work in accordance with Department of Energy requirements; and

WHEREAS, the Department of Energy has determined that the proposed work to be performed for the University will not place the Department of Energy facility and its contractor in competition with the domestic private sector;

NOW THEREFORE, the Department of Energy has authorized the **Battelle Memorial Institute** to perform the work identified in Appendix A, Statement of Work, of this Agreement in accordance with the terms and conditions of this Agreement.

ARTICLE I. PARTIES TO THE AGREEMENT

The U.S. Department of Energy Contractor, Battelle Memorial Institute, Pacific Northwest Division, hereinafter referred to as the "Contractor," has been requested by University of North Carolina, Chapel Hill, hereinafter referred to as the "University," to perform the work set forth in the Statement of Work, attached hereto as Appendix A. It is understood by the Parties that, except for the intellectual property provisions of this Agreement, the Contractor is obligated to comply with the terms and conditions of its M&O contract with the United States Government (hereinafter called the "Government") represented by the United States Department of Energy (hereinafter called the "Department" or "DOE") when providing goods, services, products, processes, materials, or information to the University under this Agreement. It is further understood that the Contractor must not allow this work to adversely impact execution of DOE assigned programs at the facility.

ARTICLE II. TERM OF THE AGREEMENT

The term of this Agreement shall be effective as of the latter date of the date on which it is signed by the last of the Parties thereto. **The completion date is May 31, 2020.**

ARTICLE III. COSTS

A. The Contractor estimated cost for the work to be performed under this Agreement is 5 U.S.C. § 552(b)(4)

B. The authorized funding is 5 U.S.C. § 552(b)(4) This amount shall constitute the maximum funding obligation of the University, unless amended by mutual Agreement of the Parties. The Contractor has no obligation to continue performance of the work at a cost in excess of the authorized funding.

C. The Contractor agrees to provide at least 30 days' notice to the University if the actual cost to complete performance will exceed the authorized funding or the estimated cost of the work.

ARTICLE IV. FUNDING AND PAYMENT

The Sponsor shall provide sufficient funds in advance to reimburse the Facility Contractor for costs to be incurred in performance of the work described in this Agreement, and the Facility Contractor shall have no obligation to perform in the absence of adequate advance funds Upon termination or completion, any excess funds shall be refunded by the Facility Contractor to the Sponsor. The Sponsor shall pay the Facility Contractor as follows

A. Advance Payment. **The Sponsor shall advance** 5 U.S.C. § 552(b)(4) payable upon execution of the Agreement. Advance payment shall be recorded in the Contractor's account.

B. Monthly Payments. The Sponsor shall pay monthly thereafter at Net 30 upon submittal of invoices, in accordance with the format identified in Appendix B, representing actual costs incurred until the last 60 days of the Agreement term. At this time, the advance payment account shall be liquidated by charging costs incurred during this last period. Advance payment in excess of total costs incurred by the Facility Contractor under this Agreement shall be refunded to the Sponsor.

Invoices will be submitted electronically to the Sponsor at the following address:

University of North Carolina at Chapel Hill
Attn: Eve Van Buren evevb@email.unc.edu

Check Payment:
Battelle
For Project Number: 75881
P. O. Box 84391, ATTN: Cashier
Seattle, WA 98124-5691

Wire Transfer:
U.S. Bank
Richland, WA 99352
ABA No.
Account I
SWIFT Co

5 U.S.C. § 552(b)(4)

For check payments, include Project Number 75881 and all invoice numbers being paid on the check. For wire transfers, include contract number and invoice number on the receiver info-line and list all invoice numbers being paid on the sender info-line.

A. Applicable Currency. All payments due the Contractor under this Agreement, including cost estimates and obligations of funds, shall be in United States dollars (U.S.$).

ARTICLE V. SOURCE OF FUNDS

The University hereby warrants and represents that, if the funding it brings to this Agreement has been secured through other Agreements such other Agreements do not have any terms and conditions (including intellectual property) that conflict with the terms of this Agreement.

ARTICLE VI. PROPERTY

Property or equipment produced or acquired in conducting the work under this Agreement shall be owned by DOE. No Federal funds of the Contractor will be used to purchase property or equipment for this Agreement. Property or equipment produced or acquired as part of this Agreement will be accounted for and maintained during the term of the Agreement in the same manner as Department property or equipment.

ARTICLE VII. PUBLICATION MATTERS

The publishing Party shall provide the other Party a 30-day period in which to review and comment on proposed publications that disclose technical developments and/or research findings generated in the course of this Agreement. The publishing Party shall not publish or otherwise disclose Proprietary Information identified by the other Party, except as provided by law.

ARTICLE VIII. LEGAL NOTICE

The Parties agree that the following Legal Disclaimer Notice shall be affixed to each report furnished to the University under this Agreement and to any report resulting from this Agreement which may be distributed by the University:

DISCLAIMER

This report was prepared by Battelle Memorial Institute on behalf of the U.S. Department of Energy (DOE), as an account of work sponsored by University of North Carolina, Chapel Hill. Neither Battelle Memorial Institute, DOE, the United States Government nor any agency thereof, nor Battelle Memorial Institute, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or Battelle Memorial Institute. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

PACIFIC NORTHWEST NATIONAL LABORATORY
operated by
BATTELLE
for the
UNITED STATES DEPARTMENT OF ENERGY
under Contract DE-AC05-76RL01830

ARTICLE IX. DISCLAIMER

THE GOVERNMENT AND THE CONTRACTOR MAKE NO EXPRESS OR IMPLIED WARRANTY AS TO THE CONDITIONS OF THE RESEARCH OR ANY INTELLECTUAL PROPERTY, GENERATED INFORMATION, OR PRODUCT MADE OR DEVELOPED UNDER THIS STRATEGIC PARTNERSHIP PROJECTS AGREEMENT, OR THE OWNERSHIP, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE OF THE RESEARCH OR RESULTING PRODUCT; THAT THE GOODS, SERVICES, MATERIALS, PRODUCTS, PROCESSES, INFORMATION, OR DATA TO BE FURNISHED HEREUNDER

WILL ACCOMPLISH INTENDED RESULTS OR ARE SAFE FOR ANY PURPOSE INCLUDING THE INTENDED PURPOSE; OR THAT ANY OF THE ABOVE WILL NOT INTERFERE WITH PRIVATELY OWNED RIGHTS OF OTHERS. NEITHER THE GOVERNMENT NOR THE CONTRACTOR SHALL BE LIABLE FOR SPECIAL, CONSEQUENTIAL, OR INCIDENTAL DAMAGES ATTRIBUTED TO SUCH RESEARCH OR RESULTING PRODUCT, INTELLECTUAL PROPERTY, GENERATED INFORMATION, OR PRODUCT MADE OR DELIVERED UNDER THIS STRATEGIC PARTNERSHIP PROJECTS AGREEMENT.

ARTICLE X. GENERAL INDEMNITY

To the extent permitted by law applicable to the University, the University agrees to indemnify and hold harmless the Government, the Department, the Contractor, and persons acting on their behalf from all liability, including costs and expenses incurred, to any person, including the University, for injury to or death of persons or other living things or injury to or destruction of property arising out of the performance of the Agreement by the Government, the Department, the Contractor, or persons acting on their behalf, or arising out of the use of the services performed, materials supplied, or information given hereunder by the University or persons acting upon behalf of the University, and not directly resulting from the fault or negligence of the Government, the Department, the Contractor, or persons acting on their behalf.

ARTICLE XI. PRODUCT LIABILITY INDEMNITY

Except for any liability resulting from any negligent acts or omissions of the Government or the Contractor, the University agrees to indemnify the Government and the Contractor for all damages, costs, and expenses, including attorney's fees, arising from personal injury or property damage occurring as a result of the making, using, or selling of a product, process, or service by or on behalf of the University, its assignees, or licensees, which was derived from the work performed under this Strategic Partnership Projects Agreement. In respect to this Article, neither the Government nor the Contractor shall be considered assignees or licensees of the University, as a result of reserved Government and Contractor rights. The indemnity set forth in this paragraph shall apply only if the University shall have been informed as soon and as completely as practical by the Contractor and/or the Government of the action alleging such claim and shall have been given an opportunity, to the maximum extent afforded by applicable laws, rules, or regulations, to participate in and control its defense, and the Contractor and/or Government shall have provided all reasonably available information and reasonable assistance requested by the University. No settlement for which the University would be responsible shall be made without the University's consent, unless required by final decree of a court of competent jurisdiction.

ARTICLE XII. INTELLECTUAL PROPERTY INDEMNITY - LIMITED

If and to the extent permitted by law applicable to the University, the University shall indemnify the Government and the Contractor and their officers, agents, and employees against liability, including costs, for infringement of any United States patent, copyright, or other intellectual property arising out of any acts required or directed by the University to be performed under this

Agreement to the extent such acts are not already performed at the facility. Such indemnity shall not apply to a claimed infringement that is settled without the consent of the University unless required by a court of competent jurisdiction.

ARTICLE XIII. NOTICE AND ASSISTANCE REGARDING PATENT AND COPYRIGHT INFRINGEMENT

The University shall report to the Department and the Contractor, promptly and in reasonable written detail, each claim of patent or copyright infringement based on the performance of this Agreement of which the University has knowledge. The University shall furnish to the Department and the Contractor, when requested by the Department or the Contractor, all evidence and information in the possession of the University pertaining to such claim.

ARTICLE XIV. PATENT RIGHTS CLASS WAIVER DECLINED NON-EXCLUSIVE LICENSE TO UNIVERSITY

1. Definitions.

   A. "Subject Invention" means any invention or discovery of the Contractor, or, to the extent the University is performing any work under this Agreement, of the University, conceived in the course of or under this Agreement, or, in the case of an invention previously conceived by the University, first actually reduced to practice in the course of or under this Agreement. "Subject Invention" includes any art, method, process, machine, manufacture, design or composition of matter, or any new and useful improvement thereof, or any variety of plant, whether patented under the patent laws of the United States of America or any foreign country, or unpatented.

   B. "Facility Contractor" means BATTELLE MEMORIAL INSTITUTE as operator of PACIFIC NORTHWEST NATIONAL LABORATORY operating under DOE Prime Contract No. DE-AC05-76RL01830 or any successor contractor thereof.

2. Any subject invention made by the Facility Contractor under this Agreement will be governed by the provisions of the Facility Prime Contract with the DOE. In the event that the Government patents a Facility Contractor Invention, University retains a non-exclusive license.

3. The University and Facility subcontractor(s) as applicable, may retain title to their own Subject Inventions, subject to, the Government retaining a non-exclusive, non-transferable, irrevocable, paid-up license to practice or have practiced by on or behalf of the United States the Subject Inventions throughout the world, a requirement to report their Subject Inventions to DOE within 6 months after conception or first actual reduction to practice, whichever occurs first, in the course of or under this Agreement, U.S.

Preference (35 USC §204) and such other conditions consistent with DOE patent waiver policy.

4. Facility Contractor grants to University a non-exclusive, irrevocable, non-transferable royalty free-license to all of Facility Contractor's inventions arising under this Agreement.

ARTICLE XV. RIGHTS IN TECHNICAL DATA — UNLIMITED RIGHTS NON-PROPRIETARY

1. The following definitions shall be used.

   A. "Facility Contractor" means BATTELLE MEMORIAL INSTITUTE as operator of PACIFIC NORTHWEST NATIONAL LABORATORY operating under DOE Prime Contract No. DE-AC05-76RL01830 or any successor contractor thereof.

   B. "Generated Information" means information produced in the performance of this Agreement.

   C. "Proprietary Information" means information which is developed at private expense, is marked as Proprietary Information, and embodies (1) trade secrets or (2) commercial or financial information which is privileged or confidential under the Freedom of Information Act (5 U.S.C. 552 (b)(4)).

   D. "Unlimited Rights" means the right to use, disclose, reproduce, prepare derivative works, distribute copies to the public, and perform publicly and display publicly, in any manner and for any purpose, and to have or permit others to do so.

2. For work performed at the DOE Facility, the University agrees to furnish to the Facility Contractor or leave at the facility that information, if any, which is (1) essential to the performance of work by the Facility Contractor personnel or (2) necessary for the health and safety of such personnel in the performance of the work. Any information furnished to the Facility Contractor shall be deemed to have been delivered with Unlimited Rights unless marked as Proprietary Information. The University agrees that it has the sole responsibility for appropriately identifying and marking all documents containing Proprietary Information, whether such documents are furnished by the University or produced under this Agreement and made available to the University for review.

3. The Government and Facility Contractor agree not to disclose properly marked Proprietary Information to anyone other than the University without written approval of the University, except to Government employees who are subject to the statutory provisions against disclosure of confidential information set forth in the Trade Secrets Act (18 U.S.C. 1905). The Government and Facility Contractor shall have the right, at reasonable times up to 3 years after the termination or completion of the Agreement, to inspect any information designated as Proprietary Information by the University, for the

purpose of verifying that such information has been properly identified as Proprietary Information.

4. The University is solely responsible for the removal of all of its Proprietary Information from the facility by or before termination of this Agreement. The Government and Facility Contractor shall have Unlimited Rights in any information which is not removed from the facility by termination of this Agreement. The Government and Facility Contractor shall have Unlimited Rights in any Proprietary Information which is incorporated into the facility or equipment under this Agreement to such extent that the facility or equipment is not restored to the condition existing prior to such incorporation.

5. The University agrees that the Facility Contractor will provide to the Department a nonproprietary description of the work performed under this Agreement.

6. The Government shall have Unlimited Rights in all Generated Information produced or information provided by the Parties under this Agreement, except for information which is disclosed in a Subject Invention disclosure being considered for patent protection, or which is marked as being Proprietary Information.

7. Copyrights. The University may assert copyright in any of its Generated Information, and may also require the Contractor, at the University's expense, to register copyright and assign copyright in any Generated Information produced by the Contractor which the University wishes to copyright. Subject to the other provisions of this article, and to the extent that copyright is asserted, the Government reserves for itself a royalty-free, worldwide, irrevocable, non-exclusive license for Governmental purposes to publish, disclose, distribute, translate, duplicate, exhibit, prepare derivative works, and perform any such copyrighted works.

8. The terms and conditions of this article shall survive the Agreement, in the event that the Agreement is terminated before completion of the Statement of Work.

ARTICLE XVI. ASSIGNMENT

Neither this Agreement nor any interest therein or claim thereunder shall be assigned or transferred by either Party, except as authorized in writing by the other Party to this Agreement, provided, the Contractor may transfer it to the Department, or its designee, with notice of such transfer to the University, and the Contractor shall have no further responsibilities except for the confidentiality, use, and/or non-disclosure obligations of this Agreement.

ARTICLE XVII. SIMILAR OR IDENTICAL SERVICES

The Government and/or Contractor shall have the right to perform similar or identical services in the Statement of Work for other Sponsors.

ARTICLE XVIII. EXPORT CONTROL

Each Party is responsible for its own compliance with laws and regulations governing export control.

ARTICLE XIX. DISPUTES

The Parties shall attempt to jointly resolve all disputes arising from this Agreement. In the event a dispute arises under this Agreement, the University is encouraged to contact Contractor's Ombudsperson in order to further resolve such dispute before pursuing third- party mediation or other remedies. If the Parties are unable to jointly resolve a dispute within a reasonable period of time, they agree to submit the dispute to a third-party mediation process that is mutually agreed upon by the Parties. To the extent that there is no applicable U.S. Federal law, this Agreement and performance thereunder shall be governed by the laws of the State of Washington, without reference to that state's conflict of laws provisions.

ARTICLE XX. TERMINATION

Performance of work under this Agreement may be terminated at any time by either Party, without liability, except as provided above, upon giving a 60-day written notice to the other Party. The Contractor shall terminate this Agreement only when the Contractor determines, after direction from DOE, that such termination is in the best interest of the Government, provided however, that the Contractor shall have the right to terminate unilaterally if the University shall have failed to advance the funds required by Article IV. In the event of termination, the University shall be responsible for the Contractor's costs (including closeout costs) through the effective date of termination, but in no event shall the University's cost responsibility exceed the total cost to the University as described in Article III, above.

It is agreed that any obligations of the Parties regarding intellectual property will remain in effect, despite early termination of the Agreement.

In witness whereof, the Parties hereto have executed this Agreement.

BATTELLE MEMORIAL INSTITUTE PACIFIC NORTHWEST DIVISION		**UNIVERSITY OF NORTH CAROLINA CHAPEL HILL**	
Name	Barb Hays	Name	
Title	Senior Contracts Specialist	Title	
Date	March 2, 2020	Date	

Pacific Northwest NATIONAL LABORATORY

Battelle *The Business of Innovation*

ADVANCE PAYMENT INVOICE

P.O. Box 84391
Seattle, WA 98124-5691
Tel (509) 375-2121
Fax (509) 371-7600

Federal Tax ID: 31-4379427

Date	1/29/2020
Invoice No.	0120018
Customer Order No.	
PNNL Contract No.	75881
Full Advance	
Total Amount Due	5 U.S.C. § 552(b)(4)

University of North Carolina, Chapel Hill
Attn: Accounts Receivable
Box 2200
Chapel Hill, NC 27599-2200

Description	Amount (U.S. Funds)
Advance Payment Invoice	5 U.S.C. § 552(b)(4)
Billing in Accordance with Terms of the agreement	

Send check payable in U.S. funds to:
Battelle
Attn: CASHIER
PO BOX 84391
Seattle, WA 98124-5691

Wire Information:
US Bank, Richland, WA
ABA No.
Account N
SWIFT C
5 U.S.C. § 552(b)(4)

Approved by: Lea Gonzalez for Barb Hays

PLEASE RETURN COPY OF INVOICE OR REFER TO INVOICE NUMBER WITH REMITTANCE.

Pacific Northwest
NATIONAL LABORATORY

SPONSOR REGISTRATION

Date:

To accurately identify your organization for the Lab's records and to facilitate the processing of your transaction, please provide the following information and sign below:

Legal Business Name:

Also Known As:

Address:

Website:

Dun & Bradstreet Number (DUNS) Number:

Contracts/Business Point of Contact (Name, Phone Number, email):

Technical Point of Contact (Name, Phone Number, email):

Invoice Point of Contact (Name, Phone Number, email):

Type of Organization:

☐ Foreign/International Organization
☐ Corporation incorporated under the laws of the State of _____,
☐ State or Municipal Government Entity
☐ University/Academic
  ☐ Public
  ☐ Private
☐ Nonprofit organization
☐ Other (please specify):

U.S. SMALL BUSINESS PROGRAM REPRESENTATIONS[1].

Representations. The Sponsor represents and certifies that it:

☐ **IS** a U. S. small business concern, **OR**
☐ **IS NOT** a U. S. small business concern

Pacific Northwest
NATIONAL LABORATORY

The sponsor represents (check all that apply):

☐ Business enterprise or legal entity organized, chartered or incorporated under the laws of any country other than the United States or its territories. (name of country)

☐ Organization's parent company is a foreign organization. (name of country)

☐ Organization is owned or controlled by a foreign government, agency, firm, corporation or individual. (name of country)

☐ Non-U.S. citizens serve as members of organization's board of directors (or similar governing body), officers, executive personnel, general partners, regents, trustees or senior management officials. (name of country(s))

I hereby certify that the above business classification representation is current, accurate and complete.	
Signature :	Date:
Print Name:	
Title:	
Email Address:	

Please email this form to PNNL Contracts Specialist barb.hays@pnnl.gov and copy: **SPP@pnnl.gov**

Note: During the course of the agreement, if the above information changes, please update.

[1] *Definitions. "Small business concern," as used in this provision, means a concern, including its affiliates, that is independently owned and operated, not dominant in the field of operation in which it is bidding on Government contracts and subcontracts, and qualified as a small business under the criteria in 13 CFR 121. Any person who misrepresents a firm's status as a small business concern in order to obtain favorable consideration for cost reduction is subject to the penalties set forth in the False Claims Act (18 USC 1001).*

From: Van Buren, Eve[evevb@email.unc.edu]
Sent: Tue 3/3/2020 7:43:10 AM (UTC-08:00)
To: Hays, Barbara A[barb.hays@pnnl.gov]
Cc: Farrell, Ronda Lee[farrelrl@email.unc.edu]; Waters, Katrina M[Katrina.Waters@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Parrish, Kalyn[klparrish@unc.edu]
Subject: RE: Subaward 5116540 Between UNC Chapel Hill and Battelle/PNNL
Attachment: 75881 5116540_Sheahan_Battelle PNWD_For Signature.pdf
Attachment: Signed Sponsor Registration Form.pdf
Attachment: Subrecipient Committment Form_05-2019.pdf

Hi Barb,

Thank you for your agreement to our proposed revision. I've attached the revised agreement with Appendices for your review. If all looks ok, please let me know and I will countersign asap. Also attached is the completed Sponsor Registration Form you requested.

I've attached here our Subrecipient Commitment Form, required by UNC for all subaward projects. I will need this completed and signed before I can fully execute the agreement.

Thanks again and please let me know if you have any questions.

Best regards,
Eve

Eve Van Buren
Subaward Specialist
Office of Sponsored Research
University of North Carolina at Chapel Hill
104 Airport Drive, Suite 2200
Campus Box 1350
Chapel Hill, NC 27599
evevb@email.unc.edu
(919) 962-3115

UNC | RESEARCH

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Monday, March 2, 2020 5:05 PM
To: Van Buren, Eve <evevb@email.unc.edu>
Cc: Farrell, Ronda Lee <farrelrl@email.unc.edu>; Parrish, Kalyn <klparrish@unc.edu>; Hays, Barbara A <barb.hays@pnnl.gov>; Waters, Katrina M <Katrina.Waters@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: RE: Subaward 5116540 Between UNC Chapel Hill and Battelle/PNNL

Eve, we are willing to accept [5 U.S.C. § 552(b)(4)] advance payment. The attached revised Agreement and invoice reflect the change. It's important to note, however, that we are not allowed to use DOE funding to "finance" non-DOE work. Therefore, the [5 U.S.C. § 552(b)(4)] will authorize PNNL to start work. At the end of each month, we will submit an invoice for actual costs that we expect to be reimbursed net 30. The advance funding and the invoice reimbursements will allow PNNL

to continue working; if we run out of cash on-hand, we will have to stop work until invoice payments are reimbursed. With this revised agreement to reduce the amount of advance pay, it's important that invoices are reimbursed in a timely manner.
The attached revised Agreement explains the process in Article IV Funding and Payment.

Because of the urgency of getting this Agreement in place and PNNL starting work, I also revised Article III, Term, to change the effective date to be when the Agreement is fully signed/executed (instead of the date we receive the advance payment). With an executed Agreement, I will try to get approval to use Battelle funding to allow us to start work while we wait for the advance payment to arrive

If you approve, please counter-sign the Agreement and return to me as soon as possible.

Also, I'm not sure if I requested a sponsor registration form when we submitted our proposal. Can you please complete and sign the attached and return it to me as soon as possible. Thank you

Barb Hays
Senior Contracts Specialist
Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999
Richland, WA 99352 USA
Tel: 509-372-4008

barb.hays@pnnl.gov

From: Van Buren, Eve <evevb@email.unc.edu>
Sent: Monday, March 02, 2020 11:17 AM
To: Hays, Barbara A <barb.hays@pnnl.gov>
Cc: Farrell, Ronda Lee <farrelrl@email.unc.edu>; Parrish, Kalyn <klparrish@unc.edu>
Subject: Subaward 5116540 Between UNC Chapel Hill and Battelle/PNNL

Hello Barb,

I'm in UNC's Office of Sponsored Research and am working on the subaward referenced above.

I'm writing to see if you would be amenable to an advance payment o 5 U.S.C. § 552(b)(4) instead of the full amount. If so, we could execute this agreement without further delay. An advance payment of 100%, however, will require additional upper level approvals.

Thank you,
Eve

Eve Van Buren
Subaward Specialist
Office of Sponsored Research
University of North Carolina at Chapel Hill
104 Airport Drive, Suite 2200
Campus Box 1350
Chapel Hill, NC 27599
evevb@email.unc.edu
(919) 962-3115

UNC | RESEARCH

Pacific Northwest
NATIONAL LABORATORY

SPONSOR REGISTRATION

Date: March 3, 2020

To accurately identify your organization for the Lab's records and to facilitate the processing of your transaction, please provide the following information and sign below:

Legal Business Name: The University of North Carolina at Chapel Hill

Also Known As: UNC Chapel Hill

Address: 104 Airport Drive, Suite 2200, CB# 1350, Chapel Hill, NC 27599-1350

Website: www.unc.edu

Dun & Bradstreet Number (DUNS) Number: 608195277

Contracts/Business Point of Contact (Name, Phone Number, email): Ronda Farrell, 919-966-3411, ResAdminOSR@unc.edu

Technical Point of Contact (Name, Phone Number, email): Timothy Sheahan, PI, 919-966-3809, sheahan@email.unc.edu

Invoice Point of Contact (Name, Phone Number, email): Kalyn Parrish, 919-966-7425, kparrish@unc.edu

Type of Organization:

☐ Foreign/International Organization
☐ Corporation incorporated under the laws of the State of _____,
☐ State or Municipal Government Entity
X☐ University/Academic
  X☐ Public
  ☐ Private
☐ Nonprofit organization
☐ Other (please specify):

U.S. SMALL BUSINESS PROGRAM REPRESENTATIONS[1].

Representations. The Sponsor represents and certifies that it:

☐ **IS** a U. S. small business concern, **OR**
X☐ **IS NOT** a U. S. small business concern

Pacific Northwest
NATIONAL LABORATORY

The sponsor represents (check all that apply):

☐ Business enterprise or legal entity organized, chartered or incorporated under the laws of any country other than the United States or its territories. (name of country)

☐ Organization's parent company is a foreign organization. (name of country)

☐ Organization is owned or controlled by a foreign government, agency, firm, corporation or individual. (name of country)

☐ Non-U.S. citizens serve as members of organization's board of directors (or similar governing body), officers, executive personnel, general partners, regents, trustees or senior management officials. (name of country(s))

I hereby certify that the above business classification representation is current, accurate and complete.

Signature : Jill Van Buren	Date: March 3, 2020
for Print Name: Terry Magnuson	
Title: Vice Chancellor for Research	
Email Address:n ResAdminOSR@unc.edu	

Please email this form to PNNL Contracts Specialist barb.hays@pnnl.gov and copy: SPP@pnnl.gov

Note: During the course of the agreement, if the above information changes, please update.

[1] *Definitions. "Small business concern," as used in this provision, means a concern, including its affiliates, that is independently owned and operated, not dominant in the field of operation in which it is bidding on Government contracts and subcontracts, and qualified as a small business under the criteria in 13 CFR 121. Any person who misrepresents a firm's status as a small business concern in order to obtain favorable consideration for cost reduction is subject to the penalties set forth in the False Claims Act (18 USC 1001).*

From: Hays, Barbara A[barb.hays@pnnl.gov]
Sent: Tue 3/3/2020 11:28:46 AM (UTC-08:00)
To: Van Buren, Eve[evevb@email.unc.edu]
Cc: Farrell, Ronda Lee[farrelrl@email.unc.edu]; Waters, Katrina M[Katrina.Waters@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Parrish, Kalyn[klparrish@unc.edu]; Hays, Barbara A[barb.hays@pnnl.gov]
Subject: RE: Subaward 5116540 Between UNC Chapel Hill and Battelle/PNNL
Attachment: 75881_Subrecipient Committment Form_05-2019 (1).pdf

Eve, the Agreement with Appendices is acceptable. Please see attached signed subrecipient form. I look forward to receiving the counter-signed fully executed Agreement and advance payment. Thank you

Barb Hays

From: Van Buren, Eve <evevb@email.unc.edu>
Sent: Tuesday, March 03, 2020 7:43 AM
To: Hays, Barbara A <barb.hays@pnnl.gov>
Cc: Farrell, Ronda Lee <farrelrl@email.unc.edu>; Waters, Katrina M <Katrina.Waters@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Parrish, Kalyn <klparrish@unc.edu>
Subject: RE: Subaward 5116540 Between UNC Chapel Hill and Battelle/PNNL

Hi Barb,

Thank you for your agreement to our proposed revision. I've attached the revised agreement with Appendices for your review. If all looks ok, please let me know and I will countersign asap. Also attached is the completed Sponsor Registration Form you requested.

I've attached here our Subrecipient Commitment Form, required by UNC for all subaward projects. I will need this completed and signed before I can fully execute the agreement.

Thanks again and please let me know if you have any questions.

Best regards,
Eve

Eve Van Buren
Subaward Specialist
Office of Sponsored Research
University of North Carolina at Chapel Hill
104 Airport Drive, Suite 2200
Campus Box 1350
Chapel Hill, NC 27599
evevb@email.unc.edu
(919) 962-3115

UNC | RESEARCH

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Monday, March 2, 2020 5:05 PM
To: Van Buren, Eve <evevb@email.unc.edu>
Cc: Farrell, Ronda Lee <farrelrl@email.unc.edu>; Parrish, Kalyn <klparrish@unc.edu>; Hays, Barbara A <barb.hays@pnnl.gov>; Waters, Katrina M <Katrina.Waters@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: RE: Subaward 5116540 Between UNC Chapel Hill and Battelle/PNNL

Eve, we are willing to accept 5 U.S.C. § 552(b)(4) advance payment. The attached revised Agreement and invoice reflect the change. It's important to note, however, that we are not allowed to use DOE funding to "finance" non-DOE work. Therefore, the 5 U.S.C. § 552(b)(4) will authorize PNNL to start work. At the end of each month, we will submit an invoice for actual costs that we expect to be reimbursed net 30. The advance funding and the invoice reimbursements will allow PNNL to continue working; if we run out of cash on-hand, we will have to stop work until invoice payments are reimbursed. With this revised agreement to reduce the amount of advance pay, it's important that invoices are reimbursed in a timely manner.
The attached revised Agreement explains the process in Article IV Funding and Payment.

Because of the urgency of getting this Agreement in place and PNNL starting work, I also revised Article III, Term, to change the effective date to be when the Agreement is fully signed/executed (instead of the date we receive the advance payment). With an executed Agreement, I will try to get approval to use Battelle funding to allow us to start work while we wait for the advance payment to arrive

If you approve, please counter-sign the Agreement and return to me as soon as possible.

Also, I'm not sure if I requested a sponsor registration form when we submitted our proposal. Can you please complete and sign the attached and return it to me as soon as possible. Thank you

Barb Hays
Senior Contracts Specialist
Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999
Richland, WA 99352 USA
Tel: 509-372-4008

barb.hays@pnnl.gov

From: Van Buren, Eve <evevb@email.unc.edu>
Sent: Monday, March 02, 2020 11:17 AM
To: Hays, Barbara A <barb.hays@pnnl.gov>
Cc: Farrell, Ronda Lee <farrelrl@email.unc.edu>; Parrish, Kalyn <klparrish@unc.edu>
Subject: Subaward 5116540 Between UNC Chapel Hill and Battelle/PNNL

Hello Barb,

I'm in UNC's Office of Sponsored Research and am working on the subaward referenced above.

I'm writing to see if you would be amenable to an advance payment of 5 U.S.C. § 552(b)(4) instead of the full amount. If so, we could execute this agreement without further delay. An advance payment of 100%, however, will require additional upper level approvals.

Thank you,
Eve

Eve Van Buren
Subaward Specialist
Office of Sponsored Research
University of North Carolina at Chapel Hill
104 Airport Drive, Suite 2200
Campus Box 1350
Chapel Hill, NC 27599
evevb@email.unc.edu
(919) 962-3115



UNC RESEARCH

Subaward Number 5116540

Subrecipient Commitment Form

Subrecipients **MUST** submit form prior to execution of an agreement and on an annual basis to the University of North Carolina at Chapel Hill (UNC-CH)

1. General Information

Subrecipient Legal Name: Battelle, PNWD, operator of PNNL for the U.S. Department of Energy		
Subrecipient PI: Katrina Waters		
Project Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells		
Prime Sponsor: The University of North Carolina at Chapel Hill		
Prime Sponsor Number:		
Budget Period: to	Project Period: to	
DUNS: 032987476	EIN: 31-4379427	Registered on SAM.gov? (•) Yes ( ) No

2. Where is your organization located and operated?

(•) US Domestic ( ) Foreign

Please select your Business Status: _____

3. Does this project involve research on Human Subjects?

( ) Yes (•) No

4. Does this project involve research on Animal Subjects?

( ) Yes (•) No

5. Please select ONE of the following options that represent the applicable Indirect Costs.

(•) Federally Negotiated Indirect Cost Rate ____ %

( ) Other Indirect Cost Rate ____ %

( ) No Applicable Indirect Cost Rate

Rate URL Address: _____

6. Does your organization have Federally negotiated Fringe Benefits?

( ) Yes (•) No

Please select the most applicable type of Fringe Benefits rate: Other Fringe Rate ____ %

Please indicate the reason for the different Fringe Benefits rate:

Fringe benefits are calculated and applied consistent with PNNL's Disclosure Statement.

7. Answer the following questions about Conflict of Interest (COI) Requirements.

a) Please select the type of COI requirement that best describes your institutional practices:

(•) This project is funded by PHS, NSF, or a Sponsor which has adopted PHS/NSF federal financial disclosure requirements (includes NIH).

( ) This project is funded by a Sponsor which has its own Conflict of Interest (COI) or financial disclosure requirements that differ from PHS and NSF. Subrecipient Institution hereby certifies it will comply with the Sponsor's standards for Conflict of Interest or financial disclosure.

( ) Not Applicable

Please check either OPTION 1 or OPTION 2.

☒ **OPTION 1:** Subrecipient Institution hereby certifies that it has an active and enforced Conflict of Interest policy that is consistent with the provision of 42 CFR Part 50, Subpart F, "Responsibility of Applicants for Promoting Objectivity in Research," or the NSF Award and Administration Procedure Guide, Chapter IV. Subrecipient also certifies that, to the best of the Institution's knowledge:

1)All financial disclosures have been made related to the activities that may be funded by or through a resulting agreement, and required by its Conflict of Interest policy;
2)All identified Conflict of Interest have been or will have been satisfactorily managed, reduced, or eliminated in accordance with Subrecipient's Conflict of Interest policy prior to expenditure of any funds under an resulting agreement;
3)Any Financial Conflicts of Interest (FCOI) will be reported to UNC-CH before funding begins and throughout the term of the project.

☐ **OPTION 2:** Subrecipient does not have an active and/or enforced Conflict of Interest policy which meets the PHS or NSF standards and hereby agrees to abide by the UNC-CH Individual Conflicts of Interest policy. The UNC-CH published policy is located at **http://research.unc.edu/offices/coi**.

---

8. Does your organization receive an annual financial audit in accordance with US Federal Regulation 2 CFR 200 Subpart F (Commonly referred to as Uniform Guidance)?

○ Yes ◉ No

Subrecipients without 'Uniform Guidance' Annual Audits:

Does your organization receive an annual financial audit by an external organization? ◉ Yes ○ No

What was the date of your most recent audit? 9/30/19

What is your organization's Fiscal Year? October 1 to September 30

Your organization is classified as: ◉ Non-Profit Entity ○ For-Profit Entity ○ Government Entity

Please provide a copy of the Audit Report. Submit a copy with this form or provide the URL location.

Audit Report URL:

Questionnaire for Subrecipients without 'Uniform Guidance' Annual Audits:

Question 1. ***General Information***

a) Does your organization have its financial statements reviewed by an independent public accounting firm? ◉ Yes ○ No
b) Are duties separate so that no one individual has complete authority over an entire financial transaction? ◉ Yes ○ No
c) Does your organization have controls to prevent expenditure of funds in excess of approved, budgeted amounts? ◉ Yes ○ No
d) Other than financial statements, has any aspects of your organization's activities been audited within the last two years by a government agency or independent public accountant? ◉ Yes ○ No

Question 2. ***Cash Management***

a) Does the accounting system identify the receipts and expenditures of program funds separately for each award? ◉ Yes ○ No
b) Are all disbursements properly documented with evidence of receipt of goods or performance of service? ◉ Yes ○ No
c) Are all bank accounts reconciled monthly? ◉ Yes ○ No

Question 3. ***Payroll***

a) Are payroll charges checked against program budgets? ◉ Yes ○ No
b) What system does your organization use to control paid time, especially time charged to sponsored agreements?

Battelle, as the operator of the Pacific Northwest National Laboratory (PNNL) is a Department of Energy prime contractor. Battelle's contract (DE-AC05-76RL01830) is administered by the Department of Energy's Pacific Northwest Site Office. In the terms of that contract, Battelle, as operator of the Pacific Northwest National Laboratory:
• is obligated to follow Cost Accounting Standards (CAS) 48CFR9904
• must fully recover all costs, in compliance with the CAS, by establishing a direct and indirect cost policy in accordance with 48CFR9904.418 to facilitate the full recovery of all costs
• has the capability to identify, in its accounts, all awards received and expended under which they were received
• has an adequate accounting system to support cost reimbursement awards including internal controls to ensure appropriate staff charging by maintaining an electronic timekeeping system for staff to appropriately and precisely record their activities.

Question 4. *Procurement*

a) Are there procedures to ensure procurement at competitive prices? (●) Yes ( ) No
b) Is there an effective system of authorization and approval for capital equipment expenditures? (●) Yes ( ) No
c) Is there an effective system of authorization and approval for travel expenditures? (●) Yes ( ) No

Question 5. *Property Management*

a) Are detailed records of individual capital assets kept and periodically balanced with the general ledger accounts? (●) Yes ( ) No
b) Are there effective procedures for authorizing and accounting for the disposal of property and equipment? (●) Yes ( ) No
c) Are detailed property records periodically checked by physical inventory? (●) Yes ( ) No

Question 6. *Cost Transfers*

a) How does the subrecipient ensure that all cost transfers are legitimate and appropriate?

Battelle, as the operator of the Pacific Northwest National Laboratory (PNNL) is a Department of Energy prime contractor. Battelle's contract (DE-AC05-76RL01830) is administered by the Department of Energy's Pacific Northwest Site Office. In the terms of that contract, Battelle, as operator of the Pacific Northwest National Laboratory, sub-recipient has the appropriate cost accounting system to receive Government Awards.

Question 7. *Indirect Costs*

a) Does the organization have an indirect cost allocation or Federally negotiated indirect cost rate agreement? (●) Yes ( ) No
b) Does the organization have procedures which provide assurance that consistent treatment is applied in the distribution of charges to all grants? (●) Yes ( ) No

Question 8. *Cost Sharing*

a) How does your organization determine it has met its costs sharing commitments?

NA

Question 9. *Assurances*

a) Does your organization engage in any lobbying or partisan political activity which is charged, directly or indirectly, to a Federally assisted program? ○ Yes ◉ No

b) Does your organization have a formal policy of nondiscrimination and a formal system for complying with US Federal civil rights requirements? ◉ Yes ○ No

c) Does your organization have a cash-forecasting process which will minimize the time elapsed between the receipt of funds and the disbursement of those funds in cases where a cash advance is used? ◉ Yes ○ No

d) Is your organization familiar with US Federal financial reporting so that it can complete financial reports in an accurate and timely manner when required? ◉ Yes ○ No

e) What was the total amount of US Federal award to your organization during the last fiscal year? **5 U.S.C. § 552(b)(4)**

f) Does your organization have a formal system for complying with the Davis-Bacon Act which requires payment of prevailing wages on US Federal contracts? ◉ Yes ○ No

Who is your organization's contact for Audit Requests?

Name: NA

Title: _____

Email: _____

9. Answer each of the following questions about your organization.

Subrecipient Organization Financial Compliance

a) Does your organization have the capability to identify, in its accounts, all US Federal awards received and expended and the Federal programs under which they were received. ◉ Yes ○ No

b) Does your organization maintain internal controls to assure that it manages US Federal awards in compliance with applicable laws, regulations and the provision of contracts and grants? ◉ Yes ○ No

c) Does your organization comply with applicable law and regulations?

d) Is your organization able to prepare appropriate financial statements, including the schedule of expenditures on federal awards? ◉ Yes ○ No ◉ Yes ○ No

e) Does your organization have any outstanding audit findings which would impact agreement costs? If there are findings, submit a copy of the most recent report that describes the findings and steps to be taken to correct the findings. ○ Yes ◉ No

Subrecipient Organization Eligibility to Receive Sponsored Funding

a) Is your organization and/or any participating individuals presently debarred, suspended, proposed for debarment, or declared ineligible for US Federal contracts? ○ Yes ◉ No

b) Is your organization and/or any participating individuals presently indicted for, or otherwise criminally or civilly charged by a government entity? ○ Yes ◉ No

c) Has your organization and/or any participating individuals within three (3) years preceding this offer, had one or more contracts terminated for default by any US Federal agency? ○ Yes ◉ No

d) Has your organization and/or any participating individuals within three (3) years preceding this proposed agreement, been convicted of or had a civil judgement rendered against them for commission of fraud or criminal offense in connection with obtaining, attempting to obtain, or preforming a public (Federal, state or local government) contract or subcontract; violated US Federal or State antitrust statutes relating to the submission of offers; commissioned embezzlement, theft, forgery, bribery, falsification or destruction of records, making false statements or receiving stolen property? ○ Yes ◉ No

Subrecipient Authorized Official's Name:	Subrecipient Authorized Official's Signature:
	Barb Hays Digitally signed by Barb Hays Date: 2020.03.03 11:25:05 -08'00'
Title:	Date:
Email:	Phone:
Address:	
City:	State/Province:
Postal Code:	Country: United States of America

From: Sutherland, Holly Ann[hsutherl@live.unc.edu]

Sent: Mon 3/9/2020 6:06:20 AM (UTC-07:00)

To: APInvoices[apinvoices@gilead.com]

Cc: Burkhart, Carol J.[carol_burkhart@unc.edu]; Moore, Victoria L[victoria_moore@unc.edu]; Sims, Amy C[amy.sims@pnnl.gov]; DiLello, Dawn M[dawn_dilello@unc.edu]; Kelly, Jim[jpkelly@email.unc.edu]; Gumm, Helen B[gumm@email.unc.edu]; Joy Feng[Joy.Feng@gilead.com]

Subject: Invoice for PO# 801467602

Attachment: 5107841_GM00149069.pdf

Good Morning,

Enclosed, please find an invoice for the attached Purchase Order. If you have any questions regarding the invoice, please let me know.

Thank You.

Kind Regards,

Holly Sutherland

Sponsored Projects Accountant
Office of Sponsored Research
University of North Carolina at Chapel Hill
104 Airport Drive, Suite 2200; Campus Box 1350
Chapel Hill, NC 27599
Hsutherl@live.unc.edu
(919)962-6488

INVOICE

The University of North Carolina at Chapel Hill

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Remit Payment To:

Office of Sponsored Research
The University of North Carolina at Chapel Hill
C/O Bank of America Lockbox Services
PO Box 402420
Atlanta GA,30384-2420

Federal Tax ID # 56-6001393
Duns # 608195277

Invoice #: GM00149069

Name of Sponsor:	Gilead Sciences, Inc. Attn: Accounts Payable P.O. Box 5469 United States	•Interim Billing ○ Final Billing	Award Amount 5 U.S.C. § 552(b)(4)
Sponsor Ref No.:	215360.1		
UNC Award No.:	A17-1458-001		
Award Title:	Testing of Gilead Nucleoside Analog Compounds	Budget Period:	
Project ID:	5107841	From: 06/07/2017	To: 06/06/2018

DESCRIPTION OF SERVICES

Funded Research with UNC Amy Sims' lab--Interim payment REFERENCE PO 801467602	5 U.S.C. § 552(b)(4)
TOTAL THIS INVOICE	5 U.S.C. § 552(b)(4)
TOTAL BILLED TO DATE	5 U.S.C. § 552(b)(4)

Payment due upon receipt of invoice

****

PLEASE RETURN A COPY OF THIS INVOICE WITH YOUR PAYMENT

I hereby certify that the foregoing report is true in all respects and that the expenditures have been made solely for the purposes set forth in the application for the grant as approved and that I am authorized to sign this report for the institution named.

Typed Name of Fiscal Officer	Signature	Date
Office of Sponsored Research		03/9/2020

For questions regarding invoice, please contact Holly Sutherland
Phone: 919/962-6488 FAX: 919/962-5011
OSRBILLING@unc.edu

ACH Payments
Account Name: NC State Treasurer
Financial Institution: Bank of America, Chapel Hill, NC
5 U.S.C. § 552(b)(4)

GILEAD

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City CA
United States 94404

Purchase Order

Date	3/6/2020
P.O.Number	801467602
Revision No	0
Release No.	

Supplier: UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
OFFICE OF SPONSORED RESEARCH
c/o BOFA LOCKBOX SERVICES
PO BOX 402420
ATLANTA GA 30384-2420
United States

Ship To: Gilead Sciences, Inc.
368 Lakeside Dr
Foster City, CA 94404
United States

Currency : USD

This Purchase Order is subject to Gilead Standard Purchase Order Terms & Conditions which can be found at www.gilead.com/pdf/north_america_terms.pdf and are incorporated into the face hereof.

Order Date	Request Date	Ship Via:	FOB & Freight Terms:	Misc. Information:
03/06/20	03/09/20		DESTINATION & Due	

Line#	Catalog#/Item#	Description	Qty	UOM	Unit Price	Extended Amount	Promise Date
1-1		Interim payment to Gilead-UNC FRA at Dr. Amy Sims' lab. Attn: Porter, Danielle L Danielle.Porter@gilead.com	5 U.S.C. § 552(b)(4)	Each	1.00	5 U.S.C. § 552(b)(4)	03/09/20

Payment Terms: Net 7	Tax Rate:	Sales Tax/VAT	Total Order Amount
Buyer: System	Authorized Signature:		5 U.S.C. § 552(b)(4)

From: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Sent: Wed 3/18/2020 5:51:05 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]; Schaefer, Alexandra[aschaefe@email.unc.edu]
Subject: Fwd: Funds remaining on R21

Begin forwarded message:

From: "Parrish, Kalyn" <klparrish@unc.edu>
Date: March 18, 2020 at 8:46:17 AM EDT
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: RE: Funds remaining on R21

HI Tim,

The R21 has [redacted] left to spend in supplies until the end of May.

Thanks,
Kalyn

From: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Sent: Tuesday, March 17, 2020 10:10 PM
To: Parrish, Kalyn <klparrish@unc.edu>
Subject: FW: Funds remaining on R21

Hi Kalyn,

Could you please do a quick check on Amy's R21? I'll let Alex know how much she has to spend on reagents.

T

From: Amy Sims <amy.sims@pnnl.gov>
Date: Monday, March 16, 2020 at 5:55 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: Funds remaining on R21

Hi Tim,

I had a call with Alex today and she is going to need some more reagents.

How much is left on the R21 for UNC? Just curious. Thank you, Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 3/18/2020 5:59:02 AM (UTC-07:00)
To: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Subject: Re: Funds remaining on R21

Thank you. Sorry to bug you. Should have just asked Kalyn. Thank you again. Amy

Get Outlook for iOS

From: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Sent: Wednesday, March 18, 2020 5:51:05 AM
To: Sims, Amy C <amy.sims@pnnl.gov>; Schaefer, Alexandra <aschaefe@email.unc.edu>
Subject: Fwd: Funds remaining on R21

Begin forwarded message:

From: "Parrish, Kalyn" <klparrish@unc.edu>
Date: March 18, 2020 at 8:46:17 AM EDT
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: RE: Funds remaining on R21

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To: Parrish, Kalyn <klparrish@unc.edu>
Subject: FW: Funds remaining on R21

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Date: Monday, March 16, 2020 at 5:55 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: Funds remaining on R21

Hi Tim,

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How much is left on the R21 for UNC? Just curious. Thank you, Amy

A. COVER PAGE

Project Title: Phenome-wide association of protein function-altering variants in a family study	
Grant Number: 5R21HL140385-02	Project/Grant Period: 09/15/2017 - 08/31/2019
Reporting Period: 09/15/2017 - 08/31/2018	Requested Budget Period: 09/01/2018 - 08/31/2019
Report Term Frequency: Annual	Date Submitted:
Program Director/Principal Investigator Information: NORA FRANCESCHINI , MD MPH Phone number: 9199661305 Email: noraf@unc.edu	Recipient Organization: UNIV OF NORTH CAROLINA CHAPEL HILL UNIVERSITY OF NORTH CAROLINA CHAPEL HILL Office of Sponsored Research CHAPEL HILL, NC 275990001 DUNS: 608195277 EIN: 1566001393A1 RECIPIENT ID:
Change of Contact PD/PI: N/A	
Administrative Official: R DAVID PAUL 104 Airport Dr. Suite 2200 Chapel Hill, NC 275991350 Phone number: 919-966-3411 Email: resadminosr@unc.edu	Signing Official: KATI CHIPPS 104 Airport Drive Suite 2200 Chapel Hill, NC 27599 Phone number: 9199624665 Email: kati_chipps@unc.edu
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	Vertebrate Animals: No
hESC: No	Inventions/Patents: No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

We hypothesize that novel heart and blood phenotype associations will be identified in carriers of predicting protein function-altering rare variants using phenome-wide association approaches. We propose a systematic phenotypic analysis of American Indians in the SHFS. All participants have comprehensive data on lifestyle/behaviors, cardio-metabolic assessments, clinical phenotypes, and biomarkers for hematologic, lipid, metabolic, inflammatory, liver and kidney traits, available over two clinical visits, in addition to longitudinal surveillance data on cardiovascular disease outcomes. Using existing WES-selected genotypes and the rich longitudinal phenotypes for heart and blood traits in SHFS participants, we propose the following aims:
1. Identify novel clinical and biomarker phenotypic associations among 1,127 American Indian carriers of LoF and missense variants that are predicted to be damaging. We will link the genotypes to the high quality phenotypic and biomarker data to perform single-trait phenome-wide association analyses and will use multi-trait approaches with the intent to identify shared genetic effects for clinical phenotypes. The family data will allow mapping individuals with these variants in pedigrees to better understand their phenotypic correlations and inheritance.
2. Validate the most significant genotype-phenotype associations in population-based studies of Southwest American Indians and in Hispanics/Latinos from the Hispanic Community Health Study/Study of Latinos participants in the Trans-Omics for Precision Medicine (TOPMed) Program. These studies have whole genome sequencing and comprehensive phenotypic data.
This proposal addresses important gaps in our knowledge of the clinical phenotypes associated with rare protein function-altering variants in humans, which may have implications for precision medicine.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: Opportunities.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

For Year 02, we plan to run the linkage/association single trait analyses and start testing new methods for multi-trait analyses that account for family data (Aim 2). For any significant findings, we plan to pursue replication in American Indians studies (Southwest American Indians) and Hispanic studies (Hispanic Community Health Study/Study of Latinos and Multi-ethnic Study of Atherosclerosis, Women's Health Initiative, which are studies that participate in TOPMed and have available whole genome sequencing data). We will also compare our novel variants to those available in TOPMed. Lastly, we plan to submit an abstract to the 2019 American Heart Association EPI-Lifestyle conference this fall for the preliminary data on association/linkage analyses and work on 1-2 papers related to findings of this study.

R21 HL140385-02: Phenome-wide association of protein function-altering variants in a family study
PI: Nora Franceschini, MD MPH

What was accomplished under the goals/specific aims for the current year?

During Year 01 of the grant (Sept/2017 to June/2018) we worked on tasks related to Aim 1. Aim 2 tasks will be accomplished in the 2nd year of the proposal.

Aim 1. Identify novel clinical and biomarker phenotypic associations among 1,127 American Indian carriers of LoF and missense variants that are predicted to be damaging. We will link the genotypes to the high quality phenotypic and biomarker data to perform single-trait phenome-wide association analyses and will use multi-trait approaches with the intent to identify shared genetic effects for clinical phenotypes. The family data will allow mapping individuals with these variants in pedigrees to better understand their phenotypic correlations and inheritance.

In collaboration with Dr. Yun Lin, UNC Biostatistics & Genetics, the following tasks related to Aim 1 have been completed:
Phenotypes: We have applied extensive quality control to the phenotypic data, including trait transformation for quantitative traits and definitions of categories for qualitative traits. These traits include heart and blood phenotypes, measures of obesity, liver and kidney function, and lipid and inflammatory biomarkers.
Genotypes: We performed extensive annotation of all exonic variants using the Whole Genome Sequencing Annotator (WGSA) (PMCID:PMC5124490), which is based on reference hg19 and annotates both single nucleotide variants (SNVs) and small indels. Variants were annotated as loss of function (essential splice sites, stop gain, stop lost, start lost, frameshift splice), missense, synonymous, protein altering indels. This annotation also includes scores pertaining to functionality (LRT score, Mutation Taster, FATHMM-MKL, MetaSMV, CADD), conservation (SIFT, Polyphen2), population allele frequencies (1000 Genomes Project, Exome Aggregation Consortium [ExAC], Exome Sequencing Project [ESP], gnomAD) and disease-related annotations (CLINVAR). The Fathmm-MKL scores were used only for nonsynonymous variants. This annotation will be used to assess the potential functional impact of these variants in protein function and to identify SNVs/indels present in other populations to guide our replication efforts. Below is a summary of these results:

Among 1,125 genotyped variants that passed quality control (1,066 genes, 1,081 SNVs, 44 indels), 1,106 are exonic SNVs/indels and n=14 are located in splicing regions. Nine-four percent of exonic SNVs/indels are non-synonymous (n=1,038) and 55 are frameshift substitutions, stop-gain or stop-loss SNVs. Of missense SNVs/indels, 673 are predicted damaging by FATHMM-MKL. Most variants had an allele frequency less than 5%, and the median minor allele count is 10 copies (0.4%), with a range of 1 to 1064 copies. In summary, our genotyped exome sample is composed of mostly low frequency and rare variants, and it is enriched for variants with predicted functionality.

We queried our SNVs/indels in publicly available databases and identified 434 SNVs/indels that are not present in dbSNP, 1000 Genomes Project, ExAC and ESP databases. Most of the variants were nonsynonymous SNVs/indels (n=396), 5.2% are frameshift substitutions, and stop-gain or stop-loss SNVs (n=22), and 1% are synonymous. Sixty-five percent (n=269) of nonsynonymous SNVs are predicted deleterious by FATHMM-MKL or other tools such as MetaSMV.

We next queried these 434 variants in the Genome Aggregation Database (gnomAD) that includes both whole exome and whole genome sequencing of diverse populations. There were 177 low frequency/rare SNVs/indels that are present in this database, and a total of 257 SNVs/indels not present in any publicly available datasets, which we considered novel variants that are specific to American Indians. These novel variants include nonsynonymous (n=229), and frameshift, stop-gain, and stop-loss variants (n=16), of which 166 are predicted deleterious by FATHMM-MLK and other functional annotation tools and six are intronic splicing SNVs/indels. We are currently comparing our novel variants with variants available in the TOPMed Program. In summary, 39% of our variants are not present in publicly available databases of genetic variants and 21% variants are just found in our sample. Although they are rare/low frequency, most of the variants in our sample included the novel ones are not singletons and may be present in other populations with Amerindian admixture.

The following tasks are ongoing:
Statistical methods for family data: We are currently working on implementing statistical methods that account for our complex family data. This includes reformatting the data to implement analyses in software that accommodate family relationships. We plan to first jointly test linkage and association for each SNV in single trait analyses before implementing multi-trait approaches.

Aim 2. Validate the most significant genotype-phenotype associations in population-based studies of Southwest American Indians and in Hispanics/Latinos from the Hispanic Community Health Study/Study of Latinos participants in the Trans-Omics for Precision Medicine (TOPMed) Program. These studies have whole genome sequencing and comprehensive phenotypic data.

We have ongoing collaborations for potential replications in American Indians and Hispanic studies, which will be done in Year 02 of the application.

What opportunities for training and professional development has the project provided? (include participation in conference , workshops, seminar, etc)

The PI Dr. Franceschini participated in TOPMed Steering Committee/External Advisory Panel meeting in Tysons, VA (Nov 29-Dec 1), which provided updates on whole genome sequencing pipelines, analyses and resources for investigators including annotation tools. The P.I. also participated in the GSP-TOPMed workshop at the University of Vanderbilt, Nashville, TN Jan 31st to Feb 1st, 2018, which focused on collaborations for whole genome sequencing projects between the NHGRI-funded Genome Sequencing Project (GSP) and the NHLBI-funded Trans-Omics for Precision Medicine (TOPMed). The workshop provided opportunities to learn about new genomic tools for statistical analyses and visualization of data.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
NORAFRANC	Y	Franceschini, Nora	MPH,MD	PD/PI	4.0	0.0	0.0			NA
YUE_SHAN	N	Shan, Yue	PHD,MS,BS	Graduate Student (research assistant)	4.0	0.0	0.0			NA
CHEYNNA_CROWLEY	N	Crowley, Cheynna Anne	MS,BS	Graduate Student (research assistant)	4.0	0.0	0.0			NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: Other Support_ALL.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

Other Support

Franceschini, Nora

ACTIVE

R01MD012765 (Franceschini) 09/24/17 – 04/30/22 4.80 Cal Mos
NIMHD
5 U.S.C. § 552(b)(4)
Leveraging Ancestry to Map Kidney Loci
We propose to identify genomic regions containing genetic variants with differential allele frequencies in the ancestral populations that associate with chronic kidney disease phenotypes, and validate the findings through replication and using experimental models.
Role: PI

R21HL140385 (Franceschini) 09/15/17 – 08/31/19 3.78 Cal Mos
NHLBI
5 U.S.C. § 552(b)(4)
Phenome-wide association of protein function-altering variants in a family study
We propose to identify novel clinical and biomarker phenotypic heart, blood and kidney associations among 1,127 American Indian carriers of loss of function and missense variants that are predicted to be damaging.
Role: PI

R56DK104806 (Franceschini, Reiner) 09/16/16 – 08/31/18 1.56 Cal Mos
NIDDK
5 U.S.C. § 552(b)(4)
Pilot study of African-specific variants and chronic kidney disease
This pilot study will provide additional phenotyping of kidney function in the Women's Health Initiative African American participants to increase the sample for genetic studies of kidney disease in this population.
Role: MPI

R01HL118305 (Rao) 01/15/14 – 12/31/18 1.26 Cal Mos
NIH/NHLBI
5 U.S.C. § 552(b)(4)
A Multi-Ethnic Study of Gene-Lifestyle Interactions in Cardiovascular Traits
The goal is to identify novel loci for blood pressure by investigating gene-by-environmental interaction including physical activity, alcohol intake and smoking exposure.
Role: Subcontract PI

NHLBI-WH-11-10 (Shumaker) 10/15/16 – 10/14/18 0.60 Cal Mos
Wake Forest Univ/NIH
5 U.S.C. § 552(b)(4)
Women's Health Initiative
The major goal of this project is to launch the next generation of cardiovascular health research projects that target older women in the Women's Health Initiative.
Role: Investigator

PENDING

R01DK113632 (Le) 08/01/18 – 05/31/20 1.56 Cal Mos
Univ of Virgina/NIH
5 U.S.C. § 552(b)(4)
Renal Mechanisms of Blood Pressure Regulation and Salt Sensitivity by Collectrin
Our objective is to precisely delineate the renal tissue-collectrin-NOS axis through which collectrin regulates AP homeostasis and salt sensitivity; and to determine its influence on AP in human populations that include salt- sensitive (SS)/-resistant (SR) cohorts.
Role: Subcontract PI

R01DK117445 (Franceschini) 09/01/18 – 08/31/23 4.8 Cal Mos
NIDDK/NIH 5 U.S.C. § 552(b)(4)
Genetics of kidney disease in diverse populations
Our aims are to characterize already know population-specific variants (APOL1, sickle cell, American Indian variant) in relation to incident CKD in Hispanics/Latinos, identify genetic variants relevant to all ethnic groups using a large sample of Hispanics/Latinos, and individuals of African, East and South Asian, and European ancestry and trans-ethnic GWAS meta-analyses, and to provide evidence for the functional role of identified genes using in vitro and in vivo experimental models.
Role: PI

OVERLAP: If any of the pending grants are awarded, Dr. Franceschini will reduce her effort on grants R21HL140385 and R01MD012765.

OTHER SUPPORT

Li, Yun

ACTIVE

5R01HL129132-02 (Li, Reiner) 07/15/2016-02/29/2020 2.40 calendar
NIH (5105069) 5 U.S.C. § 552(b)(4)
Genetic Studies of Blood Cell Traits in Multi-Ethnic Cohorts
The goal of this study is to preform genetic studies of blood cell and related traits in multi-ethnic cohorts, particularly admixed populations including African Americans and Hispanics.

4U54 HD079124-05 (Piven) 09/24/2013-05/31/2019 1.20 calendar
NIH/NICHD (5108367) 5 U.S.C. § 552(b)(4)
Clinical Translational Research Center for Neurodevelopmental Disorders
Intellectual and Developmental Disabilities Research Center.

5R01MH106611-03 (Szatkiewicz) 05/15/2015-02/28/2020 0.84 calendar
NIH/NIMH (5101312) 5 U.S.C. § 552(b)(4)
Finding causal variants within schizophrenia risk loci
The goal of this project is to resequence loci identified in schizophrenia genome-wide association studies (GWAS) in order to identify causal genetic variants. This would be the first large-scale fine-mapping follow-up study of a psychiatric GWAS.

5216282-5500000980 (Li) 05/01/2017-10/30/2018 0.12 calendar
Broad Institute/NIH/NIDDK (5107888) **5 U.S.C. § 552(b)(4)**
TOPMed Whole Genome Sequence Analysis of Type 2 Diabetes and Related Traits
The goal of this project is to test the association of common, rare, and structural variation with type 2 diabetes and related traits using TOPMed Whole Genome Sequence data.

2R01 DK093757-06 (Mohlke) 09/05/2011-07/31/2022 0.60 calendar
NIH/NIDDK (5107937) 5 U.S.C. § 552(b)(4)
Genetic epidemiology of rare and regulatory variants for metabolic traits
The goal of this project is to identify novel variants that influence traits related to diabetes, obesity and the metabolic syndrome and mechanisms by which DNA variants influence gene expression and disease.

1R21HL140385-01 (Franceschini) 09/15/2017-08/31/2019 0.60 calendar
NIH (5108750) 5 U.S.C. § 552(b)(4)
Phenome-wide association of protein function-altering variants in a family study
This project will leverage existing genotypes and the extensive clinical and biomarker data in a population-based family study of American Indians to better understand the clinical implications of rare protein function-altering variants in populations.

7R01HL130733-02 (Lange/Mohlke) 08/01/2017-04/30/2020 1.20 calendar
University of Colorado Denver/NIH (5109172) **5 U.S.C. § 552(b)(4)**
Sequence analysis of hematological traits in African Americans
The goal is to use sequence and genotyping data in African Americans to discover and functionally characterize novel genetic associations for blood cell traits.

5P01CA142538-08 (Kosorok) 04/01/2010-03/31/2020 1.94 calendar
NIH/NCI (5101326) 5 U.S.C. § 552(b)(4)
Statistical Methods for Cancer Clinical Trials
Project 3: Statistical/Computational Methods for Pharmacogenomics and Individualized Therapy
This research intends to develop novel and high-impact statistical and computational tools for discovering genetic variants associated with interindividual differences in the efficacy and toxicity of cancer medications and for optimizing drug therapy on the basis of each patient's genetic constitution.

1R01MD011609-01 (Manuck) 08/08/2017-03/31/2022 1.20 calendar
NIH/NIMHHD (5108526) 5 U.S.C. § 552(b)(4)
The Pharmacoepigenomics of Recurrent Preterm Birth in Non-Hispanic Black Women
The rationale for this work is that it will provide new insight and increased understanding into the pathophysiology and biologic mechanisms of non-response to 17P for PTB prevention among NH black women, a group of women who are at disproportionately high risk of 17P treatment failure.

3U01HL120393-04S1 (Rice) 03/01/2018-08/31/2018 0.12 calendar
University of Washington/NIH (5109864) **5 U.S.C. § 552(b)(4)**
Annotation of dbGaP variable for TOPMed
The aims of the project are to annotate data in each cohort's parent dbGaP accession, so that the NIH Commons developers can index phenotypes for easy use with TOPMed sequencing and other future 'omics datasets.

PENDING

1R01MD013349-01 (Aiello/Harris) 07/01/2018-06/30/2023 0.60 calendar
NIH 5 U.S.C. § 552(b)(4)
The Add Health Epigenome Resource: Life course stressors and epigenomic modifications in adulthood
The overall goals of this project are to investigate the influence of life course psychosocial stressors on DNA methylation and gene expression that may influence cardiometabolic health and depression in a US representative study of young adults.

No number (Styblo) 09/01/2018-08/31/2023 1.20 calendar
Cornell University/NIH 5 U.S.C. § 552(b)(4)
MicroRNAs as candidate mechanistic links between arsenic exposure and diabetes

No number (Zou) 09/01/2018-03/31/2022 0.84 calendar
Fred Hutchinson/NIH 5 U.S.C. § 552(b)(4)
Statistical Methods for RNA-seq Data Analysis

1R01MH118349-01 (Stein) 09/01/2018-08/31/2023 0.60 calendar
NIH 5 U.S.C. § 552(b)(4)
pathQTL: Integrative Multi-Omics Causal Inference of Molecular Mechanisms Leading to Neuropsychiatric Illness

No number (Hu) 09/01/2018-03/31/2023 2.40 calendar
Cleveland Clinic/NIH/NHGRI 5 U.S.C. § 552(b)(4)
Genetics of mammalian chromatin interactome

No number (Le/Franceschini) 07/01/2018-06/30/2020 0.60 calendar
University of Virginia/NIH **5 U.S.C. § 552(b)(4)**
Renal mechanisms of blood pressure regulation and salt sensitivity by collectrin

No number (Bulik) 09/30/2018-09/29/2022 1.80 calendar
USUHS/DoD 5 U.S.C. § 552(b)(4)
Military Eating Disorders: Genetics, Environment, and the Microbiota (MEDGEM)

No number (Reiner) 07/01/2018-06/30/2023 1.80 calendar
University of Washington/NIH 5 U.S.C. § 552(b)(4)
The Collaborative Network for Hemotopoietic Genetics (HemeNet)

OVERLAP

There is no scientific or budgetary overlap. Effort will be reduced as necessary to equal no more than 12 calendar months if any of the pending grants are awarded.

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES? Not Applicable
E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE? NOTHING TO REPORT
E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER? Not Applicable
E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)? NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE Not Applicable
F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM NOTHING TO REPORT
F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS F.3.a Human Subjects No Change
F.3.b Vertebrate Animals No Change
F.3.c Biohazards No Change
F.3.d Select Agents No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

No

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: Phenome-wide association of protein function-altering variants in a family study

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

No

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional	Address

		District	
Primary: The University of North Carolina at Chapel Hill	608195277	NC-004	104 Airport Drive, CB 1350 Suite 2200 Chapel Hill NC 275991350

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

Inclusion Enrollment Report

Inclusion Data Record (IDR) #: 183679

Using an Existing Dataset or Resource: Yes

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Domestic

NIH Defined Phase III Clinical Trial: No

Study Title: Phenome-wide association of protein function-altering variants in a family study

Planned Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reporte	
American Indian/Alaska Native	710	417		0	0					**1127**
Asian	0	0		0	0					**0**
Native Hawaiian or Other Pacific Islander	0	0		0	0					**0**
Black or African American	0	0		0	0					**0**
White	0	0		0	0					**0**
More than One Race	0	0		0	0					**0**
Unknown or Not Reported										
Total	**710**	**417**		**0**	**0**					**1127**

Cumulative Enrollment

This study involves an existing dataset and does not include cumulative enrollment.

Other Support

SMITH, BRIAN

ACTIVE

R01-CA153892 (Brown) 04/09/15-03/31/21 3.0 cal month
NIH 5 U.S.C. § 552(b)(4)
Cancer Screening in African American Women
The proposed study will investigate whether cancer screening coverage among AA women could be improved through medical insurance records and genealogy records.
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R21CA231470 (Andrews) 09/10/19-08/31/21 1.20 cal month
NIH 5 U.S.C. § 552(b)(4)
Cervical cancer screen-and-treat demonstration project with HPV self-testing and thermocoagulation for HIV-infected women in Malawi
This study will provide essential data to inform national policy in Malawi and other countries where both HIV and ICC prevalence are high, and it will also facilitate applications for future cooperative clinical trials groups in cervical cancer and global oncology.
Role: Investigator
Foreign component funded by grant: Yes
Foreign investigators: Dr. Maga Chagomerana (UNC Project Malawi – Lilongwe, Malawi)
Dr. Tamiwe Tomoka (University of Malawi, College of Medicine – Blantyre, Malawi)
Supplied by foreign site: Patient Samples
Appointment or Technology transfer to foreign site: No

PEER (Tang) 03/29/19-12/31/21 1.8 cal month
USAID/National Academy of Sciences 5 U.S.C. § 552(b)(4)
Implementation of an HPV-based Screen-and-Treat Strategy for Cervical Cancer Prevention in Malawi
To implement and evaluate 2 new models for cervical cancer screening and preventive therapy (CCS&PT), which will decrease the need for provider-performed pelvic exams and utilize a novel portable technology called thermocoagulation to treat precancerous cervical lesions.
Role: Investigator
Foreign component funded by grant: Yes
Foreign investigators: Dr. Bagrey Ngwira (University of Malawi, College of Medicine – Blantyre, Malawi)
Supplied by foreign site: Data Analysis
Appointment or Technology transfer to foreign site: No

P50CA058223 (Perou) 09/01/18-08/31/23 2.40 cal month
NIH/NCI 5 U.S.C. § 552(b)(4)
SPORE in Breast Cancer (Project 1: The Carolina Breast Cancer Study)
The Carolina Breast Cancer Study Phase III is a continuation of highly successful SPORE-supported population-based studies examining genetic and epidemiologic risk factors and characteristics of breast cancer with a focus on African-American and premenopausal breast cancer.
Role: Investigator
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

RESEARCH SUPPORT INVOLVING NO EFFORT OR FUNDING BUT FOREIGN COMPONENT

No Number (PI: Brown) 10/31/2017 – 12/31/2021 0 calendar
International AIDS Vaccine Institute 5 U.S.C. § 552(b)(4)
Extended high viremia by HIV viral subtype in sub-Saharan Africa
I am conducting an analysis of HIV viremia according to HIV viral subtype using data from the International AIDS Vaccine Institute.
Foreign component: Yes (no funding)
Foreign investigators: Etienne Karita (Project San Francisco Rwanda), Anatoli Kamali (Uganda Virus Research Institute), William Kilembe, Shabir Lakhi, Mubiano Inambao (Zambia-Emory Research Project), Linda-Gail Bekker (University of Cape Town), Omu Anzala (University of Nairobi), Eduard Sanders (Kenya Medical Research Institute
Technology transfer to foreign site: No

No Number (PI: Wong) 09/30/2017 – 12/31/2020 0 calendar
UNC Project China 5 U.S.C. § 552(b)(4)
Modeling the impact of sex work crackdown events on syphilis transmission in China
This modeling study seeks to estimate the effects on syphilis transmission of sex work crackdown events in South China.
Role: Advisor
Foreign component: Yes (no funding)
Foreign investigators: Ngai Sze Wong (UNC Project China, Chinese University of Hong Kong), Kate Mitchell (Imperial College London)
Technology transfer to foreign site: No

RESEARCH INVOLVING NO EFFORT OR FUNDING

No Number (PI: Olshan) 2014- 2021 0 calendar
UNC 5 U.S.C. § 552(b)(4)
Breast Cancer Association Consortium (BCAC)
The Breast Cancer Association Consortium (BCAC) is an international forum of investigators interested in the inherited risk of breast cancer. BCAC includes 107 studies covering 36 different countries (25 domestic, 82 foreign), approximately 108 lead investigators in total, considered collaborators because we share ideas and data that directly benefits my research. Full details can be provided upon request

PENDING

UG3HL152189-01 (Lessler) 06/01/20-05/31/25 1.2 cal month
NIH 5 U.S.C. § 552(b)(4)
Enhancing Blood Donation at Schools and Beyond: An Implementation Science Study
To conduct critical epidemiology surveillance and hemovigilance and qualitative research to understand facilitators and motivators of blood donation and strategies for engaging youth. Using this information, we will conduct a cluster randomized clinical trial to evaluate the effectiveness of an enhanced school-based donor program to increase both initial donation and long term retention as a donor.
Role: Investigator
Foreign component funded by grant: Yes
Foreign investigators: Dr. Maga Chagomerana (UNC Project Malawi – Lilongwe, Malawi)
Dr. Tamiwe Tomoka (University of Malawi, College of Medicine – Blantyre, Malawi)
Supplied by foreign site: Patient Samples
Appointment or Technology transfer to foreign site: No

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 4/6/2020 11:27:10 AM (UTC-07:00)
To: Caldwell, Chandra[ccaldwel@email.unc.edu]
Cc: Sheahan, Timothy Patrick[sheahan@email.unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]
Subject: Science for R21 progress report
Attachment: B2. Sims Sheahan R21 what was accomplised only.docx
Attachment: science draft R21 Year 1 progress report 4_6_2020 to chandra.docx

Hi Chandra,

I typed out a template and used it for the progress report. If this means I missed any of your sections please let me know. I know you will.

I have included the science accomplishments as a separate document as you requested.

Tim, right now I have the direct dollars broken up for year 2 as follows.

UNC direct dollars 5 U.S.C. § 552(b)(4)

PNNL direct dollars

For now this is FYI only as Chandra is going to wait until after the progress report gets done to work on Year 2 budget issues.

Please let me know if you have any questions or if I missed anything.
Thank you very much, Amy

From: Parrish, Kalyn[klparrish@unc.edu]
Sent: Tue 4/7/2020 10:38:45 AM (UTC-07:00)
To: Schaefer, Alexandra[aschaefe@email.unc.edu]
Cc: Sims, Amy C[amy.sims@pnnl.gov]
Subject: FW: Amy's R21 grant - statement to NIH

Hi Alex and Amy,

I hope you both are well. Can you provide an estimate amount you plan to spend on the prime 5113910 before 5/31?

Amy – I will also need to know if Battelle/PNNL plans to send another invoice to be paid on the subcontract. Is this something you can help with?

Thanks,
Kalyn

From: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Sent: Tuesday, April 7, 2020 1:04 PM
To: Parrish, Kalyn <klparrish@unc.edu>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Kalyn,

I'd ask Amy and Alex. I know they were planning on doing some spending in the near future but I have not kept up with their plans. Do you want to ask or have me ask?

T

From: "Parrish, Kalyn" <klparrish@unc.edu>
Date: Tuesday, April 7, 2020 at 12:09 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: Amy's R21 grant - statement to NIH

Hi Tim,

I hope you are doing well. Attached is report for Amy's R21, 5113910. Right now there is a remaining balance of [redacted]. Do you plan on spending this out? If not, can you give me an estimate on how much you do plan to spend before 5/31?

I ask because we have to issue a statement to NIH in order to move this grant to Amy at PNNL for Year 2. It's my understanding that any remaining funds will be rolled over to PNNL and UNC will then become a subcontract in year 2 once Amy decides on how much she wants to allocate to UNC for that budget period.

Thanks,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435

5 U.S.C. § 552(b)(6)

klparrish@unc.edu

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Thur 4/9/2020 12:02:56 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Science for R21 progress report

Thanks for sending the science, etc. and the only thing missing is your other support document!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, April 6, 2020 2:27 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Cc: Sheahan, Timothy Patrick <sheahan@email.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Science for R21 progress report

Hi Chandra,

I typed out a template and used it for the progress report. If this means I missed any of your sections please let me know. I know you will.

I have included the science accomplishments as a separate document as you requested.

Tim, right now I have the direct dollars broken up for year 2 as follows.

UNC direct dollars 5 U.S.C. § 552(b)(4)

PNNL direct dollars 5 U.S.C. § 552(b)(4)

For now this is FYI only as Chandra is going to wait until after the progress report gets done to work on Year 2 budget issues.

Please let me know if you have any questions or if I missed anything.
Thank you very much, Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 4/9/2020 12:08:13 PM (UTC-07:00)
To: Caldwell, Chandra[ccaldwel@email.unc.edu]
Subject: Re: Science for R21 progress report

Hi,

I generated one but sent it to my administrative people at their request.

I will make sure you get it! Thank you, Amy

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Thursday, April 9, 2020 at 12:03 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Science for R21 progress report

Thanks for sending the science, etc. and the only thing missing is your other support document!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, April 6, 2020 2:27 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Cc: Sheahan, Timothy Patrick <sheahan@email.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Science for R21 progress report

Hi Chandra,

I typed out a template and used it for the progress report. If this means I missed any of your sections please let me know. I know you will.

I have included the science accomplishments as a separate document as you requested.

Tim, right now I have the direct dollars broken up for year 2 as follows.

UNC direct dollars 5 U.S.C. § 552(b)(4)

PNNL direct dollars

For now this is FYI only as Chandra is going to wait until after the progress report gets done to work on Year 2 budget issues.

Please let me know if you have any questions or if I missed anything.
Thank you very much, Amy

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Thur 4/9/2020 12:11:31 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Science for R21 progress report

Thanks for checking on it!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, April 9, 2020 3:08 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: Science for R21 progress report

Hi,

I generated one but sent it to my administrative people at their request.

I will make sure you get it! Thank you, Amy

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Thursday, April 9, 2020 at 12:03 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Science for R21 progress report

Thanks for sending the science, etc. and the only thing missing is your other support document!

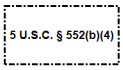
From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, April 6, 2020 2:27 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Cc: Sheahan, Timothy Patrick <sheahan@email.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Science for R21 progress report

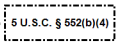
Hi Chandra,

I typed out a template and used it for the progress report. If this means I missed any of your sections please let me know. I know you will.

I have included the science accomplishments as a separate document as you requested.

Tim, right now I have the direct dollars broken up for year 2 as follows.

UNC direct dollars 

PNNL direct dollars 

For now this is FYI only as Chandra is going to wait until after the progress report gets done to work on Year 2 budget issues.

Please let me know if you have any questions or if I missed anything.
Thank you very much, Amy

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Thur 4/9/2020 12:22:41 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Science for R21 progress report
Attachment: 2590-fp7_all personnel report.docx

One more thing, are you the only one being paid from these funds at PNNL/Battelle? If yes, I will just wait to receive your other support next week to denote the amount of effort you are contributing on the project. If the answer is no, I will need the attached personnel form completed to account for everyone outside of you.

Thanks,
C.

From: Caldwell, Chandra
Sent: Thursday, April 9, 2020 3:12 PM
To: Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Science for R21 progress report

Thanks for checking on it!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, April 9, 2020 3:08 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: Science for R21 progress report

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Subject: RE: Science for R21 progress report

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Sent: Monday, April 6, 2020 2:27 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Cc: Sheahan, Timothy Patrick <sheahan@email.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Science for R21 progress report

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I have included the science accomplishments as a separate document as you requested.

Tim, right now I have the direct dollars broken up for year 2 as follows.

UNC direct dollars 5 U.S.C. § 552(b)(4)

PNNL direct dollars 5 U.S.C. § 552(b)(4)

For now this is FYI only as Chandra is going to wait until after the progress report gets done to work on Year 2 budget issues.

Please let me know if you have any questions or if I missed anything.
Thank you very much, Amy

A. COVER PAGE

Project Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells	
Grant Number: 5R21AI146872-02	**Project/Grant Period:** 06/05/2019 - 05/31/2021
Reporting Period: 06/05/2019 - 05/31/2020	**Requested Budget Period:** 06/01/2020 - 05/31/2021
Report Term Frequency: Annual	**Date Submitted:**
Program Director/Principal Investigator Information: TIMOTHY PATRICK SHEAHAN , PHD BS **Phone number:** 9196191698 **Email:** sheahan@email.unc.edu	**Recipient Organization:** UNIV OF NORTH CAROLINA CHAPEL HILL UNIVERSITY OF NORTH CAROLINA CHAPEL HILL Office of Sponsored Research CHAPEL HILL, NC 275990001 **DUNS:** 608195277 **EIN:** 1566001393A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: R DAVID PAUL 104 Airport Dr. Suite 2200 Chapel Hill, NC 275991350 **Phone** **Email:** r 5 U.S.C. § 552(b)(6)	**Signing Official:** RONDA FARRELL 104 Airport Dr Suite 2200 Chapel Hill, NC 27599 **Phone** **Email:** 5 U.S.C. § 552(b)(6)
Human Subjects: No	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The major goals of the project are to determine if primary human lung cells infected with Middle East respiratory syndrome coronavirus (MERS-CoV) use epigenetic mechanisms to regulate the expression of interferon stimulated genes (ISG). Specific Aim 1: Does histone methylation status coordinate with ISG expression patterns in MERS-CoV infected MVE, HAE, and/or FB? Aim 1 focuses on defining cell type specific type I and III ISG for primary human lung airway epithelial cell cultures (HAE), microvascular endothelial cells (MVE) and fibroblasts (FB), identifying if transcription factors mediate any regulation of ISG expression, and determining if MERS-CoV infection affects the methylation state of lysine 4 or 27 on cellular histones which determine whether chromatin in in an open state and accessible for transcription or in a closed state preventing transcription from occurring. Specific Aim 2: Exploring modulation of host chromatin remodeling enzymes following MERS-COV infection of primary human lung MVE, HAE, FB. Aim 2 seeks to define the DNA/histone methyltransfersae and deaceytylatse enzymes MERS-CoV may be modulating to regulate ISG expression. Assays will determine if host chromatin remodeling enzymes are active or inhibited following MERS-CoV replication and whether MERS-CoV replication and/or ISG expression are affected by inhibition of methyltransferase/deaceytlse enzyme activity. Finally, we will use novel protein-protein interaction technologies to determine MERS-CoV proteins that may mediate the epigenetic regulation of ISG expression.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Though there may be delays in completing experiments due to the shelter in place requirements for CoVID-19 - Prior to the end of the funding period we anticipate completing the following. Experiments to determine if histone modification plays a role in ISG differential expression in MERS-CoV infected FB will begin as soon as the shelter in place bans have been removed as all samples have been harvested and are in the freezer awaiting analysis. Existing lysate (from both MVE and FB) will also be used to explore if transcription factors contribute to regulation of ISG expression following MERS-CoV infection. Experiments to determine if the genes responsible for modifying chromatin structure are differentially expressed following MERS-CoV infection of primary human lung MVE and FB will be performed as described in Aim 2 using BioRad's PrimerPCR Pathway arrays. To determine if inhibition of enzymes that mediate chromatin structure rearrangement alters coronavirus replication and or changes the innate immune response to virus, drug efficacy studies will be performed, and infected treated samples will be assayed to determine levels of viral replication and cellular viability. If changes are detected in levels of viral replication additional samples will be generated to determine how ISG expression has been altered. We anticipate obtaining sufficient preliminary data for the submission of an RO1 by fall of 2021.

B.2 What was accomplished under these goals?

The ongoing MERS-CoV epidemic and recent identification of SARS-CoV 2 as the causative agent of coronavirus infectious disease 2019 (COVID-19) highlight the need for a better understanding of how highly pathogenic human coronaviruses manipulate the host immune response. Previous studies demonstrated that MERS-CoV infects an expanded range of human primary cell types including microvascular endothelial cells and lung fibroblasts which are not permissive for the 2002 SARS-CoV strain. In immortalized human lung epithelial cells, MERS-CoV downregulates the expression of several interferon stimulated genes (ISG) restricting the host innate immune response and previous studies suggest that this downregulation is mediated by epigenetic mechanisms that regulate the methylation state of histones keeping the chromatin in an inaccessible or closed state and upregulating the methylation of host DNA leading to a decrease in the expression of major histocompatibility complex genes. The goal of these studies was to determine if MERS-CoV uses epigenetic mechanisms to regulate the innate immune response in primary human lung endothelial cells (MVE) and fibroblasts (FB). Initial studies evaluated levels of infection in more than 20 donor tissues (all cell types collected for each donor) to determine which were best for the MERS-CoV epigenetic studies. Three donors were selected, and the University of North Carolina at Chapel Hill Tissue Procurement Core earmarked these frozen cell aliquots for these studies and sufficient numbers of cells are available for all studies within this funding application (**Figure 1**).

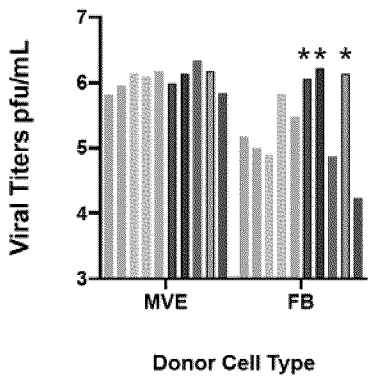

Figure 1. Representative MERS-CoV titers from tissue donor candidates for epigenetic experiments. MVE and FB from 20 donors were plated and infected with MERS-CoV for 24 hours and supernatants assessed by plaque assay to determine levels of viral replication. Three stars indicate the donors (only FB shown) used for downstream epigenetic testing. * highlight chosen donors.

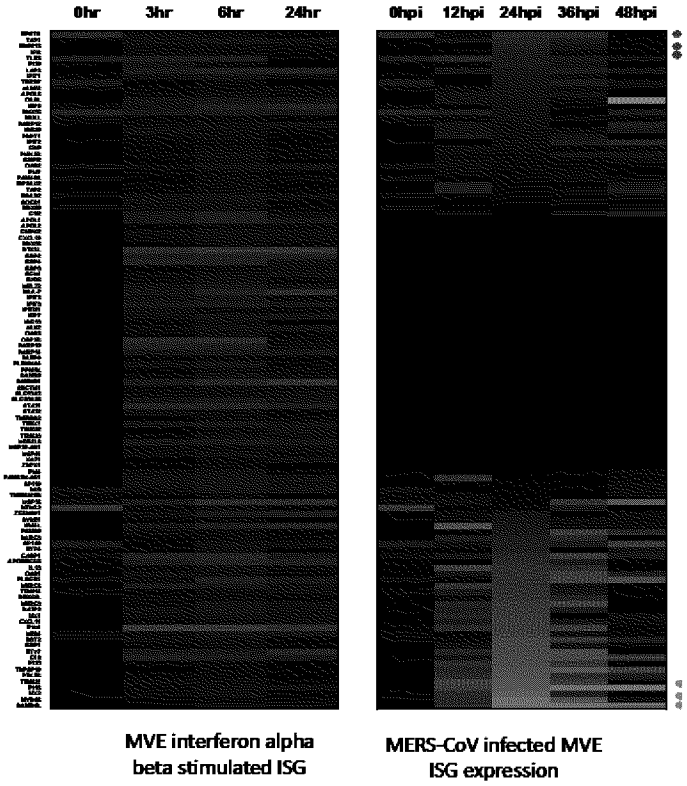

Figure 2 MERS-CoV regulates the innate immune response in primary human lung MVE. Left panel: Human lung MVE were treated with interferon alpha beta for the indicated times and ISG identified following microarray analysis. Right panel: ISG list identified in left panel following MERS-CoV infection of MVE. Red dots indicate up-regulated ISG used for ChIP-PCR studies; green dots indicate down-regulated ISG used for ChIP-PCR studies

Cell type specific lists of ISG from MVE and FB were generated following treatment of MVE and FB with interferon alpha/beta and the top six upregulated and downregulated (12 genes total per cell type) for each cell type were identified (**Table** and **Figure 2**). Triplicate samples of MVE and FB for all three donors were infected with MERS-CoV, protein and DNA crosslinked by formaldehyde, samples were safety tested and removed from biosafety level three. Due to the number of total samples to process analysis of one cell type at a time will be performed. Batch one analysis was performed on MERS-CoV infected MVE cells and has been completed. We anticipate that batch two analysis on MERS-CoV infected FB will be completed by the end of Year 1/May 2020,

but this work may be delayed until the shelter in place requirement has been removed. Formalin treated lysates from MERS-CoV infected MVE were assayed by chromatin immunoprecipitation-PCR (ChIP-PCR) using antisera specific for the open, transcriptionally active form of histone bound chromatin (lysine 4 in histone 3 (H3K4)) or for the closed transcriptionally inactive form of histone bound chromatin (lysine 27 in histone 3 (H3K27)) to determine if histone modifications could explain the differential expression of specific ISG. PCR is used to amplify the promoter regions of the ISG following immunoprecipitation to determine if the chromatin precipitated is in the active or inactive state following MERS-CoV infection (**Table**). Representative results are shown in **Figure 3** for two ISG with increased differential expression (interferon gamma inducible protein 6 (IFI 6) and ring finger protein 213 (RNF213)) or decreased expression (myeloid differentiation primary response protein 88 (MyD88) and sterile alpha motif domain containing 9L (SMAD9L)). Histones bound to the promoter regions of ISG that had upregulated expression (IFI 6 and RNF213) following MERS-CoV infection of MVE were predominantly methylated on lysine 4 and in the active confirmation for all three tissue donors (Figure 3 top panels) with little if any associate with histones in the closed confirmation. In contrast, histones bound to ISG promoter regions with decreased expression levels (SMAD9L and MyD88) were predominantly methylated on lysine 27 and in the closed confirmation with little associate with histones in the active confirmation. This data suggests that epigenetic regulation may play a role in down regulation of the innate immune response to MERS-CoV in primary human lung microvascular endothelial cells.

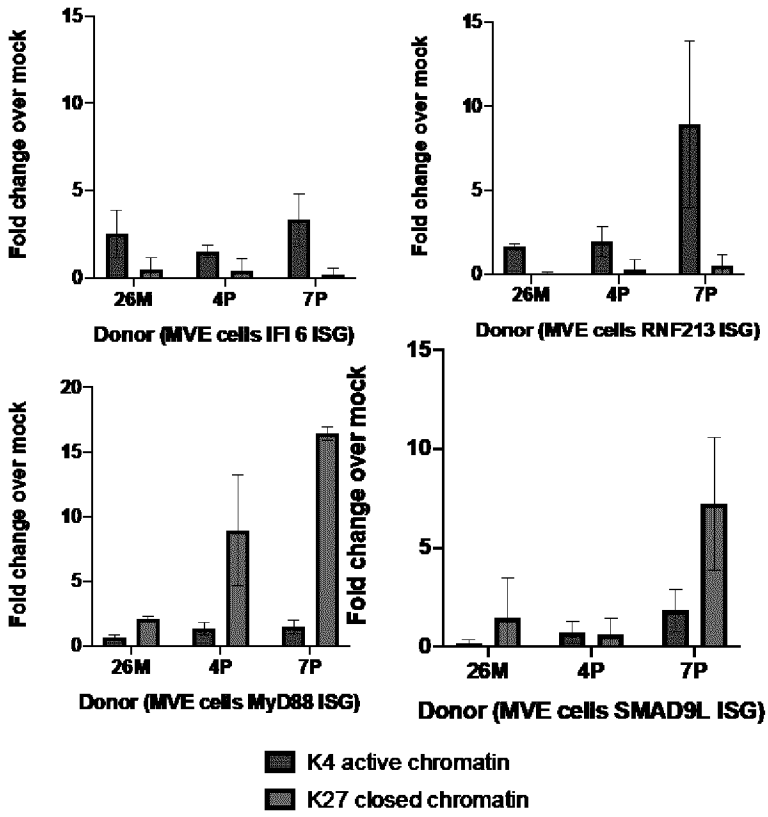

Figure 3 Altered histone methylation patterns suggest mechanism for ISG expression following MERS-CoV infection in primary human lung MVE. ChIP-PCR was performed on MERS-CoV infected MVE lysate for three donors. Antibodies specific for histones with lysine 4 methylation (shown in red) or for histones with lysine 27 methylation (shown in green) were used to precipitate chromatin and assayed by real time PCR. Top panels are ISG with increased expression following MERS-CoV infection and bottom panels are ISG with decreased expression following infection.

We are excited by the results from MERS-CoV infected MVE that suggest epigenetic regulation controls ISG expression in endothelial as well as epithelial lung cells. We anticipate similar findings from MERS-CoV infected fibroblasts and look forward to expanding our understanding of which enzymes that modify chromatin structure contribute to the regulation of the innate immune response following MERS-CoV infection.

On January 6, 2020 Dr. Sims began a new position as a senior scientist at the Pacific Northwest National Laboratory in Richland, Washington. She will continue the studies within this award as a collaboration with Drs. Timothy Sheahan and Alexandra Schaefer at the University of North Carolina at Chapel Hill.

Cell Type	Gene Name	Differential Gene Expression	Primer Pairs	Analysis as Predicted
MVE	Sterile alpha motif domain containing 9L (SMAD9L)	Down	cagcctcattttcgtagccctcat ggccatctacaagccaaggagaga	Yes
MVE	Interferon gamma inducible protein 16 (IFI 16)	Down	tcatagcagacatttccccaacca gcttcttctcccctcctttcctgt	Mixed between donors
MVE	Myeloid differentiation primary response 88 (MyD88)	Down	Cccctcctcacaggttcagtccta gagcatggcacaaccaagaaaaga	Yes
MVE	Epithelial stromal interaction 1 (EPSTI 1)	Up	ccaggttggagtacagtggcatga tacaacaattagctgggcgtggtg	Yes
MVE	Interferon alpha inducible protein 6 (IFI 6)	Up	cagcaggcagcacacaaatgttc agccaatccctgtcggagtttcta	Yes
MVE	Ring finger protein 213 (RNF213)	Up	ggatgaaggggtgagaggagaagg gtgtgaccagggacctccgtttta	Yes

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
TSHEAHAN	Y	Sheahan, Timothy Patrick	BS,PHD	PD/PI	1.0	0.0	0.0			NA
AMY_SIMS	Y	SIMS, AMY C	PHD	PD/PI	2.4	0.0	0.0			NA
	N	Schaefer, Alexandra		Technician	3.0	0.0	0.0			NA
	N	Lam, Mariam		Technician	1.8	0.0	0.0			NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: OtherSupport_ALL.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

OTHER SUPPORT

SHEAHAN, TIMOTHY

ACTIVE

R21AI146872 (PI: Sheahan/Sims) 06/05/19-05/30/21 0.60 cal months (5%
NIH **{THIS GRANT}** 5 U.S.C. § 552(b)(4)
How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
This proposal will build on foundational studies performed in continuous human lung cell lines and define ways that MERS-CoV regulates innate immunity in primary human lung fibroblasts and microvascular endothelial cells.
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

U19AI142759 CETR (PI: Whitley) 03/01/14-02/28/24 3.6 cal months (30%)
UAB/NIH/NIAID 5 U.S.C. § 552(b)(4)
Antiviral Drug Discovery and Development Center
The specific aims of the proposal will identify small molecule inhibitors of CoV fidelity and RNA capping, define their mechanism of action, and determine their efficacy against SARS-CoV and across CoV families using in vivo mouse models of acute and persistent CoV disease.
Role: Investigator
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01 AI131688-01 (PI: Rice) 03/15/17-02/281/22 1.8 cal months (15%)
Rockefeller/NIH 5 U.S.C. § 552(b)(4)
Analysis of immunity, viral adaptation and pathogenesis in a new mouse model of HCV-related rodent hepacivirus infection
Mechanisms that contribute to the persistence of hepatotropic viruses, such as HCV, are not well understood. We have recently established the first immune-competent mouse model of an HCV-related virus. With this new model, we propose to systematically study immunity and host-virus interactions during a hepatotropic RNA virus infection in vivo.
Role: Subcontract PI
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01 AI132178-01 (MPI: Sheahan/Baric) 08/09/17-07/31/22 2.4 cal months (20%)
NIH 5 U.S.C. § 552(b)(4)
Broad-spectrum antiviral GS-5734 to treat MERS-CoV and related emerging CoV
In partnership with Gilead Sciences, we aim to accelerate the preclinical development of GS-5734 and promote IND licensure. We define the pharmacokinetics, pharmacodynamics, resistance profile, efficacy breadth and mechanism of action of GS-5734 against MERS-CoV and related emerging CoV.
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01AI108197-06 (MPI: Baric/Denison) 03/01/18-02/28/23 1.8 cal months (15%)
Vanderbilt/NIH 5 U.S.C. § 552(b)(4)
Determinants of Coronavirus Fidelity in Replication and Pathogenesis
To identify common and unique determinants of CoV nsp14-ExoN functions CoV replication, fidelity and IFN sensitivity across CoVs; To determine pathways of adaptation to loss of nsp14-ExoN activity in vitro and in vivo; and to define mechanisms of ExoN-regulated CoV sensitivity to the innate antiviral immune response.
Role: Co-Investigator

Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

U01AI149644 (PI: Baric) 04/19/19-03/31/24 1.8 cal months (15%)
NIH
5 U.S.C. § 552(b)(4)
Respiratory Virus Vaccine and Adjuvant Exploration
Vaccination is one of the most effective public health measures for protecting against infectious disease, and the proposed studies will identify adjuvants and adjuvant combinations that safely elicit long lived protective immunity against emerging pathogens in at risk populations.
Role: Investigator
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

PENDING:
R01 (PI: Meshnick) 04/01/20-03/31/25 0.36 cal months (3%)
NIH
5 U.S.C. § 552(b)(4)
Molecular epidemiology of arboviruses in the Democratic Republic of the Congo
The grant is innovative in its multidisciplinarity, combining epidemiological, entomological, serological, phylogenetic and basic sciences approaches. Together, this research will, for the first time, provide data on the incidence, types, sources, and genomic traits of this important group of viruses in Central Africa.
Foreign component funded by this grant: Yes
Foreign investigators: Antoinette Tshefu, University of Kinshasa (Congo, Democratic Republic)
Supplied by foreign site: Patient Samples
Technology transfer to foreign site: No

R21 (PI: Sheahan) 07/01/20-06/30/22 0.90 cal months (7.5%)
NIH
5 U.S.C. § 552(b)(4)
Characterization of hepacivirus pathogenesis, viral adaptation and the mapping of host susceptibility alleles in the Collaborative Cross
The goals of this proposal are to: 1) phenotype the kinetics of virus replication/adaptation, pathogenesis and the host response in CC lines with delayed clearance and chronic infection and 2) to map the genetic determinants driving virus titer, viral evolution, clearance, weight loss, blood leukocyte modulation, and chronic infection
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

Not Assigned (PI: Baric) 07/01/20-06/30/25 0.36 cal months (3%)
EcoHealth Alliance
5 U.S.C. § 552(b)(4)
US-China Collab: Spillover, co-infection, and control of bat-origin livestock coronaviruses
To develop an economic model of farm profit maximization linked to the compartmental epidemiological model of co-infection disease.*Foreign component funded by this grant: No*

OVERLAP: If any of the pending awards are funded, Dr. Sheahan will reduce is effort accordingly to not exceed 12 calendar months.

Other Support

SIMS, AMY

ACTIVE

R21AI146872 (Sims/Sheahan) 06/05/19-05/31/21 2.4 cal months
UNC Chapel Hill/NIH 5 U.S.C. § 552(b)(4) **{THIS GRANT}**
How MERS-CoV regulates the innate immune response
The major goal of the project is to determine if primary human lung cells infected with Middle East respiratory syndrome coronavirus (MERS-CoV) use epigenetic mechanisms to regulate the expression of interferon stimulated genes.

Foreign component funded by grant: No

There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

LDRD (Sims) 03/07/20-09/30/21 4.4 cal months
Pacific Northwest National Laboratory $150,000
Defining coronavirus lipidomic response
The goal of this project is to characterize the lipid response to coronavirus infection.

Foreign component funded by grant: No

There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

PENDING

5 U.S.C. § 552(b)(4)

Not Applicable

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

On January 6, 2020 Dr. Sims began a new position at Pacific Northwest National Laboratory (PNNL) in Richland, Washington. Dr. Sims will continue to collaborate with Drs. Sheahan and Schaefer at the University of North Carolina at Chapel Hill (UNC) to meet the goals of this funded project. Funds for Year 1 have been appropriately distributed between the PNNL and UNC to allow work to continue at both sites. Prior to the start of Year 2, we anticipate petitioning NIH/NIAID/UNC to transition the award to PNNL allowing Dr. Sims to resume as Principle Investigator. Funds would then be distributed to UNC via subcontract to continue the collaboration and to ensure forward progress on the proposed work.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: University of North Carolina at Chapel Hill	608195277	NC-004	104 Airport Drive, Suite 2200, CB 1350 Chapel Hill NC 275991350
Pacific Northwest National Laboratory	032987476	WA-004	902 Battelle Boulevard P.O. Box 999, MSIN J4-02 Richland WA 993520999

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

A. COVER PAGE

Project Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells	
Grant Number: 5R21AI146872-02	**Project/Grant Period:** 06/05/2019 - 05/31/2021
Reporting Period: 06/05/2019 - 05/31/2020	**Requested Budget Period:** 06/01/2020 - 05/31/2021
Report Term Frequency: Annual	**Date Submitted:**
Program Director/Principal Investigator Information: TIMOTHY PATRICK SHEAHAN , PHD BS **Phone number:** 9196191698 **Email:** sheahan@email.unc.edu	**Recipient Organization:** UNIV OF NORTH CAROLINA CHAPEL HILL UNIVERSITY OF NORTH CAROLINA CHAPEL HILL Office of Sponsored Research CHAPEL HILL, NC 275990001 **DUNS:** 608195277 **EIN:** 1566001393A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: R DAVID PAUL 104 Airport Dr. Suite 2200 Chapel Hill, NC 275991350 **Phone:** **5 U.S.C. § 552(b)(6)** **Email:**	**Signing Official:** RONDA FARRELL 104 Airport Dr Suite 2200 Chapel Hill, NC 27599 **Pho** **5 U.S.C. § 552(b)(6)** **Ema**
Human Subjects: No	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The major goals of the project are to determine if primary human lung cells infected with Middle East respiratory syndrome coronavirus (MERS-CoV) use epigenetic mechanisms to regulate the expression of interferon stimulated genes (ISG). Specific Aim 1: Does histone methylation status coordinate with ISG expression patterns in MERS-CoV infected MVE, HAE, and/or FB? Aim 1 focuses on defining cell type specific type I and III ISG for primary human lung airway epithelial cell cultures (HAE), microvascular endothelial cells (MVE) and fibroblasts (FB), identifying if transcription factors mediate any regulation of ISG expression, and determining if MERS-CoV infection affects the methylation state of lysine 4 or 27 on cellular histones which determine whether chromatin in in an open state and accessible for transcription or in a closed state preventing transcription from occurring. Specific Aim 2: Exploring modulation of host chromatin remodeling enzymes following MERS-COV infection of primary human lung MVE, HAE, FB. Aim 2 seeks to define the DNA/histone methyltransfersae and deaceytylatse enzymes MERS-CoV may be modulating to regulate ISG expression. Assays will determine if host chromatin remodeling enzymes are active or inhibited following MERS-CoV replication and whether MERS-CoV replication and/or ISG expression are affected by inhibition of methyltransferase/deaceytlse enzyme activity. Finally, we will use novel protein-protein interaction technologies to determine MERS-CoV proteins that may mediate the epigenetic regulation of ISG expression.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Though there may be delays in completing experiments due to the shelter in place requirements for CoVID-19 - Prior to the end of the funding period we anticipate completing the following. Experiments to determine if histone modification plays a role in ISG differential expression in MERS-CoV infected FB will begin as soon as the shelter in place bans have been removed as all samples have been harvested and are in the freezer awaiting analysis. Existing lysate (from both MVE and FB) will also be used to explore if transcription factors contribute to regulation of ISG expression following MERS-CoV infection. Experiments to determine if the genes responsible for modifying chromatin structure are differentially expressed following MERS-CoV infection of primary human lung MVE and FB will be performed as described in Aim 2 using BioRad's PrimerPCR Pathway arrays. To determine if inhibition of enzymes that mediate chromatin structure rearrangement alters coronavirus replication and or changes the innate immune response to virus, drug efficacy studies will be performed, and infected treated samples will be assayed to determine levels of viral replication and cellular viability. If changes are detected in levels of viral replication additional samples will be generated to determine how ISG expression has been altered. We anticipate obtaining sufficient preliminary data for the submission of an RO1 by fall of 2021.

B.2 What was accomplished under these goals?

The ongoing MERS-CoV epidemic and recent identification of SARS-CoV 2 as the causative agent of coronavirus infectious disease 2019 (COVID-19) highlight the need for a better understanding of how highly pathogenic human coronaviruses manipulate the host immune response. Previous studies demonstrated that MERS-CoV infects an expanded range of human primary cell types including microvascular endothelial cells and lung fibroblasts which are not permissive for the 2002 SARS-CoV strain. In immortalized human lung epithelial cells, MERS-CoV downregulates the expression of several interferon stimulated genes (ISG) restricting the host innate immune response and previous studies suggest that this downregulation is mediated by epigenetic mechanisms that regulate the methylation state of histones keeping the chromatin in an inaccessible or closed state and upregulating the methylation of host DNA leading to a decrease in the expression of major histocompatibility complex genes. The goal of these studies was to determine if MERS-CoV uses epigenetic mechanisms to regulate the innate immune response in primary human lung endothelial cells (MVE) and fibroblasts (FB). Initial studies evaluated levels of infection in more than 20 donor tissues (all cell types collected for each donor) to determine which were best for the MERS-CoV epigenetic studies. Three donors were selected, and the University of North Carolina at Chapel Hill Tissue Procurement Core earmarked these frozen cell aliquots for these studies and sufficient numbers of cells are available for all studies within this funding application (**Figure 1**).

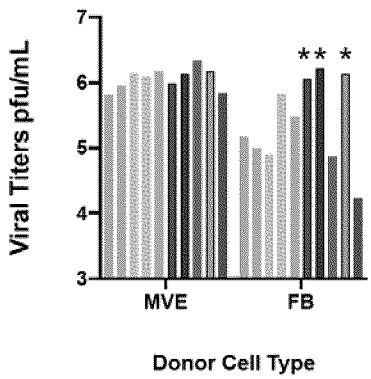

Figure 1. Representative MERS-CoV titers from tissue donor candidates for epigenetic experiments. MVE and FB from 20 donors were plated and infected with MERS-CoV for 24 hours and supernatants assessed by plaque assay to determine levels of viral replication. Three stars indicate the donors (only FB shown) used for downstream epigenetic testing. * highlight chosen donors.

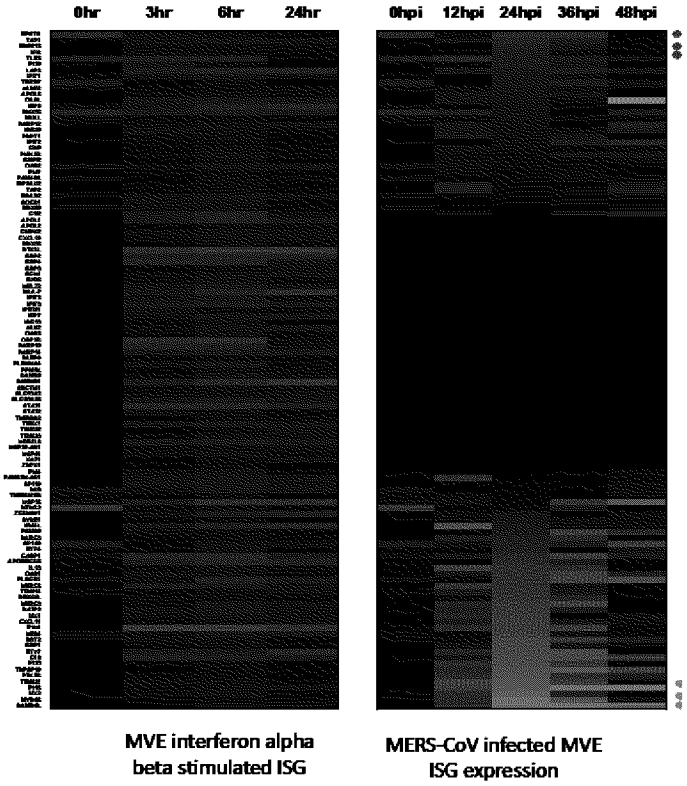

Figure 2 MERS-CoV regulates the innate immune response in primary human lung MVE. Left panel: Human lung MVE were treated with interferon alpha beta for the indicated times and ISG identified following microarray analysis. Right panel: ISG list identified in left panel following MERS-CoV infection of MVE. Red dots indicate up-regulated ISG used for ChIP-PCR studies; green dots indicate down-regulated ISG used for ChIP-PCR studies

Cell type specific lists of ISG from MVE and FB were generated following treatment of MVE and FB with interferon alpha/beta and the top six upregulated and downregulated (12 genes total per cell type) for each cell type were identified (**Table** and **Figure 2**). Triplicate samples of MVE and FB for all three donors were infected with MERS-CoV, protein and DNA crosslinked by formaldehyde, samples were safety tested and removed from biosafety level three. Due to the number of total samples to process analysis of one cell type at a time will be performed. Batch one analysis was performed on MERS-CoV infected MVE cells and has been completed. We anticipate that batch two analysis on MERS-CoV infected FB will be completed by the end of Year 1/May 2020,

but this work may be delayed until the shelter in place requirement has been removed. Formalin treated lysates from MERS-CoV infected MVE were assayed by chromatin immunoprecipitation-PCR (ChIP-PCR) using antisera specific for the open, transcriptionally active form of histone bound chromatin (lysine 4 in histone 3 (H3K4)) or for the closed transcriptionally inactive form of histone bound chromatin (lysine 27 in histone 3 (H3K27)) to determine if histone modifications could explain the differential expression of specific ISG. PCR is used to amplify the promoter regions of the ISG following immunoprecipitation to determine if the chromatin precipitated is in the active or inactive state following MERS-CoV infection (**Table**). Representative results are shown in **Figure 3** for two ISG with increased differential expression (interferon gamma inducible protein 6 (IFI 6) and ring finger protein 213 (RNF213)) or decreased expression (myeloid differentiation primary response protein 88 (MyD88) and sterile alpha motif domain containing 9L (SMAD9L)). Histones bound to the promoter regions of ISG that had upregulated expression (IFI 6 and RNF213) following MERS-CoV infection of MVE were predominantly methylated on lysine 4 and in the active confirmation for all three tissue donors (Figure 3 top panels) with little if any associate with histones in the closed confirmation. In contrast, histones bound to ISG promoter regions with decreased expression levels (SMAD9L and MyD88) were predominantly methylated on lysine 27 and in the closed confirmation with little associate with histones in the active confirmation. This data suggests that epigenetic regulation may play a role in down regulation of the innate immune response to MERS-CoV in primary human lung microvascular endothelial cells.

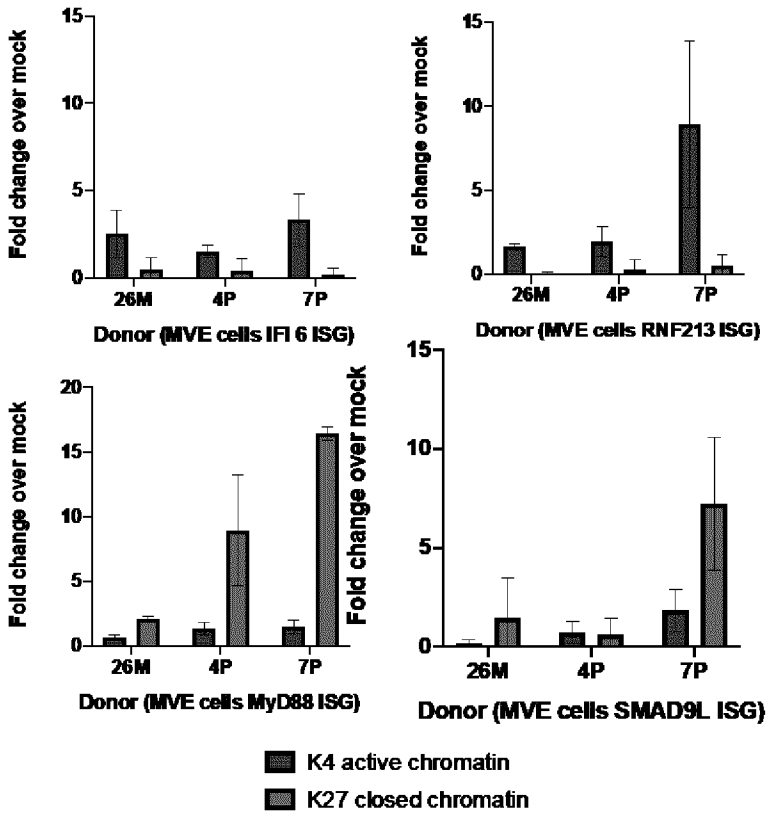

Figure 3 Altered histone methylation patterns suggest mechanism for ISG expression following MERS-CoV infection in primary human lung MVE. ChIP-PCR was performed on MERS-CoV infected MVE lysate for three donors. Antibodies specific for histones with lysine 4 methylation (shown in red) or for histones with lysine 27 methylation (shown in green) were used to precipitate chromatin and assayed by real time PCR. Top panels are ISG with increased expression following MERS-CoV infection and bottom panels are ISG with decreased expression following infection.

We are excited by the results from MERS-CoV infected MVE that suggest epigenetic regulation controls ISG expression in endothelial as well as epithelial lung cells. We anticipate similar findings from MERS-CoV infected fibroblasts and look forward to expanding our understanding of which enzymes that modify chromatin structure contribute to the regulation of the innate immune response following MERS-CoV infection.

On January 6, 2020 Dr. Sims began a new position as a senior scientist at the Pacific Northwest National Laboratory in Richland, Washington. She will continue the studies within this award as a collaboration with Drs. Timothy Sheahan and Alexandra Schaefer at the University of North Carolina at Chapel Hill.

Cell Type	Gene Name	Differential Gene Expression	Primer Pairs	Analysis as Predicted
MVE	Sterile alpha motif domain containing 9L (SMAD9L)	Down	cagcctcattttcgtagccctcat ggccatctacaagccaaggagaga	Yes
MVE	Interferon gamma inducible protein 16 (IFI 16)	Down	tcatagcagacatttccccaacca gcttcttctcccctcctttcctgt	Mixed between donors
MVE	Myeloid differentiation primary response 88 (MyD88)	Down	Cccctcctcacaggttcagtccta gagcatggcacaaccaagaaaaga	Yes
MVE	Epithelial stromal interaction 1 (EPSTI 1)	Up	ccaggttggagtacagtggcatga tacaacaattagctgggcgtggtg	Yes
MVE	Interferon alpha inducible protein 6 (IFI 6)	Up	cagcaggcagcacacaaatgttc agccaatccctgtcggagtttcta	Yes
MVE	Ring finger protein 213 (RNF213)	Up	ggatgaaggggtgagaggagaagg gtgtgaccagggacctccgtttta	Yes

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
TSHEAHAN	Y	Sheahan, Timothy Patrick	BS,PHD	PD/PI	1.0	0.0	0.0			NA
AMY_SIMS	Y	SIMS, AMY C	PHD	PD/PI	2.4	0.0	0.0			NA
	N	Schaefer, Alexandra		Staff scientist (Doctoral level)	3.0	0.0	0.0			NA
	N	Lam, Mariam		Technician	1.8	0.0	0.0			NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: OtherSupport_ALL.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

OTHER SUPPORT

SHEAHAN, TIMOTHY

ACTIVE

R21AI146872 (PI: Sheahan/Sims) 06/05/19-05/30/21 0.60 cal months (5%
NIH **{THIS GRANT}** 5 U.S.C. § 552(b)(4)
How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
This proposal will build on foundational studies performed in continuous human lung cell lines and define ways that MERS-CoV regulates innate immunity in primary human lung fibroblasts and microvascular endothelial cells.
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

U19AI142759 CETR (PI: Whitley) 03/01/14-02/28/24 3.6 cal months (30%)
UAB/NIH/NIAID 5 U.S.C. § 552(b)(4)
Antiviral Drug Discovery and Development Center
The specific aims of the proposal will identify small molecule inhibitors of CoV fidelity and RNA capping, define their mechanism of action, and determine their efficacy against SARS-CoV and across CoV families using in vivo mouse models of acute and persistent CoV disease.
Role: Investigator
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01 AI131688-01 (PI: Rice) 03/15/17-02/281/22 1.8 cal months (15%)
Rockefeller/NIH 5 U.S.C. § 552(b)(4)
Analysis of immunity, viral adaptation and pathogenesis in a new mouse model of HCV-related rodent hepacivirus infection
Mechanisms that contribute to the persistence of hepatotropic viruses, such as HCV, are not well understood. We have recently established the first immune-competent mouse model of an HCV-related virus. With this new model, we propose to systematically study immunity and host-virus interactions during a hepatotropic RNA virus infection in vivo.
Role: Subcontract PI
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01 AI132178-01 (MPI: Sheahan/Baric) 08/09/17-07/31/22 2.4 cal months (20%)
NIH 5 U.S.C. § 552(b)(4)
Broad-spectrum antiviral GS-5734 to treat MERS-CoV and related emerging CoV
In partnership with Gilead Sciences, we aim to accelerate the preclinical development of GS-5734 and promote IND licensure. We define the pharmacokinetics, pharmacodynamics, resistance profile, efficacy breadth and mechanism of action of GS-5734 against MERS-CoV and related emerging CoV.
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01AI108197-06 (MPI: Baric/Denison) 03/01/18-02/28/23 1.8 cal months (15%)
Vanderbilt/NIH 5 U.S.C. § 552(b)(4)
Determinants of Coronavirus Fidelity in Replication and Pathogenesis
To identify common and unique determinants of CoV nsp14-ExoN functions CoV replication, fidelity and IFN sensitivity across CoVs; To determine pathways of adaptation to loss of nsp14-ExoN activity in vitro and in vivo; and to define mechanisms of ExoN-regulated CoV sensitivity to the innate antiviral immune response.
Role: Co-Investigator

Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

U01AI149644 (PI: Baric) 04/19/19-03/31/24 1.8 cal months (15%)
NIH
5 U.S.C. § 552(b)(4)
Respiratory Virus Vaccine and Adjuvant Exploration
Vaccination is one of the most effective public health measures for protecting against infectious disease, and the proposed studies will identify adjuvants and adjuvant combinations that safely elicit long lived protective immunity against emerging pathogens in at risk populations.
Role: Investigator
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

PENDING:
R01 (PI: Meshnick) 04/01/20-03/31/25 0.36 cal months (3%)
NIH
5 U.S.C. § 552(b)(4)
Molecular epidemiology of arboviruses in the Democratic Republic of the Congo
The grant is innovative in its multidisciplinarity, combining epidemiological, entomological, serological, phylogenetic and basic sciences approaches. Together, this research will, for the first time, provide data on the incidence, types, sources, and genomic traits of this important group of viruses in Central Africa.
Foreign component funded by this grant: Yes
Foreign investigators: Antoinette Tshefu, University of Kinshasa (Congo, Democratic Republic)
Supplied by foreign site: Patient Samples
Technology transfer to foreign site: No

R21 (PI: Sheahan) 07/01/20-06/30/22 0.90 cal months (7.5%)
NIH
5 U.S.C. § 552(b)(4)
Characterization of hepacivirus pathogenesis, viral adaptation and the mapping of host susceptibility alleles in the Collaborative Cross
The goals of this proposal are to: 1) phenotype the kinetics of virus replication/adaptation, pathogenesis and the host response in CC lines with delayed clearance and chronic infection and 2) to map the genetic determinants driving virus titer, viral evolution, clearance, weight loss, blood leukocyte modulation, and chronic infection
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

Not Assigned (PI: Baric) 07/01/20-06/30/25 0.36 cal months (3%)
EcoHealth Alliance
5 U.S.C. § 552(b)(4)
US-China Collab: Spillover, co-infection, and control of bat-origin livestock coronaviruses
To develop an economic model of farm profit maximization linked to the compartmental epidemiological model of co-infection disease.*Foreign component funded by this grant: No*

OVERLAP: If any of the pending awards are funded, Dr. Sheahan will reduce is effort accordingly to not exceed 12 calendar months.

Other Support

SIMS, AMY

ACTIVE

R21AI146872 (Sims/Sheahan) 06/05/19-05/31/21 2.4 cal months
UNC Chapel Hill/NIH 5 U.S.C. § 552(b)(4) **{THIS GRANT}**
How MERS-CoV regulates the innate immune response
The major goal of the project is to determine if primary human lung cells infected with Middle East respiratory syndrome coronavirus (MERS-CoV) use epigenetic mechanisms to regulate the expression of interferon stimulated genes.

Foreign component funded by grant: No

There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

LDRD (Sims) 03/07/20-09/30/21 4.4 cal months
Pacific Northwest National Laboratory 5 U.S.C. § 552(b)(4)
Defining coronavirus lipidomic response
The goal of this project is to characterize the lipid response to coronavirus infection.

Foreign component funded by grant: No

There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

PENDING

Not Applicable

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

On January 6, 2020 Dr. Sims began a new position at Pacific Northwest National Laboratory (PNNL) in Richland, Washington. Dr. Sims will continue to collaborate with Drs. Sheahan and Schaefer at the University of North Carolina at Chapel Hill (UNC) to meet the goals of this funded project. Funds for Year 1 have been appropriately distributed between the PNNL and UNC to allow work to continue at both sites. Prior to the start of Year 2, we anticipate petitioning NIH/NIAID/UNC to transition the award to PNNL allowing Dr. Sims to resume as Principle Investigator. Funds would then be distributed to UNC via subcontract to continue the collaboration and to ensure forward progress on the proposed work.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: University of North Carolina at Chapel Hill	608195277	NC-004	104 Airport Drive, Suite 2200, CB 1350 Chapel Hill NC 275991350
Pacific Northwest National Laboratory	032987476	WA-004	902 Battelle Boulevard P.O. Box 999, MSIN J4-02 Richland WA 993520999

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 4/23/2020 2:05:21 PM (UTC-07:00)
To: Parrish, Kalyn[klparrish@unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Moore, Victoria L[victoria_moore@unc.edu]; Hays, Barbara A[barb.hays@pnnl.gov]
Cc: Caldwell, Chandra[ccaldwel@email.unc.edu]
Subject: Re: Amy's R21 grant - statement to NIH

Hi Kalyn and Vicki,

Now that the progress report has been submitted, I would like to move towards getting the relinquish statement finalized and submitted.

Both Barb Hays and Norma Sandoval will be assisting me with this from PNNL's end. Both of which are cc'd on this email.

Please let us know what you need to move forward with this request.
I hope all of you are doing well in these crazy times.

Thank you in advance for your assistance! Best wishes, Amy

From: "Parrish, Kalyn" <klparrish@unc.edu>
Date: Wednesday, April 8, 2020 at 6:18 AM
To: "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>
Cc: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Amy's R21 grant - statement to NIH

Hi Norma,

Nice to meet you as well! I appreciate your timely response. I will relay this information to our grant manager to proceed with relinquish statement for Year 2 funding. I'll let you know if we have any further questions.

Thanks so much,
Kalyn

From: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Sent: Tuesday, April 7, 2020 6:15 PM
To: Parrish, Kalyn <klparrish@unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Amy's R21 grant - statement to NIH

Hi Kalyn,
Very pleased to meet you! Expenditures through 3/31/2020 were less th[5 U.S.C. § 552(b)(4)] however with the advance in hand it allows Amy to continue working on the grant without interruption.

As Amy indicated the current plan is to exhaust funds by end of May. In order to do that seamlessly, our contracts, Barb Hays, will be sending a second invoice for the remaining[5 U.S.C. § 552(b)(4)] funds.

Our monthly processing dates don't coincide with actual month end date, therefore you'll see an 'do not pay' invoice for effort through March 20, 2020 the remainder of the months effort will be reflected in April's monthly invoice.

Monthly Invoices:

March expenditures – 2/22/2020 – 3/20/2020 - 5 U.S.C. § 552(b)(4)
April expenditures – 3/21/2020 – 4/25/2020
May expenditures – 4/26/2020 – 5/20/2020
Remainder of May expenditures through 5/31/2020 will appear in the June monthly invoice

Let me know if you have any further questions if you prefer to discuss over phone, my contact information is below.

Thx.

Norma Sandoval
Principal Project Coordinator
Biological Sciences Division, **EBSD**

Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999, MSIN J4-18
Richland, WA 99352 USA
Tel: 509-371-6553
norma.sandoval@pnnl.gov
www.pnnl.gov

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Tuesday, April 7, 2020 12:34 PM
To: Sims, Amy C <amy.sims@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: RE: Amy's R21 grant - statement to NIH

Hi Amy,

I am well. Just trying to stay safe during this time of social distancing. I hope you and your family are safe as well. Thank you for the information.

Norma – hello – I'm hoping you can provide me with an estimated amount that will be invoiced through 3/31/2020 beyond the 5 U.S.C. § 552(b)(4) advance invoice that has already been paid. If expenditures through 3/31 is less than the 5 U.S.C. § 552(b)(4) please simply confirm.

Thanks so much,
Kalyn

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, April 7, 2020 3:05 PM
To: Parrish, Kalyn <klparrish@unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Kalyn,

I hope you are doing well. It's good to hear from you! Yes, PNNL will send another invoice and it is our plan to use all funds by the end of May.

Norma Sandoval coordinates the financial side of projects here and is a great resource if you have any questions. She is cc'd above and will have more "real time" information than I will on the status of invoices from PNNL etc.

Please let me know if you need any additional information. Thank you, Amy

From: "Parrish, Kalyn" <klparrish@unc.edu>

Date: Tuesday, April 7, 2020 at 10:39 AM
To: "Schaefer, Alexandra" <aschaefe@email.unc.edu>
Cc: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: FW: Amy's R21 grant - statement to NIH

Hi Alex and Amy,

I hope you both are well. Can you provide an estimate amount you plan to spend on the prime 5113910 before 5/31?

Amy – I will also need to know if Battelle/PNNL plans to send another invoice to be paid on the subcontract. Is this something you can help with?

Thanks,
Kalyn

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 4/27/2020 4:38:33 PM (UTC-07:00)
To: Caldwell, Chandra[ccaldwel@email.unc.edu]
Subject: FW: 75881- 5116540 2nd advance payment request
Attachment: 75881_2nd advance payment invoice_0420011.pdf

Hi,

Second email from PNNL. Just wanted to make sure you saw this. Thank you! Amy

PS. You guys doing okay?

From: "Hays, Barbara A" <barb.hays@pnnl.gov>
Date: Monday, April 27, 2020 at 12:13 PM
To: "Moore, Victoria L" <victoria_moore@unc.edu>
Cc: "Burkhart, Carol J." <carol_burkhart@unc.edu>, "Parrish, Kalyn" <klparrish@unc.edu>, "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>, "Sims, Amy C" <amy.sims@pnnl.gov>, "Hays, Barbara A" <barb.hays@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Vicki. I'm following up to check if the 2nd advance payment has been issued. Thank you

Barb Hays

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Thursday, April 09, 2020 2:03 PM
To: Moore, Victoria L <victoria_moore@unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>; Hays, Barbara A <barb.hays@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Thank you Vicki. Yes, we plan to expend the entire 5 U.S.C. § 552(b)(4) 1st and 2nd advances) by the end of May. Thank you

Barb Hays

From: Moore, Victoria L <victoria_moore@unc.edu>
Sent: Thursday, April 09, 2020 12:32 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Hope you are doing well and staying safe! Just to make sure we are all on the same page, are you going to be able to expend all of the funds (1st and 2nd advances) by the May 31 end date? I don't want to advance you funds then have

you return them to us. If not, please project how much you will need through May 31 and we will advance you the balance between that and the first advance. We will also use that to calculate the amount we should put on the relinquishing statement.

Best,

Vicki

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Thursday, April 9, 2020 3:19 PM
To: Moore, Victoria L <victoria_moore@unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>
Subject: FW: 75881- 5116540 2nd advance payment request

Hi Vicki,

FYI – please let me know if this is sufficient information to process the 2nd invoice.

Thanks,
Kalyn

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Thursday, April 9, 2020 3:04 PM
To: Parrish, Kalyn <klparrish@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Hays, Barbara A <barb.hays@pnnl.gov>
Subject: 75881- 5116540 2nd advance payment request

Kalyn, costs through March 20, 2020 were 5 U.S.C. § 552(b)(4)
There is a pending commitment of 5 U.S.C. § 552(b)(4) supplies that were purchased for the project and we are projecting to be out of funds in hand 5 U.S.C. § 552(b)(4) by end of April. If you agree to pay the second advance, then we will send you a 'do not pay' invoice can be sent for March and April.
Thank you

Amy Sims (PI)						
			58.5%	64.5%	69.1%	
Processing Dates			20-Mar-20	24-Apr-20	22-May-20	31-May-20	Total
Labor Hours							
Labor							
Salary & Fringe							
Service/Equipment Centers							
Procurements							
Subcontracts							
Labor Overheads							
Value Added Overheads							
Cost Distributions							
Travel							
Actual Costs Per Processing							
Cumulative Actual Costs							

5 U.S.C. § 552(b)(4)

Barb Hays

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Wednesday, April 08, 2020 12:18 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Can you please provide a reconciliation of funds from the first advance payment thus far?

Thank you,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
klparrish@unc.edu

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Subject: 75881- 5116540 2nd advance payment request

Kalyn and Eve, please see attached invoice for the remaining advance payment. As you know, we have to make sure we have funding in-house to keep PNNL working. With such a short period of performance, I'm concerned that we will expend all the funding received before we get reimbursed for the first invoice. To avoid a work stoppage situation, I'm hopeful you will be able to advance pay the remaining 5 U.S.C. § 552(b)(4) then we will be able to keep working by drawing down on the advance. Please respond and let us know if this is possible. Thank you

---

Barb Hays

Pacific Northwest NATIONAL LABORATORY

Battelle *The Business of Innovation*

ADVANCE PAYMENT INVOICE

P.O. Box 84391
Seattle, WA 98124-5691
Tel (509) 375-2121
Fax (509) 371-7600

Federal Tax ID: 31-4379427

Date	4/8/2020
Invoice No.	0420011
Customer Order No.	
PNNL Contract No.	75881
Partial Advance	
Total Amount Due	$ 5 U.S.C. § 552(b)(4)

University of North Carolina, Chapel Hill
Attn: Accounts Payable
Box 2200
Chapel Hill, NC 27599-2200

Description	Amount (U.S. Funds)
Advance Payment Invoice Remaining Advance payment for Agreement No. 75881	5 U.S.C. § 552(b)(4)
Billing in Accordance with Terms of the agreement	

Send check payable in U.S. funds to:
Battelle
Attn: CASHIER
PO BOX 84391
Seattle, WA 98124-5691

Wire Information:
US B
ABA
Accou
SWIF
5 U.S.C. § 552(b)(4)

Approved by: Kim Kaiser for Barb Hays

PLEASE RETURN COPY OF INVOICE OR REFER TO INVOICE NUMBER WITH REMITTANCE.

From: Hays, Barbara A[barb.hays@pnnl.gov]
Sent: Tue 4/28/2020 10:27:40 AM (UTC-07:00)
To: Moore, Victoria L[victoria_moore@unc.edu]; Van Buren, Eve[evevb@email.unc.edu]
Cc: Burkhart, Carol J.[carol_burkhart@unc.edu]; Parrish, Kalyn[klparrish@unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; ^PNNL Accounts Receivable[ar@pnnl.gov]; Vopalensky, Tiffany A[tiffany.vopalensky@pnnl.gov]; Hays, Barbara A[barb.hays@pnnl.gov]
Subject: 75881- 5116540 stop work notice
Attachment: 75881_2nd advance payment invoice_0420011.pdf

Vicki and Eve, this message is to notify you that PNNL will stop work on 75881 this week. As you know, we are allowed to accrue costs up to the amount of funds we have in-house. We only have § U.S.C. § 552(b)(4) remaining from the original advance payment and we are waiting for the remaining § U.S.C. § 552(b)(4) payment (attached invoice). Can you please respond to this email to confirm you received it and let us know when the payment was sent so I can track it on my end. Thank you

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Thank you Vicki. Yes, we plan to expend the entire § U.S.C. § 552(b)(4) 1st and 2nd advances) by the end of May. Thank you

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Best,

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Thanks,
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Thank you

Amy Sims (PI)					
Processing Dates	20-Mar-20	24-Apr-20	22-May-20	31-May-20	Total
Labor Hours	5 U.S.C. § 552(b)(4)	5 U.S.C. § 552(b)(4)			5 U.S.C. § 552(b)(4)
Labor					
Salary & Fringe					
Service/Equipment Centers					
Procurements					
Subcontracts					
Labor Overheads					
Value Added Overheads					
Cost Distributions					
Travel					
Actual Costs Per Processing					
Cumulative Actual Costs					

Barb Hays

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Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Can you please provide a reconciliation of funds from the first advance payment thus far?

Thank you,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
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Kalyn and Eve, please see attached invoice for the remaining advance payment. As you know, we have to make sure we have funding in-house to keep PNNL working. With such a short period of performance, I'm concerned that we will expend all the funding received before we get reimbursed for the first invoice. To avoid a work stoppage situation, I'm hopeful you will be able to advance pay the remaining [redacted] then we will be able to keep working by drawing down on the advance. Please respond and let us know if this is possible. Thank you

---

Barb Hays

Pacific Northwest NATIONAL LABORATORY

Battelle *The Business of Innovation*

ADVANCE PAYMENT INVOICE

P.O. Box 84391
Seattle, WA 98124-5691
Tel (509) 375-2121
Fax (509) 371-7600

Federal Tax ID: 31-4379427

Date	4/8/2020
Invoice No.	0420011
Customer Order No.	
PNNL Contract No.	75881
Partial Advance	5 U.S.C. § 552(b)(4)
Total Amount Due	

University of North Carolina, Chapel Hill
Attn: Accounts Payable
Box 2200
Chapel Hill, NC 27599-2200

Description	Amount (U.S. Funds)
Advance Payment Invoice Remaining Advance payment for Agreement No. 75881	5 U.S.C. § 552(b)(4)
Billing in Accordance with Terms of the agreement	

Send check payable in U.S. funds to:
Battelle
Attn: CASHIER
PO BOX 84391
Seattle, WA 98124-5691

Wire Information:
US Bank,
ABA No. 1
Account N
SWIFT Cc
5 U.S.C. § 552(b)(4)

Approved by: Kim Kaiser for Barb Hays

PLEASE RETURN COPY OF INVOICE OR REFER TO INVOICE NUMBER WITH REMITTANCE.

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 4/28/2020 11:33:45 AM (UTC-07:00)
To: Caldwell, Chandra[ccaldwel@email.unc.edu]
Subject: FW: 75881- 5116540 stop work notice
Attachment: 75881_2nd advance payment invoice_0420011.pdf

Just letting you know in case you see Vicki today. PNNL is very serious about having access to funds and whether or not we can do the work.

Thank you very much! Amy

From: "Hays, Barbara A" <barb.hays@pnnl.gov>
Date: Tuesday, April 28, 2020 at 10:27 AM
To: "Moore, Victoria L" <victoria_moore@unc.edu>, "Van Buren, Eve" <evevb@email.unc.edu>
Cc: "Burkhart, Carol J." <carol_burkhart@unc.edu>, "Parrish, Kalyn" <klparrish@unc.edu>, "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>, "Sims, Amy C" <amy.sims@pnnl.gov>, ^PNNL Accounts Receivable <ar@pnnl.gov>, "Vopalensky, Tiffany A" <tiffany.vopalensky@pnnl.gov>, "Hays, Barbara A" <barb.hays@pnnl.gov>
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Subject: RE: 75881- 5116540 2nd advance payment request

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P.O. Box 84391
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Tel (509) 375-2121
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Federal Tax ID: 31-4379427

Date	4/8/2020
Invoice No.	0420011
Customer Order No.	
PNNL Contract No.	75881
Partial Advance	
Total Amount Due	$ 5 U.S.C. § 552(b)(4)

University of North Carolina, Chapel Hill
Attn: Accounts Payable
Box 2200
Chapel Hill, NC 27599-2200

Description	Amount (U.S. Funds)
Advance Payment Invoice Remaining Advance payment for Agreement No. 75881	5 U.S.C. § 552(b)(4)
Billing in Accordance with Terms of the agreement	

Send check payable in U.S. funds to:
Battelle
Attn: CASHIER
PO BOX 84391
Seattle, WA 98124-5691

Wire Information:
US Bank,
ABA No. 1
Account N
SWIFT Cd
5 U.S.C. § 552(b)(4)

Approved by: Kim Kaiser for Barb Hays

PLEASE RETURN COPY OF INVOICE OR REFER TO INVOICE NUMBER WITH REMITTANCE.

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Tue 4/28/2020 11:55:22 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: 75881- 5116540 stop work notice

You know at this point…I wouldn't be surprised if you mentioned it to Til if you don't hear something by Friday morning since I really don't understand the delay. It is indeed mind boggling to me…thanks for the heads up (especially with you having all 3 on the email)! Kalyn did reach out to me this morning to see what she can do to get the ball rolling so she was going to have a conference call with Carol today.

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, April 28, 2020 2:34 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: FW: 75881- 5116540 stop work notice

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Sent: Thursday, April 09, 2020 2:03 PM
To: Moore, Victoria L <victoria_moore@unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>; Hays, Barbara A <barb.hays@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Thank you Vicki. Yes, we plan to expend the entire [redacted] (1st and 2nd advances) by the end of May. Thank you

---

Barb Hays

From: Moore, Victoria L <victoria_moore@unc.edu>
Sent: Thursday, April 09, 2020 12:32 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Hope you are doing well and staying safe! Just to make sure we are all on the same page, are you going to be able to expend all of the funds (1st and 2nd advances) by the May 31 end date? I don't want to advance you funds then have you return them to us. If not, please project how much you will need through May 31 and we will advance you the balance between that and the first advance. We will also use that to calculate the amount we should put on the relinquishing statement.

Best,

Vicki

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Thursday, April 9, 2020 3:19 PM
To: Moore, Victoria L <victoria_moore@unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>
Subject: FW: 75881- 5116540 2nd advance payment request

Hi Vicki,

FYI – please let me know if this is sufficient information to process the 2nd invoice.

Thanks,
Kalyn

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Thursday, April 9, 2020 3:04 PM
To: Parrish, Kalyn <klparrish@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Hays, Barbara A <barb.hays@pnnl.gov>
Subject: 75881- 5116540 2nd advance payment request

Kalyn, costs through March 20, 2020 were 5 U.S.C. § 552(b)(4)
There is a pending commitment of 5 U.S.C. § 552(b)(4) in supplies that were purchased for the project and we are projecting to be out of funds in hand 5 U.S.C. § 552(b)(4) by end of April. If you agree to pay the second advance, then we will send you a 'do not pay' invoice can be sent for March and April.
Thank you

Amy Sims (PI)					
Processing Dates	20-Mar-20	24-Apr-20	22-May-20	31-May-20	Total
Labor Hours					
Labor					
Salary & Fringe					
Service/Equipment Centers					
Procurements					
Subcontracts					
Labor Overheads					
Value Added Overheads					
Cost Distributions					
Travel					
Actual Costs Per Processing					
Cumulative Actual Costs					

5 U.S.C. § 552(b)(4)

5 U.S.C. § 552(b)(4)

Barb Hays

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Wednesday, April 08, 2020 12:18 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Can you please provide a reconciliation of funds from the first advance payment thus far?

Thank you,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
klparrish@unc.edu

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Wednesday, April 8, 2020 2:31 PM
To: Parrish, Kalyn <klparrish@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; Hays, Barbara A <barb.hays@pnnl.gov>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: 75881- 5116540 2nd advance payment request

Kalyn and Eve, please see attached invoice for the remaining advance payment. As you know, we have to make sure we have funding in-house to keep PNNL working. With such a short period of performance, I'm concerned that we will

expend all the funding received before we get reimbursed for the first invoice. To avoid a work stoppage situation, I'm hopeful you will be able to advance pay the remaining 5 U.S.C. § 552(b)(4) then we will be able to keep working by drawing down on the advance. Please respond and let us know if this is possible. Thank you

---

Barb Hays

Approved for use through 03/31/2020
OMB No. 0925-0002

Department of Health and Human Services, Public Health Service

Official Statement Relinquishing Interests and Rights in a Public Health Service Research Grant

(Return original to awarding unit)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed and completing and reviewing collection of information. **An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.** Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-0002). Do not return the completed form to this address.

04/30/2020 (date)

Name of Institution: The University of North Carolina at Chapel Hill

Address *(city and state)*: Office of Sponsored Research
CB# 1350, 104 Airport Drive
Chapel Hill, NC 27599-1350

Principal Investigator: Timothy Sheahan, PhD

on Public Health Service grant number 1 R21 AI146872

has expressed a desire to continue his/her research project at the

Battelle Memorial Institute, Pacific Northwest National Laboratory (Dr. Amy Sims)

In view of the fact that we do not wish to nominate another principal investigator or continue the research project at this Institution, this is to signify our willingness to terminate this grant as of 5/31/2020 (date) and to relinquish all claims to any unexpended and uncommitted funds remaining in the grant as of that date, as well as to all recommended future support of this project.

Equipment Costing $5,000 or More Transferring with the Project *(itemize)*	Unexpended Balance — Estimated
1. N/A	The unexpended balance on termination date of 5/31/2020 calculated on basis of total amount awarded for the grant year, will be approximately
2.	$ 5 U.S.C. § 552(b)(4) direct cost
3.	$ 5 U.S.C. § 552(b)(4) indirect cost.
4.	
5.	
6.	
Use separate page for additional items.	

That portion of the estimated unexpended balance which has been received will be returned to the Public Health Service, upon request, with a final adjustment, if required, to be made after the grant account has been audited.

Official Authorized to Sign Application

Signature

Name and Title *(print or type)*

Privacy Act Statement. Privacy Act Statement. The NIH maintains application and grant records as part of a system of records as defined by the Privacy Act: NIH 09-25-0225 https://era.nih.gov/privacy-act-and-era.htm.

From: Schaefer, Alexandra [aschaefe@email.unc.edu]
Sent: 5/5/2020 7:27:14 AM
To: Sims, Amy C [amy.sims@pnnl.gov]
Subject: Re: Amy's R21 grant - statement to NIH

Hi Amy,

I hope this email finds you well!

Sorry, for disappearing for a while, but things have been crazy busy.

However,
the plan is to get the ChIPs done for the FB samples-
for this I need to order
7x (better 8x) EpiTect ChIP OneDay Kit, Qiagen # 334471
2x anti-H3K4me3 antibodies, Cell Signaling #9751S
2x anti-H3K27me3 antibodies, Cell Signaling #9733S

I would like to put that today onto the order sheet-
could you please let me know the grant# for this?

Thanks,
Alex

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Tuesday, April 7, 2020 1:38 PM
To: Schaefer, Alexandra <aschaefe@email.unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>
Subject: FW: Amy's R21 grant - statement to NIH

Hi Alex and Amy,

I hope you both are well. Can you provide an estimate amount you plan to spend on the prime 5113910 before 5/31?

Amy – I will also need to know if Battelle/PNNL plans to send another invoice to be paid on the subcontract. Is this something you can help with?

Thanks,
Kalyn

From: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Sent: Tuesday, April 7, 2020 1:04 PM
To: Parrish, Kalyn <klparrish@unc.edu>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Kalyn,

I'd ask Amy and Alex. I know they were planning on doing some spending in the near future but I have not kept up with their plans. Do you want to ask or have me ask?

T

From: "Parrish, Kalyn" <klparrish@unc.edu>
Date: Tuesday, April 7, 2020 at 12:09 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: Amy's R21 grant - statement to NIH

Hi Tim,

I hope you are doing well. Attached is report for Amy's R21, 5113910. Right now there is a remaining balance 5 U.S.C. § 552(b)(4) Do you plan on spending this out? If not, can you give me an estimate on how much you do plan to spend before 5/31?

I ask because we have to issue a statement to NIH in order to move this grant to Amy at PNNL for Year 2. It's my understanding that any remaining funds will be rolled over to PNNL and UNC will then become a subcontract in year 2 once Amy decides on how much she wants to allocate to UNC for that budget period.

Thanks,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
919-843-6601
klparrish@unc.edu

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 5/5/2020 8:17:40 AM (UTC-07:00)
To: Schaefer, Alexandra[aschaefe@email.unc.edu]
Subject: Re: Amy's R21 grant - statement to NIH

Alex,

I am glad to hear from you. I was going to follow up with you today.

I am very happy to hear that this experiment is on your to do list.

I have emailed Kalyn to find out how much money UNC has but as I don't work there anymore I no longer have access to which grants have funds and where purchases can be made. It would also be much easier for me to provide you a reliable answer if you provided me with total dollar amounts to spend rather than catalog numbers. If you can get me that I can give you a better answer when I hear from Kalyn.

When you have a few minutes please think about Year 2 of our grant and the experiments that still need to be done. I will try to find a time that we can discuss this further next week.

Thank you, Amy

From: "Schaefer, Alexandra" <aschaefe@email.unc.edu>
Date: Tuesday, May 5, 2020 at 7:27 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Amy,

I hope this email finds you well!

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the plan is to get the ChIPs done for the FB samples-
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7x (better 8x) EpiTect ChIP OneDay Kit, Qiagen # 334471
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I would like to put that today onto the order sheet-
could you please let me know the grant# for this?

Thanks,
Alex

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Tuesday, April 7, 2020 1:38 PM
To: Schaefer, Alexandra <aschaefe@email.unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>
Subject: FW: Amy's R21 grant - statement to NIH

Hi Alex and Amy,

I hope you both are well. Can you provide an estimate amount you plan to spend on the prime 5113910 before 5/31?

Amy – I will also need to know if Battelle/PNNL plans to send another invoice to be paid on the subcontract. Is this something you can help with?

Thanks,
Kalyn

From: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Sent: Tuesday, April 7, 2020 1:04 PM
To: Parrish, Kalyn <klparrish@unc.edu>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Kalyn,

I'd ask Amy and Alex. I know they were planning on doing some spending in the near future but I have not kept up with their plans. Do you want to ask or have me ask?

T

From: "Parrish, Kalyn" <klparrish@unc.edu>
Date: Tuesday, April 7, 2020 at 12:09 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: Amy's R21 grant - statement to NIH

Hi Tim,

I hope you are doing well. Attached is report for Amy's R21, 5113910. Right now there is a remaining balance of (b) (4). Do you plan on spending this out? If not, can you give me an estimate on how much you do plan to spend before 5/31?

I ask because we have to issue a statement to NIH in order to move this grant to Amy at PNNL for Year 2. It's my understanding that any remaining funds will be rolled over to PNNL and UNC will then become a subcontract in year 2 once Amy decides on how much she wants to allocate to UNC for that budget period.

Thanks,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
919-843-6601
klparrish@unc.edu

From: Schaefer, Alexandra [aschaefe@email.unc.edu]
Sent: 5/7/2020 6:51:39 AM
To: Sims, Amy C [amy.sims@pnnl.gov]
Subject: Re: Amy's R21 grant - statement to NIH

Hi Amy,

okay
7x (better 8x) EpiTect ChIP OneDay Kit, Qiagen # 334471 - 5 U.S.C. § 552(b)(4)
2x anti-H3K4me3 antibodies, Cell Signaling #9751S - 5 U.S.C. § 552(b)(4)
2x anti-H3K27me3 antibodies, Cell Signaling #9733S

I hope that helps,
Alex

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, May 5, 2020 11:17 AM
To: Schaefer, Alexandra <aschaefe@email.unc.edu>
Subject: Re: Amy's R21 grant - statement to NIH

Alex,

I am glad to hear from you. I was going to follow up with you today.

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When you have a few minutes please think about Year 2 of our grant and the experiments that still need to be done. I will try to find a time that we can discuss this further next week.

Thank you, Amy

From: "Schaefer, Alexandra" <aschaefe@email.unc.edu>
Date: Tuesday, May 5, 2020 at 7:27 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Amy,

I hope this email finds you well!

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However,

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could you please let me know the grant# for this?

Thanks,
Alex

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Tuesday, April 7, 2020 1:38 PM
To: Schaefer, Alexandra <aschaefe@email.unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>
Subject: FW: Amy's R21 grant - statement to NIH

Hi Alex and Amy,

I hope you both are well. Can you provide an estimate amount you plan to spend on the prime 5113910 before 5/31?

Amy – I will also need to know if Battelle/PNNL plans to send another invoice to be paid on the subcontract. Is this something you can help with?

Thanks,
Kalyn

From: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Sent: Tuesday, April 7, 2020 1:04 PM
To: Parrish, Kalyn <klparrish@unc.edu>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Kalyn,

I'd ask Amy and Alex. I know they were planning on doing some spending in the near future but I have not kept up with their plans. Do you want to ask or have me ask?

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From: "Parrish, Kalyn" <klparrish@unc.edu>
Date: Tuesday, April 7, 2020 at 12:09 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: Amy's R21 grant - statement to NIH

Hi Tim,

I hope you are doing well. Attached is report for Amy's R21, 5113910. Right now there is a remaining balance o[5 U.S.C. § 552(b)(4)]
Do you plan on spending this out? If not, can you give me an estimate on how much you do plan to spend before 5/31?

I ask because we have to issue a statement to NIH in order to move this grant to Amy at PNNL for Year 2. It's my understanding that any remaining funds will be rolled over to PNNL and UNC will then become a subcontract in year 2 once Amy decides on how much she wants to allocate to UNC for that budget period.

Thanks,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
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2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
919-843-6601
klparrish@unc.edu

From: Schaefer, Alexandra [aschaefe@email.unc.edu]
Sent: 5/7/2020 6:56:19 AM
To: Sims, Amy C [amy.sims@pnnl.gov]
Subject: Re: Amy's R21 grant - statement to NIH

HI Amy,

yes, I phone call would be good to discuss goals and
also how the this grant will be organized since you are taking it to PNNL

Let me know a few time slots that work for you and we can find something,
Alex

From: Schaefer, Alexandra <aschaefe@email.unc.edu>
Sent: Thursday, May 7, 2020 9:51 AM
To: Sims, Amy C <amy.sims@pnnl.gov>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Amy,

okay
7x (better 8x) EpiTect ChIP OneDay Kit, Qiagen # 334471 - 5 U.S.C. § 552(b)(4)
2x anti-H3K4me3 antibodies, Cell Signaling #9751S 5 U.S.C. § 552(b)(4)
2x anti-H3K27me3 antibodies, Cell Signaling #9733S

I hope that helps,
Alex

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, May 5, 2020 11:17 AM
To: Schaefer, Alexandra <aschaefe@email.unc.edu>
Subject: Re: Amy's R21 grant - statement to NIH

Alex,

I am glad to hear from you. I was going to follow up with you today.

I am very happy to hear that this experiment is on your to do list.

I have emailed Kalyn to find out how much money UNC has but as I don't work there anymore I no longer have access to which grants have funds and where purchases can be made. It would also be much easier for me to provide you a reliable answer if you provided me with total dollar amounts to spend rather than catalog numbers. If you can get me that I can give you a better answer when I hear from Kalyn.

When you have a few minutes please think about Year 2 of our grant and the experiments that still need to be done. I will try to find a time that we can discuss this further next week.

Thank you, Amy

From: "Schaefer, Alexandra" <aschaefe@email.unc.edu>
Date: Tuesday, May 5, 2020 at 7:27 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Amy,

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the plan is to get the ChIPs done for the FB samples-
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I would like to put that today onto the order sheet-
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To: Schaefer, Alexandra <aschaefe@email.unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>
Subject: FW: Amy's R21 grant - statement to NIH

Hi Alex and Amy,

I hope you both are well. Can you provide an estimate amount you plan to spend on the prime 5113910 before 5/31?

Amy – I will also need to know if Battelle/PNNL plans to send another invoice to be paid on the subcontract. Is this something you can help with?

Thanks,
Kalyn

From: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Sent: Tuesday, April 7, 2020 1:04 PM
To: Parrish, Kalyn <klparrish@unc.edu>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Kalyn,

I'd ask Amy and Alex. I know they were planning on doing some spending in the near future but I have not kept up with their plans. Do you want to ask or have me ask?

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From: "Parrish, Kalyn" <klparrish@unc.edu>
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To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
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Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
919-843-6601
klparrish@unc.edu

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 5/7/2020 8:21:25 AM (UTC-07:00)
To: Schaefer, Alexandra[aschaefe@email.unc.edu]
Subject: Re: Amy's R21 grant - statement to NIH

Alex,

This is just under 5 U.S.C. § 552(b)(4) th 8 of the first kit and 2 of items 2 and 3. Kalyn emailed that there is around 5 U.S.C. § 552(b)(4) to spend on the R21 at UNC so you should be more than fine to place this order.

Project ID is 5113910

Thank you, Amy

From: "Schaefer, Alexandra" <aschaefe@email.unc.edu>
Date: Thursday, May 7, 2020 at 6:52 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Amy's R21 grant - statement to NIH

Hi Amy,

okay
7x (better 8x) EpiTect ChIP OneDay Kit, Qiagen # 334
2x anti-H3K4me3 antibodies, Cell Signaling #9751S - 5 U.S.C. § 552(b)(4)
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Thanks,
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Thanks,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
919-843-6601
klparrish@unc.edu

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 5/7/2020 8:28:32 AM (UTC-07:00)
To: Schaefer, Alexandra[aschaefe@email.unc.edu]
Subject: Re: Amy's R21 grant - statement to NIH

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Date: Thursday, May 7, 2020 at 6:57 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Amy's R21 grant - statement to NIH

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Sent: Thursday, May 7, 2020 9:51 AM
To: Sims, Amy C <amy.sims@pnnl.gov>
Subject: Re: Amy's R21 grant - statement to NIH

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From: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Sent: Tuesday, April 7, 2020 1:04 PM
To: Parrish, Kalyn <klparrish@unc.edu>
Subject: Re: Amy's R21 grant - statement to NIH

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Sent: 5/11/2020 8:17:59 AM
To: Sims, Amy C [amy.sims@pnnl.gov]
Subject: Re: Amy's R21 grant - statement to NIH

Hi Amy,

sorry, I missed have missed that email!

I am already pretty busy today-
How will Wednesday work for you?

I can do later in the afternoon, if that works for you.

Thanks,
Alex

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Sent: Monday, May 11, 2020 11:11 AM
To: Schaefer, Alexandra <aschaefe@email.unc.edu>
Subject: FW: Amy's R21 grant - statement to NIH

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Notice of Award

EXPLORATORY/DEVELOPMENT GRANT
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 05/11/2020

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 5R21AI146872-02
FAIN: R21AI146872

Principal Investigator(s):
AMY C SIMS, PHD
Timothy Patrick Sheahan (contact), PHD

Project Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells

Terry Magnuson
Research Administration Manager
104 Airport Drive, Suite 2200
CB: 1350
Chapel Hill, NC 275991350

Award e-mailed to: resadminosr@unc.edu

Period Of Performance:
Budget Period: 06/01/2020 – 05/31/2021
Project Period: 06/05/2019 – 05/31/2021

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of **5 U.S.C. § 552(b)(4)** Calculation" in Section I and "Terms and Conditions" in Section III) to UNIV OF NORTH CAROLINA CHAPEL HILL in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R21AI146872. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Michael W. Fato
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

NIH NGA R | Version: 56 - 12/26/2018 2:22:00 PM| Generated on: 5/11/2020 12:01:46 AM

SECTION I – AWARD DATA – 5R21AI146872-02

Award Calculation (U.S. Dollars)

Federal Direct Costs
Federal F&A Costs
Approved Budget
Total Amount of Federal Funds Obligated (Federal Share)
TOTAL FEDERAL AWARD AMOUNT

AMOUNT OF THIS ACTION (FEDERAL SHARE)

5 U.S.C. § 552(b)(4)

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
2	5 U.S.C. § 552(b)(4)	5 U.S.C. § 552(b)(4)

Fiscal Information:

CFDA Name: Allergy and Infectious Diseases Research
CFDA Number: 93.855
EIN: 1566001393A1
Document Number: RAI146872A
PMS Account Type: P (Subaccount)
Fiscal Year: 2020

IC	CAN	2020
AI	8472364	5 U.S.C. § 552(b)(4)

NIH Administrative Data:
PCC: M51C B / **OC**: 41025 / **Released**: FATOM 05/08/2020
Award Processed: 05/11/2020 12:01:46 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R21AI146872-02

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 5R21AI146872-02

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2. As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal

Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VI Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R21AI146872. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

This award represents the final year of the competitive segment for this grant. See the NIH Grants Policy Statement Section 8.6 Closeout for complete closeout requirements at: http://grants.nih.gov/grants/policy/policy.htm#gps.

A final expenditure Federal Financial Report (FFR) (SF 425) must be submitted through the eRA Commons (Commons) within 120 days of the period of performance end date; see the NIH Grants Policy Statement Section 8.6.1 Financial Reports, http://grants.nih.gov/grants/policy/policy.htm#gps, for additional information on this submission requirement. The final FFR must indicate the exact balance of unobligated funds and may not reflect any unliquidated obligations. There must be no discrepancies between the final FFR expenditure data and the Payment Management System's (PMS) quarterly cash transaction data. A final quarterly federal cash transaction report is not required for awards in PMS B subaccounts (i.e., awards to foreign entities and to Federal agencies). NIH will close the awards using the last recorded cash drawdown level in PMS for awards that do not require a final FFR on expenditures or quarterly federal cash transaction reporting. It is important to note that for financial closeout, if a grantee fails to submit a required final expenditure FFR, NIH will close the grant using the last recorded cash drawdown level. If the grantee submits a final expenditure FFR but does not reconcile any discrepancies between expenditures reported on the final expenditure FFR and the last cash report to PMS, NIH will close the award at the lower amount. This could be considered a debt or result in disallowed costs.

A Final Invention Statement and Certification form (HHS 568), (not applicable to training, construction, conference or cancer education grants) must be submitted within 120 days of the

expiration date. The HHS 568 form may be downloaded at: http://grants.nih.gov/grants/forms.htm. This paragraph does not apply to Training grants, Fellowships, and certain other programs—i.e., activity codes C06, D42, D43, D71, DP7, G07, G08, G11, K12, K16, K30, P09, P40, P41, P51, R13, R25, R28, R30, R90, RL5, RL9, S10, S14, S15, U13, U14, U41, U42, U45, UC6, UC7, UR2, X01, X02.

Unless an application for competitive renewal is submitted, a Final Research Performance Progress Report (Final RPPR) must also be submitted within 120 days of the period of performance end date. If a competitive renewal application is submitted prior to that date, then an Interim RPPR must be submitted by that date as well. Instructions for preparing an Interim or Final RPPR are at: https://grants.nih.gov/grants/rppr/rppr_instruction_guide.pdf. Any other specific requirements set forth in the terms and conditions of the award must also be addressed in the Interim or Final RPPR. *Note that data reported within Section I of the Interim and Final RPPR forms will be made public and should be written for a lay person audience.*

NIH strongly encourages electronic submission of the final invention statement through the Closeout feature in the Commons, but will accept an email or hard copy submission as indicated below.

Email: The final invention statement may be e-mailed as PDF attachments to: NIHCloseoutCenter@mail.nih.gov.

Hard copy: Paper submissions of the final invention statement may be faxed to the NIH Division of Central Grants Processing, Grants Closeout Center, at 301-480-2304, or mailed to:

National Institutes of Health
Office of Extramural Research
Division of Central Grants Processing
Grants Closeout Center
6705 Rockledge Drive
Suite 5016, MSC 7986
Bethesda, MD 20892-7986 (for regular or U.S. Postal Service Express mail)
Bethesda, MD 20817 (for other courier/express deliveries only)

NOTE: If this is the final year of a competitive segment due to the transfer of the grant to another institution, then a Final RPPR is not required. However, a final expenditure FFR is required and should be submitted electronically as noted above. If not already submitted, the Final Invention Statement is required and should be sent directly to the assigned Grants Management Specialist.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 5R21AI146872-02

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

Select Agents:

NIH NGA R | Version: 56 - 12/26/2018 2:22:00 PM| Generated on: 5/11/2020 12:01:46 AM

Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

- o A list of the new and/or additional Agent(s) that will be studied;
- o A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
- o The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Ashley Colette Ranellone
Email: ranelloneac@niaid.nih.gov **Phone**: 301-594-8541

Program Official: Erik J. Stemmy
Email: erik.stemmy@nih.gov **Phone**: 240-627-3380

SPREADSHEET SUMMARY
GRANT NUMBER: 5R21AI146872-02

INSTITUTION: UNIV OF NORTH CAROLINA CHAPEL HILL

Budget	Year 2
TOTAL FEDERAL DC	5 U.S.C. § 552(b)(4)
TOTAL FEDERAL F&A	
TOTAL COST	

Facilities and Administrative Costs	Year 2
F&A Cost Rate 1	5 U.S.C. § 552(b)(4)
F&A Cost Base 1	
F&A Costs 1	

NIH NGA R | Version: 56 - 12/26/2018 2:22:00 PM| Generated on: 5/11/2020 12:01:46 AM

From: Hays, Barbara A[barb.hays@pnnl.gov]
Sent: Fri 5/15/2020 7:35:25 AM (UTC-07:00)
To: Moore, Victoria L[victoria_moore@unc.edu]; Van Buren, Eve[evevb@email.unc.edu]
Cc: Burkhart, Carol J.[carol_burkhart@unc.edu]; Parrish, Kalyn[klparrish@unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Hays, Barbara A[barb.hays@pnnl.gov]
Subject: RE: 75881- 5116540 2nd advance payment request

Vicki or Eve, I'm hopeful one of you can provide an update on the 2nd advance payment. I'm told we may have to stop work if not received and as you know this project has to be complete by end of May so a stop-work would be detrimental. Can you please provide update on when the payment can be expected today? Thank you so much.

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Hi Barb,

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Best,

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Subject: RE: 75881- 5116540 2nd advance payment request

Thank you Vicki. Yes, we plan to expend the entire 5 U.S.C. § 552(b)(4) 1st and 2nd advances) by the end of May. Thank you

---

Barb Hays

From: Moore, Victoria L <victoria_moore@unc.edu>
Sent: Thursday, April 09, 2020 12:32 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

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Best,

Vicki

From: Parrish, Kalyn <klparrish@unc.edu>

Sent: Thursday, April 9, 2020 3:19 PM
To: Moore, Victoria L <victoria_moore@unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>
Subject: FW: 75881- 5116540 2nd advance payment request

Hi Vicki,

FYI – please let me know if this is sufficient information to process the 2nd invoice.

Thanks,
Kalyn

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Thursday, April 9, 2020 3:04 PM
To: Parrish, Kalyn <klparrish@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Hays, Barbara A <barb.hays@pnnl.gov>
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Thank you

Amy Sims (PI)					
Processing Dates	20-Mar-20	24-Apr-20	22-May-20	31-May-20	Total
Labor Hours					
Labor					
Salary & Fringe					
Service/Equipment Centers					
Procurements					
Subcontracts					
Labor Overheads					
Value Added Overheads					
Cost Distributions					
Travel					
Actual Costs Per Processing					
Cumulative Actual Costs	6,279	38,186	62,757	69,990	

5 U.S.C. § 552(b)(4)

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Barb Hays

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Wednesday, April 08, 2020 12:18 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Can you please provide a reconciliation of funds from the first advance payment thus far?

Thank you,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
klparrish@unc.edu

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Subject: 75881- 5116540 2nd advance payment request

Kalyn and Eve, please see attached invoice for the remaining advance payment. As you know, we have to make sure we have funding in-house to keep PNNL working. With such a short period of performance, I'm concerned that we will expend all the funding received before we get reimbursed for the first invoice. To avoid a work stoppage situation, I'm hopeful you will be able to advance pay the remaining $28K; then we will be able to keep working by drawing down on the advance. Please respond and let us know if this is possible. Thank you

---

Barb Hays

From: Parrish, Kalyn[klparrish@unc.edu]
Sent: Fri 5/15/2020 7:52:26 AM (UTC-07:00)
To: Hays, Barbara A[barb.hays@pnnl.gov]; Moore, Victoria L[victoria_moore@unc.edu]; Van Buren, Eve[evevb@email.unc.edu]
Cc: Burkhart, Carol J.[carol_burkhart@unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

The payment is scheduled to be electronically sent today. Your reference number is 0000487575. Please let us know that you have received this.

Thanks,
Kalyn

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Friday, May 15, 2020 10:35 AM
To: Moore, Victoria L <victoria_moore@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Hays, Barbara A <barb.hays@pnnl.gov>
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Thank you very much for the quick response Kayln. We'll let you know when received.

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To: Hays, Barbara A <barb.hays@pnnl.gov>; Moore, Victoria L <victoria_moore@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
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Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Unfortunately, as of yesterday morning, it had not been issued. We are rectifying that situation and have asked that the University expedite it.

Best,

Vicki

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Monday, April 27, 2020 3:14 PM
To: Moore, Victoria L <victoria_moore@unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Hays, Barbara A <barb.hays@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Vicki. I'm following up to check if the 2nd advance payment has been issued. Thank you

---

Barb Hays

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Thursday, April 09, 2020 2:03 PM
To: Moore, Victoria L <victoria_moore@unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>; Hays, Barbara A

<barb.hays@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Thank you Vicki. Yes, we plan to expend the entire [redacted] (1st and 2nd advances) by the end of May. Thank you

Barb Hays

From: Moore, Victoria L <victoria_moore@unc.edu>
Sent: Thursday, April 09, 2020 12:32 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Hope you are doing well and staying safe! Just to make sure we are all on the same page, are you going to be able to expend all of the funds (1st and 2nd advances) by the May 31 end date? I don't want to advance you funds then have you return them to us. If not, please project how much you will need through May 31 and we will advance you the balance between that and the first advance. We will also use that to calculate the amount we should put on the relinquishing statement.

Best,

Vicki

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Subject: FW: 75881- 5116540 2nd advance payment request

Hi Vicki,

FYI – please let me know if this is sufficient information to process the 2nd invoice.

Thanks,
Kalyn

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Thursday, April 9, 2020 3:04 PM
To: Parrish, Kalyn <klparrish@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
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Subject: 75881- 5116540 2nd advance payment request

Kalyn, costs through March 20, 2020 we[redacted]
There is a pending commitment o[redacted]K in supplies that were purchased for the project and we are projecting to be out of funds in ha[redacted]y end of April. If you agree to pay the second advance, then we will send you a 'do not pay' invoice can be sent for March and April.
Thank you

Amy Sims (PI)					
Processing Dates	20-Mar-20	24-Apr-20	22-May-20	31-May-20	Total
Labor Hours					
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Cost Distributions					
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Actual Costs Per Processing					
Cumulative Actual Costs					

5 U.S.C. § 552(b)(4)

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Barb Hays

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Wednesday, April 08, 2020 12:18 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Can you please provide a reconciliation of funds from the first advance payment thus far?

Thank you,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
klparrish@unc.edu

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Subject: 75881- 5116540 2nd advance payment request

Kalyn and Eve, please see attached invoice for the remaining advance payment. As you know, we have to make sure we have funding in-house to keep PNNL working. With such a short period of performance, I'm concerned that we will

expend all the funding received before we get reimbursed for the first invoice. To avoid a work stoppage situation, I'm hopeful you will be able to advance pay the remaining $28K; then we will be able to keep working by drawing down on the advance. Please respond and let us know if this is possible. Thank you

---

Barb Hays

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Fri 5/15/2020 8:46:16 AM (UTC-07:00)
To: Parrish, Kalyn[klparrish@unc.edu]; Hays, Barbara A[barb.hays@pnnl.gov]; Moore, Victoria L[victoria_moore@unc.edu]; Van Buren, Eve[evevb@email.unc.edu]
Cc: Burkhart, Carol J.[carol_burkhart@unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]
Subject: Re: 75881- 5116540 2nd advance payment request

Thank you Kalyn! We really appreciate it. Best wishes, Amy

From: "Parrish, Kalyn" <klparrish@unc.edu>
Date: Friday, May 15, 2020 at 7:52 AM
To: "Hays, Barbara A" <barb.hays@pnnl.gov>, "Moore, Victoria L" <victoria_moore@unc.edu>, "Van Buren, Eve" <evevb@email.unc.edu>
Cc: "Burkhart, Carol J." <carol_burkhart@unc.edu>, "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>, "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

The payment is scheduled to be electronically sent today. Your reference number is 0000487575. Please let us know that you have received this.

Thanks,
Kalyn

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Friday, May 15, 2020 10:35 AM
To: Moore, Victoria L <victoria_moore@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Hays, Barbara A <barb.hays@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Vicki or Eve, I'm hopeful one of you can provide an update on the 2nd advance payment. I'm told we may have to stop work if not received and as you know this project has to be complete by end of May so a stop-work would be detrimental. Can you please provide update on when the payment can be expected today? Thank you so much.

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Subject: RE: 75881- 5116540 2nd advance payment request

Vicki, to date, I have not received notice that we've received payment yet. Can you please check status and let me know if/when it was released? Thank you

---

Barb Hays

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Wednesday, April 29, 2020 2:40 PM
To: Moore, Victoria L <victoria_moore@unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Hays, Barbara A <barb.hays@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Vicki; my project team is asking me….when you say it will be expedited, when will the payment be sent and how? Electronic? Just wondering when we can expect to receive it. thank you

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Subject: RE: 75881- 5116540 2nd advance payment request

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Barb Hays

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Subject: RE: 75881- 5116540 2nd advance payment request

Thank you Vicki. Yes, we plan to expend the entire [5 U.S.C. § 552(b)(4)] (1st and 2nd advances) by the end of May. Thank you

Barb Hays

From: Moore, Victoria L <victoria_moore@unc.edu>
Sent: Thursday, April 09, 2020 12:32 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Parrish, Kalyn <klparrish@unc.edu>
Subject: RE: 75881- 5116540 2nd advance payment request

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Subject: 75881- 5116540 2nd advance payment request

Kalyn, costs through March 20, 2020 were $ 5 U.S.C. § 552(b)(4)
There is a pending commitment of 5 U.S.C. § 552(b)(4) supplies that were purchased for the project and we are projecting to be out of funds in hand 5 U.S.C. § 552(b)(4) by end of April. If you agree to pay the second advance, then we will send you a 'do not pay' invoice can be sent for March and April.
Thank you

Amy Sims (PI)						
Processing Dates		20-Mar-20	24-Apr-20	22-May-20	31-May-20	Total
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Cost Distributions						
Travel						
Actual Costs Per Processing						
Cumulative Actual Costs						

5 U.S.C. § 552(b)(4)

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Subject: RE: 75881- 5116540 2nd advance payment request

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Thank you,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
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Subject: 75881- 5116540 2nd advance payment request

Kalyn and Eve, please see attached invoice for the remaining advance payment. As you know, we have to make sure we have funding in-house to keep PNNL working. With such a short period of performance, I'm concerned that we will

expend all the funding received before we get reimbursed for the first invoice. To avoid a work stoppage situation, I'm hopeful you will be able to advance pay the remaining [redacted] then we will be able to keep working by drawing down on the advance. Please respond and let us know if this is possible. Thank you

---

Barb Hays

From: Schaefer, Alexandra [aschaefe@email.unc.edu]
Sent: 5/19/2020 6:25:08 AM
To: Sims, Amy C [amy.sims@pnnl.gov]
CC: Edwards, Caitlin E [caitedw@unc.edu]
Subject: Fw: Amy R21...

Flag: Follow Up

Hi Amy,

there are still issues with the Qiagen order.

Kalyn, is holding a particular amount of money amount back (below), which was supposed to be for the Qiagen kits
therefore, we cannot order the Magnetic bead ChIP-kits (Invitrogen) in addition-
However, since we can't get the Qiagen kits anyway, we will order the Invitrogen Kits instead (I need 4, and I think we will buy one on Baric money)
But, As understand it- then we will not be able to order the Qiagen kits from UNC?

I CC'ed Cait on this email, I am sure she has a much better understanding of all the financial/ordering stuff.

Alex

From: Edwards, Caitlin E <caitedw@unc.edu>
Sent: Tuesday, May 19, 2020 9:10 AM
To: Parrish, Kalyn <klparrish@unc.edu>
Cc: Schaefer, Alexandra <aschaefe@email.unc.edu>
Subject: Re: Amy R21...

Hey Kalyn!

Hmm okay – got it! In that case I may go ahead and place the other order for around this amount and place the Qiagen order on a different project ID once Qiagen gets it together. Their website is still not cooperating via ePro, but supposedly the rep is working on it. The other item is Fisher so I'll order today and that way it should arrive before the end of the month.

Thanks for your help! Sorry for any confusion!!
Cait

From: "Parrish, Kalyn" <klparrish@unc.edu>
Date: Tuesday, May 19, 2020 at 9:05 AM
To: "Edwards, Caitlin E" <caitedw@unc.edu>
Subject: RE: Amy R21...

Hi Cait,

We can only submit orders for the amount I set aside [5 U.S.C. § 552(b)(4)] r the Qiagen order. Because we already submitted paperwork to the NIH, we need to stick to this amount. If you can't get Qiagen order to work, we can place the other order for only [5 U.S.C. § 552(b)(4)]

Please remember that we need to receive these items by the end of the month so please place the order asap.

Thanks,
Kalyn

From: Edwards, Caitlin E <caitedw@unc.edu>
Sent: Monday, May 18, 2020 4:32 PM
To: Parrish, Kalyn <klparrish@unc.edu>
Subject: Amy R21...

Hey Kalyn!

I have to place another order on Amy's R21. Will be about [5 U.S.C. § 552(b)(4)] that still possible or create a mess? This would be in addition to the other item we set aside money for. Qiagen still won't let me place that order..

Thanks!
Cait

From: Hays, Barbara A[barb.hays@pnnl.gov]
Sent: Tue 5/19/2020 7:32:58 AM (UTC-07:00)
To: Parrish, Kalyn[klparrish@unc.edu]; Moore, Victoria L[victoria_moore@unc.edu]; Van Buren, Eve[evevb@email.unc.edu]
Cc: Burkhart, Carol J.[carol_burkhart@unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Hays, Barbara A[barb.hays@pnnl.gov]
Subject: RE: 75881- 5116540 2nd advance payment request

Kalyn, can you please let me know if the payment was issued? If yes, please provide details (when and how—electronic?) so I can track it down. Thank you

Barb Hays

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Friday, May 15, 2020 7:52 AM
To: Hays, Barbara A <barb.hays@pnnl.gov>; Moore, Victoria L <victoria_moore@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
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Sent: Friday, May 15, 2020 10:35 AM
To: Moore, Victoria L <victoria_moore@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
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Subject: RE: 75881- 5116540 2nd advance payment request

Thank you Vicki. Yes, we plan to expend the entir[5 U.S.C. § 552(b)(4)] 1st and 2nd advances) by the end of May. Thank you

---

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Amy Sims (PI)					
Processing Dates	20-Mar-20	24-Apr-20	22-May-20	31-May-20	Total
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5 U.S.C. § 552(b)(4)

5 U.S.C. § 552(b)(4)

Barb Hays

From: Parrish, Kalyn <klparrish@unc.edu>
Sent: Wednesday, April 08, 2020 12:18 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Can you please provide a reconciliation of funds from the first advance payment thus far?

Thank you,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
klparrish@unc.edu

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Cc: Burkhart, Carol J.[carol_burkhart@unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]
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Vicki, to date, I have not received notice that we've received payment yet. Can you please check status and let me know if/when it was released? Thank you

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Vicki; my project team is asking me….when you say it will be expedited, when will the payment be sent and how? Electronic? Just wondering when we can expect to receive it. thank you

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Subject: RE: 75881- 5116540 2nd advance payment request

Thank you Vicki. Yes, we plan to expend the entire [5 U.S.C. § 552(b)(4)] 1st and 2nd advances) by the end of May. Thank you

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---

Barb Hays

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 5/19/2020 8:31:42 AM (UTC-07:00)
To: Schaefer, Alexandra[aschaefe@email.unc.edu]
Cc: Edwards, Caitlin E[caitedw@unc.edu]
Subject: Re: Amy R21...

Alex,

Thank you for letting me know. I believe I understand what is going on but I have an all-day meeting today. I will see what I can figure out but most likely it will take me a couple of days.

Thank you again, Amy

From: "Schaefer, Alexandra" <aschaefe@email.unc.edu>
Date: Tuesday, May 19, 2020 at 6:26 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Cc: "Edwards, Caitlin E" <caitedw@unc.edu>
Subject: Fw: Amy R21...

Hi Amy,

there are still issues with the Qiagen order.

Kalyn, is holding a particular amount of money amount back (below), which was supposed to be for the Qiagen kits
therefore, we cannot order the Magnetic bead ChIP-kits (Invitrogen) in addition-
However, since we can't get the Qiagen kits anyway, we will order the Invitrogen Kits instead (I need 4, and I think we will buy one on Baric money)
But, As understand it- then we will not be able to order the Qiagen kits from UNC?

I CC'ed Cait on this email, I am sure she has a much better understanding of all the financial/ordering stuff.

Alex

From: Edwards, Caitlin E <caitedw@unc.edu>
Sent: Tuesday, May 19, 2020 9:10 AM
To: Parrish, Kalyn <klparrish@unc.edu>
Cc: Schaefer, Alexandra <aschaefe@email.unc.edu>
Subject: Re: Amy R21...

Hey Kalyn!

Hmm okay – got it! In that case I may go ahead and place the other order for around this amount and place the Qiagen order on a different project ID once Qiagen gets it together. Their website is still not cooperating via ePro, but supposedly the rep is working on it. The other item is Fisher so I'll order today and that way it should arrive before the

end of the month.

Thanks for your help! Sorry for any confusion!!
Cait

From: "Parrish, Kalyn" <klparrish@unc.edu>
Date: Tuesday, May 19, 2020 at 9:05 AM
To: "Edwards, Caitlin E" <caitedw@unc.edu>
Subject: RE: Amy R21...

Hi Cait,

We can only submit orders for the amount I set aside ([redacted]) for the Qiagen order. Because we already submitted paperwork to the NIH, we need to stick to this amount. If you can't get Qiagen order to work, we can place the other order for only $[redacted].

Please remember that we need to receive these items by the end of the month so please place the order asap.

Thanks,
Kalyn

From: Edwards, Caitlin E <caitedw@unc.edu>
Sent: Monday, May 18, 2020 4:32 PM
To: Parrish, Kalyn <klparrish@unc.edu>
Subject: Amy R21...

Hey Kalyn!

I have to place another order on Amy's R21. Will be about [redacted]. Is that still possible or create a mess? This would be in addition to the other item we set aside money for. Qiagen still won't let me place that order..

Thanks!
Cait

From: Hays, Barbara A[barb.hays@pnnl.gov]
Sent: Tue 5/19/2020 9:24:40 AM (UTC-07:00)
To: Parrish, Kalyn[klparrish@unc.edu]; Moore, Victoria L[victoria_moore@unc.edu]; Van Buren, Eve[evevb@email.unc.edu]
Cc: Burkhart, Carol J.[carol_burkhart@unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: 75881- 5116540 2nd advance payment request

Kayln, I was notified by Accounts Receivable this morning we have received the payment. Thank you very much

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Thank you Vicki. Yes, we plan to expend the enti[5 U.S.C. § 552(b)(4)](1st and 2nd advances) by the end of May. Thank you

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Sent: Wednesday, April 08, 2020 12:18 PM
To: Hays, Barbara A <barb.hays@pnnl.gov>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: RE: 75881- 5116540 2nd advance payment request

Hi Barb,

Can you please provide a reconciliation of funds from the first advance payment thus far?

Thank you,

Kalyn Parrish
Accounting Technician
Department of Epidemiology
The University of North Carolina at Chapel Hill
2107A McGavran-Greenberg Hall, CB#7435
Chapel Hill, NC 27599-7435
klparrish@unc.edu

From: Hays, Barbara A <barb.hays@pnnl.gov>
Sent: Wednesday, April 8, 2020 2:31 PM
To: Parrish, Kalyn <klparrish@unc.edu>; Van Buren, Eve <evevb@email.unc.edu>
Cc: Burkhart, Carol J. <carol_burkhart@unc.edu>; Farrell, Ronda Lee <farrelrl@email.unc.edu>; Hays, Barbara A <barb.hays@pnnl.gov>; ^PNNL Accounts Receivable <ar@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: 75881- 5116540 2nd advance payment request

Kalyn and Eve, please see attached invoice for the remaining advance payment. As you know, we have to make sure we have funding in-house to keep PNNL working. With such a short period of performance, I'm concerned that we will expend all the funding received before we get reimbursed for the first invoice. To avoid a work stoppage situation, I'm hopeful you will be able to advance pay the remaining $28K; then we will be able to keep working by drawing down on the advance. Please respond and let us know if this is possible. Thank you

---

Barb Hays

A. COVER PAGE

Project Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells	
Grant Number: 5R21AI146872-02	**Project/Grant Period:** 06/05/2019 - 05/31/2021
Reporting Period: 06/05/2019 - 05/31/2020	**Requested Budget Period:** 06/01/2020 - 05/31/2021
Report Term Frequency: Annual	**Date Submitted:**
Program Director/Principal Investigator Information: TIMOTHY PATRICK SHEAHAN , PHD BS 5 U.S.C. § 552(b)(6)	**Recipient Organization:** UNIV OF NORTH CAROLINA CHAPEL HILL UNIVERSITY OF NORTH CAROLINA CHAPEL HILL Office of Sponsored Research CHAPEL HILL, NC 275990001 **DUNS:** 608195277 **EIN:** 1566001393A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: R DAVID PAUL 104 Airport Dr. Suite 2200 Chapel Hill, NC 275991350 **Phone:** **Email:** 5 U.S.C. § 552(b)(6)	**Signing Official:** RONDA FARRELL 104 Airport Dr Suite 2200 Chapel Hill, NC 27599
Human Subjects: No	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The major goals of the project are to determine if primary human lung cells infected with Middle East respiratory syndrome coronavirus (MERS-CoV) use epigenetic mechanisms to regulate the expression of interferon stimulated genes (ISG). Specific Aim 1: Does histone methylation status coordinate with ISG expression patterns in MERS-CoV infected MVE, HAE, and/or FB? Aim 1 focuses on defining cell type specific type I and III ISG for primary human lung airway epithelial cell cultures (HAE), microvascular endothelial cells (MVE) and fibroblasts (FB), identifying if transcription factors mediate any regulation of ISG expression, and determining if MERS-CoV infection affects the methylation state of lysine 4 or 27 on cellular histones which determine whether chromatin in in an open state and accessible for transcription or in a closed state preventing transcription from occurring. Specific Aim 2: Exploring modulation of host chromatin remodeling enzymes following MERS-COV infection of primary human lung MVE, HAE, FB. Aim 2 seeks to define the DNA/histone methyltransfersae and deaceytylatse enzymes MERS-CoV may be modulating to regulate ISG expression. Assays will determine if host chromatin remodeling enzymes are active or inhibited following MERS-CoV replication and whether MERS-CoV replication and/or ISG expression are affected by inhibition of methyltransferase/deaceytlse enzyme activity. Finally, we will use novel protein-protein interaction technologies to determine MERS-CoV proteins that may mediate the epigenetic regulation of ISG expression.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Though there may be delays in completing experiments due to the shelter in place requirements for CoVID-19 - Prior to the end of the funding period we anticipate completing the following. Experiments to determine if histone modification plays a role in ISG differential expression in MERS-CoV infected FB will begin as soon as the shelter in place bans have been removed as all samples have been harvested and are in the freezer awaiting analysis. Existing lysate (from both MVE and FB) will also be used to explore if transcription factors contribute to regulation of ISG expression following MERS-CoV infection. Experiments to determine if the genes responsible for modifying chromatin structure are differentially expressed following MERS-CoV infection of primary human lung MVE and FB will be performed as described in Aim 2 using BioRad's PrimerPCR Pathway arrays. To determine if inhibition of enzymes that mediate chromatin structure rearrangement alters coronavirus replication and or changes the innate immune response to virus, drug efficacy studies will be performed, and infected treated samples will be assayed to determine levels of viral replication and cellular viability. If changes are detected in levels of viral replication additional samples will be generated to determine how ISG expression has been altered. We anticipate obtaining sufficient preliminary data for the submission of an RO1 by fall of 2021.

B.2 What was accomplished under these goals?

The ongoing MERS-CoV epidemic and recent identification of SARS-CoV 2 as the causative agent of coronavirus infectious disease 2019 (COVID-19) highlight the need for a better understanding of how highly pathogenic human coronaviruses manipulate the host immune response. Previous studies demonstrated that MERS-CoV infects an expanded range of human primary cell types including microvascular endothelial cells and lung fibroblasts which are not permissive for the 2002 SARS-CoV strain. In immortalized human lung epithelial cells, MERS-CoV downregulates the expression of several interferon stimulated genes (ISG) restricting the host innate immune response and previous studies suggest that this downregulation is mediated by epigenetic mechanisms that regulate the methylation state of histones keeping the chromatin in an inaccessible or closed state and upregulating the methylation of host DNA leading to a decrease in the expression of major histocompatibility complex genes. The goal of these studies was to determine if MERS-CoV uses epigenetic mechanisms to regulate the innate immune response in primary human lung endothelial cells (MVE) and fibroblasts (FB). Initial studies evaluated levels of infection in more than 20 donor tissues (all cell types collected for each donor) to determine which were best for the MERS-CoV epigenetic studies. Three donors were selected, and the University of North Carolina at Chapel Hill Tissue Procurement Core earmarked these frozen cell aliquots for these studies and sufficient numbers of cells are available for all studies within this funding application (**Figure 1**).

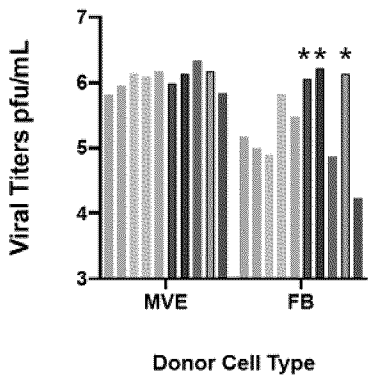

Figure 1. Representative MERS-CoV titers from tissue donor candidates for epigenetic experiments. MVE and FB from 20 donors were plated and infected with MERS-CoV for 24 hours and supernatants assessed by plaque assay to determine levels of viral replication. Three stars indicate the donors (only FB shown) used for downstream epigenetic testing. * highlight chosen donors.

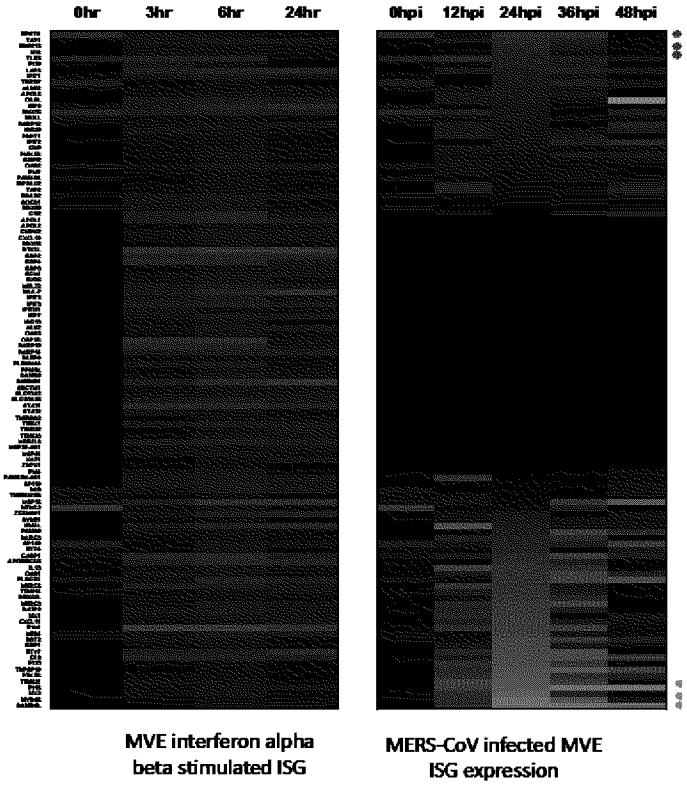

Figure 2 MERS-CoV regulates the innate immune response in primary human lung MVE. Left panel: Human lung MVE were treated with interferon alpha beta for the indicated times and ISG identified following microarray analysis. Right panel: ISG list identified in left panel following MERS-CoV infection of MVE. Red dots indicate up-regulated ISG used for ChIP-PCR studies; green dots indicate down-regulated ISG used for ChIP-PCR studies

Cell type specific lists of ISG from MVE and FB were generated following treatment of MVE and FB with interferon alpha/beta and the top six upregulated and downregulated (12 genes total per cell type) for each cell type were identified (**Table** and **Figure 2**). Triplicate samples of MVE and FB for all three donors were infected with MERS-CoV, protein and DNA crosslinked by formaldehyde, samples were safety tested and removed from biosafety level three. Due to the number of total samples to process analysis of one cell type at a time will be performed. Batch one analysis was performed on MERS-CoV infected MVE cells and has been completed. We anticipate that batch two analysis on MERS-CoV infected FB will be completed by the end of Year 1/May 2020,

but this work may be delayed until the shelter in place requirement has been removed. Formalin treated lysates from MERS-CoV infected MVE were assayed by chromatin immunoprecipitation-PCR (ChIP-PCR) using antisera specific for the open, transcriptionally active form of histone bound chromatin (lysine 4 in histone 3 (H3K4)) or for the closed transcriptionally inactive form of histone bound chromatin (lysine 27 in histone 3 (H3K27)) to determine if histone modifications could explain the differential expression of specific ISG. PCR is used to amplify the promoter regions of the ISG following immunoprecipitation to determine if the chromatin precipitated is in the active or inactive state following MERS-CoV infection (**Table**). Representative results are shown in **Figure 3** for two ISG with increased differential expression (interferon gamma inducible protein 6 (IFI 6) and ring finger protein 213 (RNF213)) or decreased expression (myeloid differentiation primary response protein 88 (MyD88) and sterile alpha motif domain containing 9L (SMAD9L)). Histones bound to the promoter regions of ISG that had upregulated expression (IFI 6 and RNF213) following MERS-CoV infection of MVE were predominantly methylated on lysine 4 and in the active confirmation for all three tissue donors (Figure 3 top panels) with little if any associate with histones in the closed confirmation. In contrast, histones bound to ISG promoter regions with decreased expression levels (SMAD9L and MyD88) were predominantly methylated on lysine 27 and in the closed confirmation with little associate with histones in the active confirmation. This data suggests that epigenetic regulation may play a role in down regulation of the innate immune response to MERS-CoV in primary human lung microvascular endothelial cells.

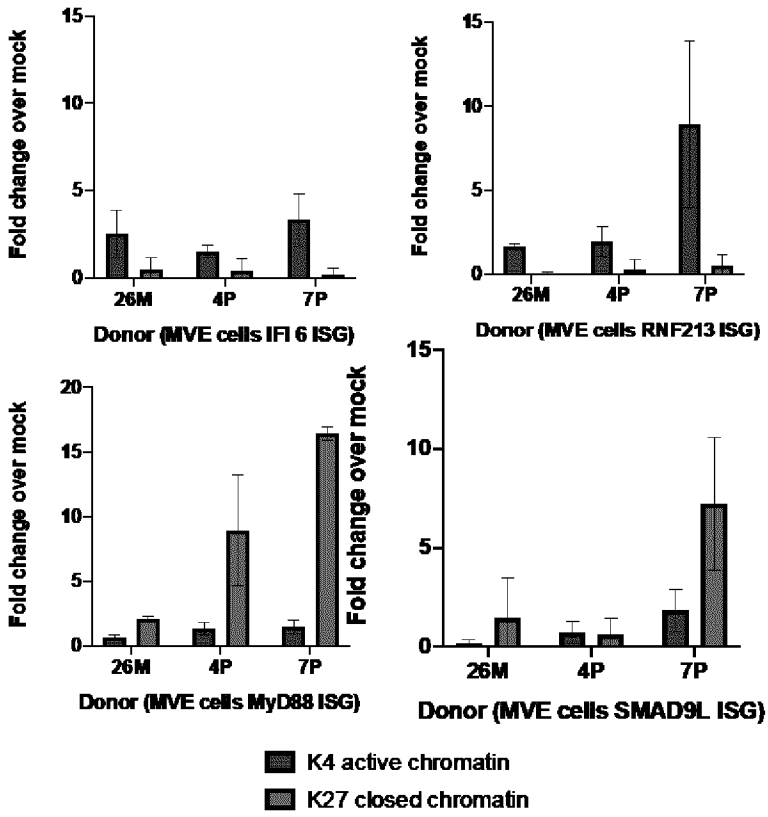

Figure 3 Altered histone methylation patterns suggest mechanism for ISG expression following MERS-CoV infection in primary human lung MVE. ChIP-PCR was performed on MERS-CoV infected MVE lysate for three donors. Antibodies specific for histones with lysine 4 methylation (shown in red) or for histones with lysine 27 methylation (shown in green) were used to precipitate chromatin and assayed by real time PCR. Top panels are ISG with increased expression following MERS-CoV infection and bottom panels are ISG with decreased expression following infection.

We are excited by the results from MERS-CoV infected MVE that suggest epigenetic regulation controls ISG expression in endothelial as well as epithelial lung cells. We anticipate similar findings from MERS-CoV infected fibroblasts and look forward to expanding our understanding of which enzymes that modify chromatin structure contribute to the regulation of the innate immune response following MERS-CoV infection.

On January 6, 2020 Dr. Sims began a new position as a senior scientist at the Pacific Northwest National Laboratory in Richland, Washington. She will continue the studies within this award as a collaboration with Drs. Timothy Sheahan and Alexandra Schaefer at the University of North Carolina at Chapel Hill.

Cell Type	Gene Name	Differential Gene Expression	Primer Pairs	Analysis as Predicted
MVE	Sterile alpha motif domain containing 9L (SMAD9L)	Down	cagcctcattttcgtagccctcat ggccatctacaagccaaggagaga	Yes
MVE	Interferon gamma inducible protein 16 (IFI 16)	Down	tcatagcagacatttccccaacca gcttcttctcccctcctttcctgt	Mixed between donors
MVE	Myeloid differentiation primary response 88 (MyD88)	Down	Cccctcctcacaggttcagtccta gagcatggcacaaccaagaaaaga	Yes
MVE	Epithelial stromal interaction 1 (EPSTI 1)	Up	ccaggttggagtacagtggcatga tacaacaattagctgggcgtggtg	Yes
MVE	Interferon alpha inducible protein 6 (IFI 6)	Up	cagcaggcagcacacaaatgttc agccaatccctgtcggagtttcta	Yes
MVE	Ring finger protein 213 (RNF213)	Up	ggatgaaggggtgagaggagaagg gtgtgaccagggacctccgtttta	Yes

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
TSHEAHAN	Y	Sheahan, Timothy Patrick	BS,PHD	PD/PI	1.0	0.0	0.0			NA
AMY_SIMS	Y	SIMS, AMY C	PHD	PD/PI	2.4	0.0	0.0			NA
	N	Schaefer, Alexandra		Staff scientist (Doctoral level)	3.0	0.0	0.0			NA
	N	Lam, Mariam		Technician	1.8	0.0	0.0			NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: OtherSupport_ALL.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

OTHER SUPPORT

SHEAHAN, TIMOTHY

ACTIVE

R21AI146872 (PI: Sheahan/Sims) 06/05/19-05/30/21 0.60 cal months (5%
NIH **{THIS GRANT}** 5 U.S.C. § 552(b)(4)
How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
This proposal will build on foundational studies performed in continuous human lung cell lines and define ways that MERS-CoV regulates innate immunity in primary human lung fibroblasts and microvascular endothelial cells.
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

U19AI142759 CETR (PI: Whitley) 03/01/14-02/28/24 3.6 cal months (30%)
UAB/NIH/NIAID 5 U.S.C. § 552(b)(4)
Antiviral Drug Discovery and Development Center
The specific aims of the proposal will identify small molecule inhibitors of CoV fidelity and RNA capping, define their mechanism of action, and determine their efficacy against SARS-CoV and across CoV families using in vivo mouse models of acute and persistent CoV disease.
Role: Investigator
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01 AI131688-01 (PI: Rice) 03/15/17-02/281/22 1.8 cal months (15%)
Rockefeller/NIH 5 U.S.C. § 552(b)(4)
Analysis of immunity, viral adaptation and pathogenesis in a new mouse model of HCV-related rodent hepacivirus infection
Mechanisms that contribute to the persistence of hepatotropic viruses, such as HCV, are not well understood. We have recently established the first immune-competent mouse model of an HCV-related virus. With this new model, we propose to systematically study immunity and host-virus interactions during a hepatotropic RNA virus infection in vivo.
Role: Subcontract PI
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01 AI132178-01 (MPI: Sheahan/Baric) 08/09/17-07/31/22 2.4 cal months (20%)
NIH 5 U.S.C. § 552(b)(4)
Broad-spectrum antiviral GS-5734 to treat MERS-CoV and related emerging CoV
In partnership with Gilead Sciences, we aim to accelerate the preclinical development of GS-5734 and promote IND licensure. We define the pharmacokinetics, pharmacodynamics, resistance profile, efficacy breadth and mechanism of action of GS-5734 against MERS-CoV and related emerging CoV.
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01AI108197-06 (MPI: Baric/Denison) 03/01/18-02/28/23 1.8 cal months (15%)
Vanderbilt/NIH 5 U.S.C. § 552(b)(4)
Determinants of Coronavirus Fidelity in Replication and Pathogenesis
To identify common and unique determinants of CoV nsp14-ExoN functions CoV replication, fidelity and IFN sensitivity across CoVs; To determine pathways of adaptation to loss of nsp14-ExoN activity in vitro and in vivo; and to define mechanisms of ExoN-regulated CoV sensitivity to the innate antiviral immune response.
Role: Co-Investigator

Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

U01AI149644 (PI: Baric) 04/19/19-03/31/24 1.8 cal months (15%)
NIH
5 U.S.C. § 552(b)(4)
Respiratory Virus Vaccine and Adjuvant Exploration
Vaccination is one of the most effective public health measures for protecting against infectious disease, and the proposed studies will identify adjuvants and adjuvant combinations that safely elicit long lived protective immunity against emerging pathogens in at risk populations.
Role: Investigator
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

PENDING:
R01 (PI: Meshnick) 04/01/20-03/31/25 0.36 cal months (3%)
NIH
5 U.S.C. § 552(b)(4)
Molecular epidemiology of arboviruses in the Democratic Republic of the Congo
The grant is innovative in its multidisciplinarity, combining epidemiological, entomological, serological, phylogenetic and basic sciences approaches. Together, this research will, for the first time, provide data on the incidence, types, sources, and genomic traits of this important group of viruses in Central Africa.
Foreign component funded by this grant: Yes
Foreign investigators: Antoinette Tshefu, University of Kinshasa (Congo, Democratic Republic)
Supplied by foreign site: Patient Samples
Technology transfer to foreign site: No

R21 (PI: Sheahan) 07/01/20-06/30/22 0.90 cal months (7.5%)
NIH
5 U.S.C. § 552(b)(4)
Characterization of hepacivirus pathogenesis, viral adaptation and the mapping of host susceptibility alleles in the Collaborative Cross
The goals of this proposal are to: 1) phenotype the kinetics of virus replication/adaptation, pathogenesis and the host response in CC lines with delayed clearance and chronic infection and 2) to map the genetic determinants driving virus titer, viral evolution, clearance, weight loss, blood leukocyte modulation, and chronic infection
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

Not Assigned (PI: Baric) 07/01/20-06/30/25 0.36 cal months (3%)
EcoHealth Alliance
5 U.S.C. § 552(b)(4)
US-China Collab: Spillover, co-infection, and control of bat-origin livestock coronaviruses
To develop an economic model of farm profit maximization linked to the compartmental epidemiological model of co-infection disease.*Foreign component funded by this grant: No*

OVERLAP: If any of the pending awards are funded, Dr. Sheahan will reduce is effort accordingly to not exceed 12 calendar months.

Other Support

SIMS, AMY

ACTIVE

R21AI146872 (Sims/Sheahan) 06/05/19-05/31/21 2.4 cal months
UNC Chapel Hill/NIH 5 U.S.C. § 552(b)(4) **{THIS GRANT}**
How MERS-CoV regulates the innate immune response
The major goal of the project is to determine if primary human lung cells infected with Middle East respiratory syndrome coronavirus (MERS-CoV) use epigenetic mechanisms to regulate the expression of interferon stimulated genes.

Foreign component funded by grant: No

There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

LDRD (Sims) 03/07/20-09/30/21 4.4 cal months
Pacific Northwest National Laboratory 5 U.S.C. § 552(b)(4)
Defining coronavirus lipidomic response
The goal of this project is to characterize the lipid response to coronavirus infection.

Foreign component funded by grant: No

There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

PENDING

Not Applicable

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

On January 6, 2020 Dr. Sims began a new position at Pacific Northwest National Laboratory (PNNL) in Richland, Washington. Dr. Sims will continue to collaborate with Drs. Sheahan and Schaefer at the University of North Carolina at Chapel Hill (UNC) to meet the goals of this funded project. Funds for Year 1 have been appropriately distributed between the PNNL and UNC to allow work to continue at both sites. Prior to the start of Year 2, we anticipate petitioning NIH/NIAID/UNC to transition the award to PNNL allowing Dr. Sims to resume as Principle Investigator. Funds would then be distributed to UNC via subcontract to continue the collaboration and to ensure forward progress on the proposed work.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: University of North Carolina at Chapel Hill	608195277	NC-004	104 Airport Drive, Suite 2200, CB 1350 Chapel Hill NC 275991350
Pacific Northwest National Laboratory	032987476	WA-004	902 Battelle Boulevard P.O. Box 999, MSIN J4-02 Richland WA 993520999

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

From: Sandoval, Norma I [Norma.Sandoval@pnnl.gov]
Sent: 6/1/2020 8:56:21 AM
To: Moore, Victoria L [victoria_moore@unc.edu]; Caldwell, Chandra [ccaldwel@email.unc.edu]
CC: Sims, Amy C [amy.sims@pnnl.gov]; Sandoval, Norma I [Norma.Sandoval@pnnl.gov]
Subject: 76382 - R21 Document Request, due by 6/5/2020
Attachments: RR_Budget_1_4_A-V1.4.pdf

Importance: High

Hi Vicki and Chandra,
I am assisting Amy with the proposal submission for the R21 Year 2 effort. Below are the specific components that I will need in order to include UNC's effort in the proposal.

The deadline for submission is 6/9/2020, therefore we'll need your documents by no later than **COB 6/5/2020.**

Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
Period of Performance: 06/01/2020 – 05/31/2021 (1 year effort)
Face page – Signed by your appropriate authorized official
Statement of Work
R&R budget form (attached) and Budget Justification:
~Budget: 5 U.S.C. § 552(b)(4) *DIRECT*
Biographical Sketches for all key personnel
Facilities and Resources
Equipment
Performance site information

Let me know if you have any questions or need additional information.

Thx.

Norma Sandoval
Principal Project Coordinator
Biological Sciences Division, **EBSD**

Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999, MSIN J4-18
Richland, WA 99352 USA
Tel: 509-371-6553
norma.sandoval@pnnl.gov
www.pnnl.gov

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 6/1/2020 9:31:49 AM (UTC-07:00)
To: Caldwell, Chandra[ccaldwel@email.unc.edu]
Subject: FW: 76382 - R21 Document Request, due by 6/5/2020
Attachment: RR_Budget_1_4_A-V1.4.pdf

Is it helpful if I get in touch with Tim and Alex and help get this paperwork moving forward? Thank you, Amy

---

From: "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>
Date: Monday, June 1, 2020 at 8:56 AM
To: "Moore, Victoria L" <victoria_moore@unc.edu>, "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Cc: "Sims, Amy C" <amy.sims@pnnl.gov>, "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>
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Face page – Signed by your appropriate authorized official
Statement of Work
R&R budget form (attached) and Budget Justification:
~Budget **5 U.S.C. § 552(b)(4)**
Biographical Sketches for all key personnel
Facilities and Resources
Equipment
Performance site information

Let me know if you have any questions or need additional information.

Thx.

Norma Sandoval
Principal Project Coordinator
Biological Sciences Division, **EBSD**

Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999, MSIN J4-18
Richland, WA 99352 USA
Tel: 509-371-6553
norma.sandoval@pnnl.gov
www.pnnl.gov

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Mon 6/1/2020 10:15:19 AM (UTC-07:00)
To: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Moore, Victoria L[victoria_moore@unc.edu]
Cc: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: 76382 - R21 Document Request, due by 6/5/2020

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From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 6/1/2020 10:18:10 AM (UTC-07:00)
To: Caldwell, Chandra[ccaldwel@email.unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Moore, Victoria L[victoria_moore@unc.edu]
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From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 6/1/2020 11:25:21 AM (UTC-07:00)
To: Caldwell, Chandra[ccaldwel@email.unc.edu]
Subject: Re: 76382 - R21 Document Request, due by 6/5/2020

Got it. I figured it couldn't hurt to ask. I looked through my emails and could not find them. I know we did them, oh well.
I will send you something you can use. Thank you very much for looking. I appreciate it. Amy

---

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Date: Monday, June 1, 2020 at 11:20 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
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Chandra,

I believe that Tim is currently being paid around 1% on the R21. I kept him there but it is up to UNC if they want to increase this amount. Vicki may argue that his effort has to be increased.

I added the rest of the categories that should be included. The numbers for the breakout might have to be changed but these should mostly cover it. I can look at a budget in excel if you want to send it to me. I tried to text Tim but he hasn't answered.

Thank you very much! Amy

Timothy Sheahan Ph.D., Principal Investigator 5 U.S.C. § 552(b)(4) Dr. Sheahan has extensive (>15 years) select agent/BSL3 experience primarily working with in vitro an in vivo models of human coronavirus infection to better understand highly pathogenic human respiratory virus pathogenicity and pathogen host interactions. Dr. Sheahan will oversee all work performed at UNC Chapel Hill and work closely with Drs. Sims and Dr. Schaefer to ensure steady progress on meeting the goals of the project. He will interact closely with Dr. Schaefer and Mr. Scobey to ensure steady progress during the course of the proposal, evaluate results and propose alternative experiments. Dr. Sheahan will manage fiscal matters associated with the work performed at UNC Chapel Hill.

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Date: Monday, June 1, 2020 at 11:20 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: 76382 - R21 Document Request, due by 6/5/2020

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Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
Period of Performance: 06/01/2020 – 05/31/2021 (1 year effort)
Face page – Signed by your appropriate authorized official
Statement of Work
R&R budget form (attached) and Budget Justification:
~Budget: 5 U.S.C. § 552(b)(4)
Biographical Sketches for all key personnel
Facilities and Resources
Equipment
Performance site information

Let me know if you have any questions or need additional information.

Thx.

Norma Sandoval
Principal Project Coordinator
Biological Sciences Division, **EBSD**

Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999, MSIN J4-18
Richland, WA 99352 USA
Tel: 509-371-6553
norma.sandoval@pnnl.gov
www.pnnl.gov

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Mon 6/1/2020 12:30:07 PM (UTC-07:00)
To: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]
Cc: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: 76382 - R21 Document Request, due by 6/5/2020
Attachment: Baric Facilities_Resources.docx
Attachment: UNC site info.jpg
Attachment: Sheahan Biosketch.docx

Hi Nora,

I need the highlighted info for UNC's LOI. Also, attached are the last few documents you requested (biosketch, facilities and performance site info).

SPONSOR	
Legal Name:	(Enter Name of Sponsor)
Lead PI:	(Enter Principal Investigator Name)
Sponsor Administrative Contact:	
Name/Title:	(Enter Sponsor Administrative Contact)
Address:	(Enter Sponsor Address)
Phone:	(Enter Sponsor Phone)
Email:	(Enter Sponsor Main Email)

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Administrative Contact (PNNL's Contract/SO)
Barb Hays, Contracting Professional
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Richland, WA 99352-0999
509-372-4008
barb.hays@pnnl.gov

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Pacific Northwest National Laboratory

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To: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
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Hi Chandra,

Thank you for taking care of this so quickly. I would recommend the following changes.

I am leaning towards having you remove the international travel. Maybe leave (b) (4) for domestic travel. We were supposed to have an international CoV meeting this year but I have no idea when that might happen. I would put the remaining funds into miscellaneous.

If you have a reason for all of the travel funds I don't have a problem with them staying but the budget isn't that big. Over 10% of the direct funds for travel seems a little strange without a specific reason.

Thank you very much! Amy

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Thanks for sending the breakdown. Attached is the budget since Tim has been slow to respond to emails given the stuff that Ralph has him working on these days. I will get this routed today.

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Chandra,

I believe that Tim is currently being paid around (b) (4) on the R21. I kept him there but it is up to UNC if they want to increase this amount. Vicki may argue that his effort has to be increased.

I added the rest of the categories that should be included. The numbers for the breakout might have to be changed but these should mostly cover it. I can look at a budget in excel if you want to send it to me. I tried to text Tim but he hasn't answered.

Thank you very much! Amy

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Attachment: Sims R21 Yr2_UNC Subcontact_RV.xlsx

Hi Amy,

See attachment since I increased Sheahan's effort to 5% with the extra travel funds since I was originally thinking both Tim and Alex would be traveling.

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Sent: Monday, June 1, 2020 4:05 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: 76382 - R21 Document Request, due by 6/5/2020

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Let me know if you have any questions or need additional information.

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Norma Sandoval
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Pacific Northwest National Laboratory
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Attachment: 76382_R21_SOW_UNC_SUBCONTRACT_Year 2.docx

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To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: 76382 - R21 Document Request, due by 6/5/2020

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R&R budget form (attached) and Budget Justification:
~Budget: (b) (4) ***DIRECT***

Biographical Sketches for all key personnel
Facilities and Resources
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Let me know if you have any questions or need additional information.

Thx.

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Please make her co-investigator. She is actually key personnel on this one. Thank you! I appreciate the reminder about the biosketch. I will need to ask for that. Amy

---

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Approved for use through 03/31/2020
OMB No. 0925-0002

Department of Health and Human Services, Public Health Service

Official Statement Relinquishing Interests and Rights in a Public Health Service Research Grant

(Return original to awarding unit)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed and completing and reviewing collection of information. **An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.** Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-0002). Do not return the completed form to this address.

May 22,2020 (date)

Name of Institution: The University of North Carolina at Chapel Hill

Address *(city and state)*: Chapel Hill, NC, United States 27599001

104 Airport Drive, Suite 2200

Principal Investigator: Sheahan, Timothy Patrick

on Public Health Service grant number: 5R21AI146872-02

has expressed a desire to continue his/her research project at the

Battelle Centers for Public Health Research and Evaluation

In view of the fact that we do not wish to nominate another principal investigator or continue the research project at this Institution, this is to signify our willingness to terminate this grant as of 5/31/2020 (date) and to relinquish all claims to any unexpended and uncommitted funds remaining in the grant as of that date, as well as to all recommended future support of this project.

Equipment Costing $5,000 or More Transferring with the Project *(itemize)*	Unexpended Balance — Estimated
1.	The unexpended balance on termination date of 5/31/2020 calculated on basis of total amount
2.	
3.	**5 U.S.C. § 552(b)(4)**
4.	
5.	
6.	
Use separate page for additional items.	

That portion of the estimated unexpended balance which has been received will be returned to the Public Health Service, upon request, with a final adjustment, if required, to be made after the grant account has been audited.

Official Authorized to Sign Application

Signature: Kati Chipps on behalf of Terry Magnuson

Digitally signed by Kati Chipps on behalf of Terry Magnuson
Date: 2020.05.22 16:40:39 -04'00'

Name and Title *(print or type)*

Terry Magnuson, Ph.D., Vice Chancellor for Research

Privacy Act Statement. Privacy Act Statement. The NIH maintains application and grant records as part of a system of records as defined by the Privacy Act: NIH 09-25-0225 https://era.nih.gov/privacy-act-and-era.htm.

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Department of Health and Human Services, Public Health Service

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Principal Investigator: Sheahan, Timothy Patrick

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1.	The unexpended balance on termination date of
2.	5/31/2020 calculated on basis of total amount
3.	awarded for the grant year, will be approximately
4.	$ 5 U.S.C. § 552(b)(4) direct cost
5.	$ indirect cost.
6.	
Use separate page for additional items.	

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Approved for use through 03/31/2020
OMB No. 0925-0002

Department of Health and Human Services, Public Health Service

Official Statement Relinquishing Interests and Rights in a Public Health Service Research Grant

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06/03/2020 (date)

Name of Institution: The University of North Carolina at Chapel Hill

Address *(city and state)*: Office of Sponsored Research
CB# 1350, 104 Airport Drive
Chapel Hill, NC 27599-1350

Principal Investigator: Timothy Sheahan, PhD

on Public Health Service grant number 1 R21 AI146872

has expressed a desire to continue his/her research project at the

Battelle Memorial Institute, Pacific Northwest National Laboratory (Dr. Amy Sims)

In view of the fact that we do not wish to nominate another principal investigator or continue the research project at this Institution, this is to signify our willingness to terminate this grant as of 5/31/2020 (date) and to relinquish all claims to any unexpended and uncommitted funds remaining in the grant as of that date, as well as to all recommended future support of this project.

Equipment Costing $5,000 or More Transferring with the Project *(itemize)*	Unexpended Balance — Estimated
1. N/A	5 U.S.C. § 552(b)(4)
2.	
3.	
4.	
5.	
6.	
Use separate page for additional items.	

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Official Authorized to Sign Application

Signature: Kati Chipps on behalf of Terry Magnuson

Digitally signed by Kati Chipps on behalf of Terry Magnuson
Date: 2020.06.03 15:49:07 -04'00'

Name and Title *(print or type)*

Terry Magnuson, Ph.D., Vice Chancellor for Research

Privacy Act Statement. Privacy Act Statement. The NIH maintains application and grant records as part of a system of records as defined by the Privacy Act: NIH 09-25-0225 https://era.nih.gov/privacy-act-and-era.htm.

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Fri 6/5/2020 1:18:08 PM (UTC-07:00)
To: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]
Cc: Sims, Amy C[amy.sims@pnnl.gov]; Hays, Barbara A[barb.hays@pnnl.gov]
Subject: RE: 76382 - R21 Document Request, due by 6/5/2020
Attachment: SignedLOI.pdf
Attachment: UNC Budget.pdf
Attachment: UNC Budget Justification.docx
Attachment: 76382_R21_SOW_UNC_SUBCONTRACT_Year 2.docx

Hi Norma,

Attached are the remaining documents from UNC.

Best,
Chandra

From: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Sent: Monday, June 1, 2020 3:41 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>; Hays, Barbara A <barb.hays@pnnl.gov>
Subject: RE: 76382 - R21 Document Request, due by 6/5/2020

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Legal Name
Battelle-PNWD, Operator of PNNL for US DOE

Administrative Contact (PNNL's Contract/SO)
Barb Hays, Contracting Professional
902 Battelle Blvd.
PO Box 999
Richland, WA 99352-0999
509-372-4008
barb.hays@pnnl.gov

Thx.

Norma Sandoval
Principal Project Coordinator
Biological Sciences Division, **EBSD**
Pacific Northwest National Laboratory

From: Caldwell, Chandra <ccaldwel@email.unc.edu>
Sent: Monday, June 1, 2020 12:30 PM
To: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Cc: Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: 76382 - R21 Document Request, due by 6/5/2020

Hi Nora,

I need the highlighted info for UNC's LOI. Also, attached are the last few documents you requested (biosketch, facilities and performance site info).

SPONSOR	
Legal Name:	(Enter Name of Sponsor)
Lead PI:	(Enter Principal Investigator Name)
Sponsor Administrative Contact:	
Name/Title:	(Enter Sponsor Administrative Contact)
Address:	(Enter Sponsor Address)
Phone:	(Enter Sponsor Phone)
Email:	(Enter Sponsor Main Email)

Thanks,
Chandra

From: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Sent: Monday, June 1, 2020 11:56 AM
To: Moore, Victoria L <victoria_moore@unc.edu>; Caldwell, Chandra <ccaldwel@email.unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: 76382 - R21 Document Request, due by 6/5/2020
Importance: High

Hi Vicki and Chandra,
I am assisting Amy with the proposal submission for the R21 Year 2 effort. Below are the specific components that I will need in order to include UNC's effort in the proposal.

The deadline for submission is 6/9/2020, therefore we'll need your documents by no later than **COB 6/5/2020.**

Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
Period of Performance: 06/01/2020 – 05/31/2021 (1 year effort)
Face page – Signed by your appropriate authorized official
Statement of Work
R&R budget form (attached) and Budget Justification:
~Budget: **5 U.S.C. § 552(b)(4)**
Biographical Sketches for all key personnel
Facilities and Resources
Equipment
Performance site information

Let me know if you have any questions or need additional information.

Thx.

Norma Sandoval
Principal Project Coordinator
Biological Sciences Division, **EBSD**

Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999, MSIN J4-18
Richland, WA 99352 USA
Tel: 509-371-6553
norma.sandoval@pnnl.gov
www.pnnl.gov

UNC RESEARCH

Subrecipient Letter of Intent To University of North Carolina at Chapel Hill

To be completed by UNC-CH Project Team

SUBRECIPIENT	SPONSOR
Legal Name: The University of North Carolina at Chapel Hill	Legal Name: Battelle-PNWD, Operator of PNNL for US DOE
DUNS: 608195277	
Lead PI: Dr. Timothy Sheahan	Lead PI: Dr. Amy Sims
Subrecipient Administrative Contact:	***Sponsor Administrative Contact:***
Name/Title: David Paul/Associate Vice Chancellor	Name/Title: Barb Hays, Contracting Professional
Address: 104 Airport Dr., Suite 2200, CB 1350 Chapel Hill, NC, 27599	Address: 902 Battelle Blvd. - PO Box 999 Richland, WA 99352-0999
Phone: 919-966-3411	Phone: 509-372-4008
Email: ResAdminOSR@unc.edu	Email: barb.hays@pnnl.gov

GENERAL INFORMATION

Project Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells

Prime Awarding Agency: NIH

RFA/RFP: PA-18-489

Project Period: Start 06/01/2020 End 05/31/2021

UNC-CH Proposal Number: 20-5613

BUDGET INFORMATION

Choose appropriate F&A Type:

(●) Federal Rate ( ) Sponsor Rate ( ) Other

Applicable F&A Rate: 55.5 %

Direct Costs:

Indirect Costs:

Total Request:

5 U.S.C. § 552(b)(4)

COMPLIANCE INFORMATION

Human Subjects: ( ) Yes (●) No

Animal Subjects: ( ) Yes (●) No

UNC-CH is a Federal Demonstration Partnership (FDP) Pilot Participant.

This LETTER OF INTENT confirms the appropriate program and administrative personnel at UNC-CH have reviewed and approve the above referenced Solicitation/RFP/RFA. Further, UNC-CH and its Principal Investigator certify that:

Information submitted within this application is true, complete, and accurate to the best of UNC-CH's and PI's knowledge; any false, fictitious, or fraudulent statements or claims may subject the UNC-CH and PI to criminal, civil, or administrative penalties; PI agrees to accept responsibility for the scientific conduct of the project and to provide the required progress reports if an award is made and a mutually agreeable subcontract is executed as a result of UNC-CH's application.

Further, UNC-CH confirms it maintains an active and enforced conflict of interest policy meeting the requirements of 42 CFR Part 5. Subpart F, and 45 CFR Part 94.

Included: Statement of Work Budget Budget Justification Other:

UNC-CH Principal Investigator: Timothy P. Sheahan

Date: 06/01/2020

UNC-CH Authorized Official: Alexie Mina Digitally signed by Alexie Mina Date: 2020.06.05 10:47:52 -04'00'

Date:

UNC Budget Justification

Personnel:

Timothy Sheahan Ph.D., Principal Investigator 5 U.S.C. § 552(b)(4) . Dr. Sheahan has extensive (>15 years) select agent/BSL3 experience primarily working with in vitro an in vivo models of human coronavirus infection to better understand highly pathogenic human respiratory virus pathogenicity and pathogen host interactions. Dr. Sheahan will oversee all work performed at UNC Chapel Hill and work closely with Drs. Sims and Dr. Schaefer to ensure steady progress on meeting the goals of the project. He will interact closely with Dr. Schaefer and Mr. Scobey to ensure steady progress during the course of the proposal, evaluate results and propose alternative experiments. Dr. Sheahan will manage fiscal matters associated with the work performed at UNC Chapel Hill.

Alexandra Schaefer, Ph.D., Co-Investigato 5 U.S.C. § 552(b)(4) Dr. Schaefer pioneered the use of ChIP-RT PCR/Seq in the laboratory and will be critical for examining the relationships between histone modifications, DNA methylation and ISG expression control. Dr. Schaefer has extensive experience working under BSL3 conditions and will perform all primary human lung cell epigenetic experiments. She will work closely with Drs. Sims and Sheahan to plan, execute, and trouble shoot the proposed studies. She will meet with Drs. Sims and Sheahan frequently to discuss and trouble shoot experimental results and issues. Dr. Schaefer will assist with the preparation of all reports and manuscripts.

Fringe Benefits: Faculty/Staff: 24.863% Social Security and Retirement; $6,306/FTE Health Insurance.

Supplies:

BL3 Protective Gear 5 U.S.C. § 552(b)(4) Personnel wear powered air purifying HEPA filtered breathing apparatuses, wear tyvek suits, tyvek aprons, hoods, booties and are double gloved when entering the BSL3 facility. These materials are expensive as the HEPA, organic chemical filters and even batteries must be replaced every ~6 months, and the tyvek suits are disposable. Moreover, the PAPR (powered air breathing apparatus) are expensive and must be replaced every ~2 years from normal wear and tear, and daily contact with EPA disinfectants. Personnel use high quantities of disinfectants like ethanol, Clorox and other EPA approved disinfectants in maintaining a safe working environment in the BSL3. Personnel spray down tyvek suits, etc. with alcohol or related disinfectants in the process of deconing and leaving the BSL3 facility. All materials that leave the BSL3 must be disinfected, packaged in disinfected, sealed containers, which are disinfected prior to removal from the BSL3 facility. In addition, funds are requested to help defray costs associated with the decontamination and maintenance of the BSL3 laboratory each year.

Miscellaneous 5 U.S.C. § 552(b)(4) Monies are requested to purchase glassware, pipettes, etc. used in day to day virologic and cell culture procedures as well as in growing, titering and characterizing virus growth in vitro. Funds are also requested to purchase chemicals, reagents, paper products, gloves, micropipetors, autoclave supplies, plastic tips, water baths, and other small equipment items that typically have short half lives in laboratory settings.

Kits and Reagents 5 U.S.C. § 552(b)(4) Funds are requested to purchase the wide variety of kits required to perform the proposed epigenetic experiments. For ChIP Seq experiments we will need the MAGnify Chromatin Immunoprecipitation system and the histone specific antisera required for pull down are obtained by purchasing the EpiTect ChIP Antibody kit and pre-sequencing PCR requires CyberGreen kits and general PCR reagents. For detecting methylated DNA, we will require the MethylMiner Methylated DNA Enrichment Kit as well as running addition general PCR reactions using the reagents listed above.

Tissue Culture Reagents 5 U.S.C. § 552(b)(4) We are requesting funds to purchase cell culture supplies and plastic ware to perform cell passage and viral plaque assays to determine viral titers.

Other Expenses:

Sequencing Reactions: 5 U.S.C. § 552(b)(4) We will work with Arraystar to sequence the chromatin immunoprecipitated DNA. In Year 1 we can perform 24 sequencing reactions and in Year 2 we can perform 16 sequencing reactions from pooled primary cell samples.

Indirect Costs (Facilities and Administration): In accordance with the University's F&A Cost Rate Agreement dated November 23, 2016, the University's predetermined F&A rate is 55.50%. This rate remains in effect through June 30, 2020. The base for calculating Facilities and Administrative cost (indirect cost) is modified total direct costs (MTDC), consisting of all salaries and wages, fringe benefits, materials and supplies, and services.

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Fri 6/5/2020 1:52:44 PM (UTC-07:00)
To: Caldwell, Chandra[ccaldwel@email.unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]
Cc: Hays, Barbara A[barb.hays@pnnl.gov]
Subject: Re: 76382 - R21 Document Request, due by 6/5/2020

Thank you, Chandra! You are a rock star!! Amy

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Friday, June 5, 2020 at 1:19 PM
To: "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>
Cc: "Sims, Amy C" <amy.sims@pnnl.gov>, "Hays, Barbara A" <barb.hays@pnnl.gov>
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To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>; Hays, Barbara A <barb.hays@pnnl.gov>
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Thx.

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Principal Project Coordinator
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Pacific Northwest National Laboratory

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Sponsor Administrative Contact:	
Name/Title:	(Enter Sponsor Administrative Contact)
Address:	(Enter Sponsor Address)
Phone:	(Enter Sponsor Phone)
Email:	(Enter Sponsor Main Email)

Thanks,
Chandra

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Sent: Monday, June 1, 2020 11:56 AM
To: Moore, Victoria L <victoria_moore@unc.edu>; Caldwell, Chandra <ccaldwel@email.unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
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Period of Performance: 06/01/2020 – 05/31/2021 (1 year effort)
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R&R budget form (attached) and Budget Justification:
~Budget: **5 U.S.C. § 552(b)(4)**
Biographical Sketches for all key personnel
Facilities and Resources
Equipment
Performance site information

Let me know if you have any questions or need additional information.

Thx.

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Principal Project Coordinator
Biological Sciences Division, **EBSD**

Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999, MSIN J4-18
Richland, WA 99352 USA
Tel: 509-371-6553
norma.sandoval@pnnl.gov
www.pnnl.gov

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Sun 6/7/2020 10:28:27 AM (UTC-07:00)
To: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Subject: Re: Sketch for R21 Year 2

Thank you very much! Amy

From: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Date: Sunday, June 7, 2020 at 4:38 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Sketch for R21 Year 2

Hi Amy,

See attached!
Thanks!
T

From: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Sent: Sun 6/7/2020 10:43:11 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Sketch for R21 Year 2

You're welcome my friend!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Sunday, June 7, 2020 1:28:26 PM
To: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Subject: Re: Sketch for R21 Year 2

Thank you very much! Amy

From: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Date: Sunday, June 7, 2020 at 4:38 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Sketch for R21 Year 2

Hi Amy,

See attached!
Thanks!
T

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 6/8/2020 2:51:13 PM (UTC-07:00)
To: Caldwell, Chandra[ccaldwel@email.unc.edu]
Subject: Re: A little help please

Hi Chandra,

I hate to bug you again but one more thing please!

The report that you sent to me still says “draft” at the top of each page of the pdf. Do you have another pdf that does not have draft on it?

Thank you, Amy

PS. I hope you are doing well! ACS

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Thursday, May 28, 2020 at 3:04 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: A little help please

Hi Amy,

Attached is the progress report. However, you can’t go by the amount that is on the progress report since the notice of award was issued to UNC before the relinquish statement was submitted. Therefore, they had to include the amount for your year 2 award along with the remaining balance from year 1.

You will have to ask Carol for the info since she completed the relinquish statement and shared it with Vicki to get her approval before sending it to OSR to submit and process.

Thanks,
Chandra

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, May 28, 2020 5:58 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: A little help please

Hi Chandra,
Is it possible for you to tell me exactly how much carry forward UNC reported to the NIH for the R21 that is being relinquished? We are working on that paperwork and I am not sure of the exact dollar amount that was left over.

If it is easier and contained within the progress report you can just send me that!

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Sent: Mon 6/8/2020 3:21:23 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: A little help please
Attachment: Sims RPPR.pdf

FYI: See attachment!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 8, 2020 5:51 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: A little help please

Hi Chandra,

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A. COVER PAGE

Project Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells	
Grant Number: 5R21AI146872-02	**Project/Grant Period:** 06/05/2019 - 05/31/2021
Reporting Period: 06/05/2019 - 05/31/2020	**Requested Budget Period:** 06/01/2020 - 05/31/2021
Report Term Frequency: Annual	**Date Submitted:** 04/14/2020
Program Director/Principal Investigator Information: TIMOTHY PATRICK SHEAHAN , PHD BS **Phone** **Email:** 5 U.S.C. § 552(b)(6)	**Recipient Organization:** UNIV OF NORTH CAROLINA CHAPEL HILL UNIVERSITY OF NORTH CAROLINA CHAPEL HILL Office of Sponsored Research CHAPEL HILL, NC 275990001 **DUNS:** 608195277 **EIN:** 1566001393A1 **RECIPIENT ID:**
Change of Contact PD/PI: N/A	
Administrative Official: R DAVID PAUL 104 Airport Dr. Suite 2200 Chapel Hill, NC 275991350 **Phone** **Email:** 5 U.S.C. § 552(b)(6)	**Signing Official:** RONDA FARRELL 104 Airport Dr Suite 2200 Chapel Hill, NC 27599 **Phone** **Email:** 5 U.S.C. § 552(b)(6)
Human Subjects: No	**Vertebrate Animals:** No
hESC: No	**Inventions/Patents:** No

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The major goals of the project are to determine if primary human lung cells infected with Middle East respiratory syndrome coronavirus (MERS-CoV) use epigenetic mechanisms to regulate the expression of interferon stimulated genes (ISG). Specific Aim 1: Does histone methylation status coordinate with ISG expression patterns in MERS-CoV infected MVE, HAE, and/or FB? Aim 1 focuses on defining cell type specific type I and III ISG for primary human lung airway epithelial cell cultures (HAE), microvascular endothelial cells (MVE) and fibroblasts (FB), identifying if transcription factors mediate any regulation of ISG expression, and determining if MERS-CoV infection affects the methylation state of lysine 4 or 27 on cellular histones which determine whether chromatin in in an open state and accessible for transcription or in a closed state preventing transcription from occurring. Specific Aim 2: Exploring modulation of host chromatin remodeling enzymes following MERS-COV infection of primary human lung MVE, HAE, FB. Aim 2 seeks to define the DNA/histone methyltransfersae and deaceytylatse enzymes MERS-CoV may be modulating to regulate ISG expression. Assays will determine if host chromatin remodeling enzymes are active or inhibited following MERS-CoV replication and whether MERS-CoV replication and/or ISG expression are affected by inhibition of methyltransferase/deaceytlse enzyme activity. Finally, we will use novel protein-protein interaction technologies to determine MERS-CoV proteins that may mediate the epigenetic regulation of ISG expression.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: Accomplishments.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Though there may be delays in completing experiments due to the shelter in place requirements for CoVID-19 - Prior to the end of the funding period we anticipate completing the following. Experiments to determine if histone modification plays a role in ISG differential expression in MERS-CoV infected FB will begin as soon as the shelter in place bans have been removed as all samples have been harvested and are in the freezer awaiting analysis. Existing lysate (from both MVE and FB) will also be used to explore if transcription factors contribute to regulation of ISG expression following MERS-CoV infection. Experiments to determine if the genes responsible for modifying chromatin structure are differentially expressed following MERS-CoV infection of primary human lung MVE and FB will be performed as described in Aim 2 using BioRad's PrimerPCR Pathway arrays. To determine if inhibition of enzymes that mediate chromatin structure rearrangement alters coronavirus replication and or changes the innate immune response to virus, drug efficacy studies will be performed, and infected treated samples will be assayed to determine levels of viral replication and cellular viability. If changes are detected in levels of viral replication additional samples will be generated to determine how ISG expression has been altered. We anticipate obtaining sufficient preliminary data for the submission of an RO1 by fall of 2021.

B.2 What was accomplished under these goals?

The ongoing MERS-CoV epidemic and recent identification of SARS-CoV 2 as the causative agent of coronavirus infectious disease 2019 (COVID-19) highlight the need for a better understanding of how highly pathogenic human coronaviruses manipulate the host immune response. Previous studies demonstrated that MERS-CoV infects an expanded range of human primary cell types including microvascular endothelial cells and lung fibroblasts which are not permissive for the 2002 SARS-CoV strain. In immortalized human lung epithelial cells, MERS-CoV downregulates the expression of several interferon stimulated genes (ISG) restricting the host innate immune response and previous studies suggest that this downregulation is mediated by epigenetic mechanisms that regulate the methylation state of histones keeping the chromatin in an inaccessible or closed state and upregulating the methylation of host DNA leading to a decrease in the expression of major histocompatibility complex genes. The goal of these studies was to determine if MERS-CoV uses epigenetic mechanisms to regulate the innate immune response in primary human lung endothelial cells (MVE) and fibroblasts (FB). Initial studies evaluated levels of infection in more than 20 donor tissues (all cell types collected for each donor) to determine which were best for the MERS-CoV epigenetic studies. Three donors were selected, and the University of North Carolina at Chapel Hill Tissue Procurement Core earmarked these frozen cell aliquots for these studies and sufficient numbers of cells are available for all studies within this funding application (**Figure 1**).

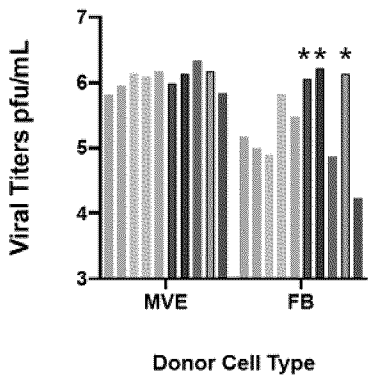

Figure 1. Representative MERS-CoV titers from tissue donor candidates for epigenetic experiments. MVE and FB from 20 donors were plated and infected with MERS-CoV for 24 hours and supernatants assessed by plaque assay to determine levels of viral replication. Three stars indicate the donors (only FB shown) used for downstream epigenetic testing. * highlight chosen donors.

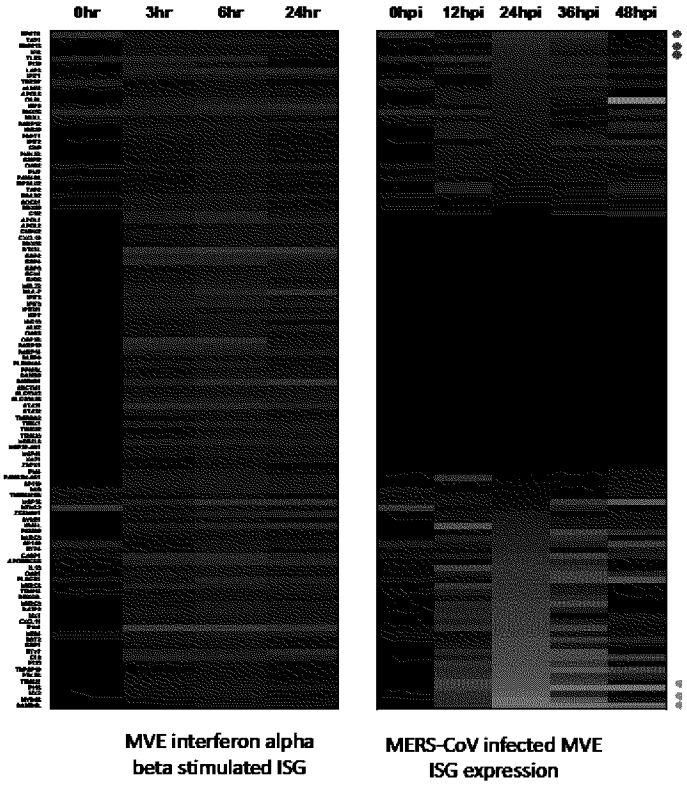

Figure 2 MERS-CoV regulates the innate immune response in primary human lung MVE. Left panel: Human lung MVE were treated with interferon alpha beta for the indicated times and ISG identified following microarray analysis. Right panel: ISG list identified in left panel following MERS-CoV infection of MVE. Red dots indicate up-regulated ISG used for ChIP-PCR studies; green dots indicate down-regulated ISG used for ChIP-PCR studies

Cell type specific lists of ISG from MVE and FB were generated following treatment of MVE and FB with interferon alpha/beta and the top six upregulated and downregulated (12 genes total per cell type) for each cell type were identified (**Table** and **Figure 2**). Triplicate samples of MVE and FB for all three donors were infected with MERS-CoV, protein and DNA crosslinked by formaldehyde, samples were safety tested and removed from biosafety level three. Due to the number of total samples to process analysis of one cell type at a time will be performed. Batch one analysis was performed on MERS-CoV infected MVE cells and has been completed. We anticipate that batch two analysis on MERS-CoV infected FB will be completed by the end of Year 1/May 2020,

but this work may be delayed until the shelter in place requirement has been removed. Formalin treated lysates from MERS-CoV infected MVE were assayed by chromatin immunoprecipitation-PCR (ChIP-PCR) using antisera specific for the open, transcriptionally active form of histone bound chromatin (lysine 4 in histone 3 (H3K4)) or for the closed transcriptionally inactive form of histone bound chromatin (lysine 27 in histone 3 (H3K27)) to determine if histone modifications could explain the differential expression of specific ISG. PCR is used to amplify the promoter regions of the ISG following immunoprecipitation to determine if the chromatin precipitated is in the active or inactive state following MERS-CoV infection (**Table**). Representative results are shown in **Figure 3** for two ISG with increased differential expression (interferon gamma inducible protein 6 (IFI 6) and ring finger protein 213 (RNF213)) or decreased expression (myeloid differentiation primary response protein 88 (MyD88) and sterile alpha motif domain containing 9L (SMAD9L)). Histones bound to the promoter regions of ISG that had upregulated expression (IFI 6 and RNF213) following MERS-CoV infection of MVE were predominantly methylated on lysine 4 and in the active confirmation for all three tissue donors (Figure 3 top panels) with little if any associate with histones in the closed confirmation. In contrast, histones bound to ISG promoter regions with decreased expression levels (SMAD9L and MyD88) were predominantly methylated on lysine 27 and in the closed confirmation with little associate with histones in the active confirmation. This data suggests that epigenetic regulation may play a role in down regulation of the innate immune response to MERS-CoV in primary human lung microvascular endothelial cells.

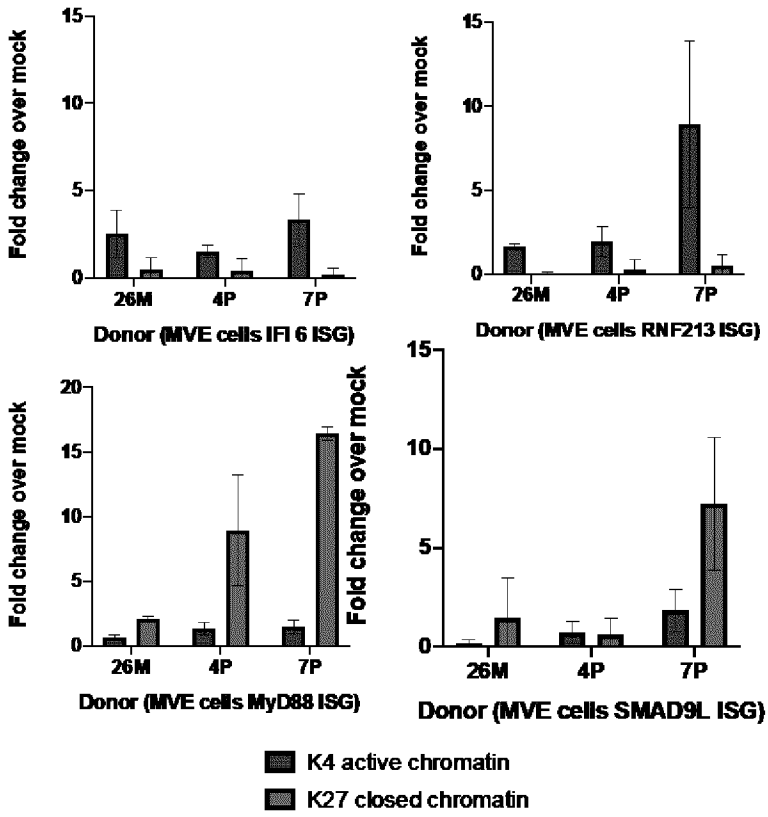

Figure 3 Altered histone methylation patterns suggest mechanism for ISG expression following MERS-CoV infection in primary human lung MVE. ChIP-PCR was performed on MERS-CoV infected MVE lysate for three donors. Antibodies specific for histones with lysine 4 methylation (shown in red) or for histones with lysine 27 methylation (shown in green) were used to precipitate chromatin and assayed by real time PCR. Top panels are ISG with increased expression following MERS-CoV infection and bottom panels are ISG with decreased expression following infection.

We are excited by the results from MERS-CoV infected MVE that suggest epigenetic regulation controls ISG expression in endothelial as well as epithelial lung cells. We anticipate similar findings from MERS-CoV infected fibroblasts and look forward to expanding our understanding of which enzymes that modify chromatin structure contribute to the regulation of the innate immune response following MERS-CoV infection.

On January 6, 2020 Dr. Sims began a new position as a senior scientist at the Pacific Northwest National Laboratory in Richland, Washington. She will continue the studies within this award as a collaboration with Drs. Timothy Sheahan and Alexandra Schaefer at the University of North Carolina at Chapel Hill.

Cell Type	Gene Name	Differential Gene Expression	Primer Pairs	Analysis as Predicted
MVE	Sterile alpha motif domain containing 9L (SMAD9L)	Down	cagcctcattttcgtagccctcat ggccatctacaagccaaggagaga	Yes
MVE	Interferon gamma inducible protein 16 (IFI 16)	Down	tcatagcagacatttccccaacca gcttcttctcccctcctttcctgt	Mixed between donors
MVE	Myeloid differentiation primary response 88 (MyD88)	Down	Cccctcctcacaggttcagtccta gagcatggcacaaccaagaaaaga	Yes
MVE	Epithelial stromal interaction 1 (EPSTI 1)	Up	ccaggttggagtacagtggcatga tacaacaattagctgggcgtggtg	Yes
MVE	Interferon alpha inducible protein 6 (IFI 6)	Up	cagcaggcagcacacaaatgttc agccaatccctgtcggagtttcta	Yes
MVE	Ring finger protein 213 (RNF213)	Up	ggatgaaggggtgagaggagaagg gtgtgaccagggacctccgtttta	Yes

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

No

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Nothing to report

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
TSHEAHAN	Y	Sheahan, Timothy Patrick	BS,PHD	PD/PI	1.0	0.0	0.0			NA
AMY_SIMS	Y	SIMS, AMY C	PHD	PD/PI	2.4	0.0	0.0			NA
	N	Schaefer, Alexandra		Staff scientist (Doctoral level)	3.0	0.0	0.0			NA
	N	Lam, Mariam		Technician	1.8	0.0	0.0			NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

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D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

OTHER SUPPORT

SHEAHAN, TIMOTHY

ACTIVE

R21AI146872 (PI: Sheahan/Sims) 06/05/19-05/30/21 0.60 cal months (5%
NIH **{THIS GRANT}** 5 U.S.C. § 552(b)(4)
How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
This proposal will build on foundational studies performed in continuous human lung cell lines and define ways that MERS-CoV regulates innate immunity in primary human lung fibroblasts and microvascular endothelial cells.
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

U19AI142759 CETR (PI: Whitley) 03/01/14-02/28/24 3.6 cal months (30%)
UAB/NIH/NIAID 5 U.S.C. § 552(b)(4)
Antiviral Drug Discovery and Development Center
The specific aims of the proposal will identify small molecule inhibitors of CoV fidelity and RNA capping, define their mechanism of action, and determine their efficacy against SARS-CoV and across CoV families using in vivo mouse models of acute and persistent CoV disease.
Role: Investigator
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01 AI131688-01 (PI: Rice) 03/15/17-02/281/22 1.8 cal months (15%)
Rockefeller/NIH 5 U.S.C. § 552(b)(4)
Analysis of immunity, viral adaptation and pathogenesis in a new mouse model of HCV-related rodent hepacivirus infection
Mechanisms that contribute to the persistence of hepatotropic viruses, such as HCV, are not well understood. We have recently established the first immune-competent mouse model of an HCV-related virus. With this new model, we propose to systematically study immunity and host-virus interactions during a hepatotropic RNA virus infection in vivo.
Role: Subcontract PI
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01 AI132178-01 (MPI: Sheahan/Baric) 08/09/17-07/31/22 2.4 cal months (20%)
NIH 5 U.S.C. § 552(b)(4)
Broad-spectrum antiviral GS-5734 to treat MERS-CoV and related emerging CoV
In partnership with Gilead Sciences, we aim to accelerate the preclinical development of GS-5734 and promote IND licensure. We define the pharmacokinetics, pharmacodynamics, resistance profile, efficacy breadth and mechanism of action of GS-5734 against MERS-CoV and related emerging CoV.
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01AI108197-06 (MPI: Baric/Denison) 03/01/18-02/28/23 1.8 cal months (15%)
Vanderbilt/NIH 5 U.S.C. § 552(b)(4)
Determinants of Coronavirus Fidelity in Replication and Pathogenesis
To identify common and unique determinants of CoV nsp14-ExoN functions CoV replication, fidelity and IFN sensitivity across CoVs; To determine pathways of adaptation to loss of nsp14-ExoN activity in vitro and in vivo; and to define mechanisms of ExoN-regulated CoV sensitivity to the innate antiviral immune response.
Role: Co-Investigator

Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

U01AI149644 (PI: Baric) 04/19/19-03/31/24 1.8 cal months (15%)
NIH 5 U.S.C. § 552(b)(4)
Respiratory Virus Vaccine and Adjuvant Exploration
Vaccination is one of the most effective public health measures for protecting against infectious disease, and the proposed studies will identify adjuvants and adjuvant combinations that safely elicit long lived protective immunity against emerging pathogens in at risk populations.
Role: Investigator
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

PENDING:
R01 (PI: Meshnick) 04/01/20-03/31/25 0.36 cal months (3%)
NIH 5 U.S.C. § 552(b)(4)
Molecular epidemiology of arboviruses in the Democratic Republic of the Congo
The grant is innovative in its multidisciplinarity, combining epidemiological, entomological, serological, phylogenetic and basic sciences approaches. Together, this research will, for the first time, provide data on the incidence, types, sources, and genomic traits of this important group of viruses in Central Africa.
Foreign component funded by this grant: Yes
Foreign investigators: Antoinette Tshefu, University of Kinshasa (Congo, Democratic Republic)
Supplied by foreign site: Patient Samples
Technology transfer to foreign site: No

R21 (PI: Sheahan) 07/01/20-06/30/22 0.90 cal months (7.5%)
NIH 5 U.S.C. § 552(b)(4)
Characterization of hepacivirus pathogenesis, viral adaptation and the mapping of host susceptibility alleles in the Collaborative Cross
The goals of this proposal are to: 1) phenotype the kinetics of virus replication/adaptation, pathogenesis and the host response in CC lines with delayed clearance and chronic infection and 2) to map the genetic determinants driving virus titer, viral evolution, clearance, weight loss, blood leukocyte modulation, and chronic infection
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

Not Assigned (PI: Baric) 07/01/20-06/30/25 0.36 cal months (3%)
EcoHealth Alliance 5 U.S.C. § 552(b)(4)
US-China Collab: Spillover, co-infection, and control of bat-origin livestock coronaviruses
To develop an economic model of farm profit maximization linked to the compartmental epidemiological model of co-infection disease.*Foreign component funded by this grant: No*

OVERLAP: If any of the pending awards are funded, Dr. Sheahan will reduce is effort accordingly to not exceed 12 calendar months.

Other Support

SIMS, AMY

ACTIVE

R21AI146872 (Sims/Sheahan) 06/05/19-05/31/21 2.4 cal months
UNC Chapel Hill/NIH 5 U.S.C. § 552(b)(4) **{THIS GRANT}**
How MERS-CoV regulates the innate immune response
The major goal of the project is to determine if primary human lung cells infected with Middle East respiratory syndrome coronavirus (MERS-CoV) use epigenetic mechanisms to regulate the expression of interferon stimulated genes.

Foreign component funded by grant: No

There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

LDRD (Sims) 03/07/20-09/30/21 4.4 cal months
Pacific Northwest National Laboratory **5 U.S.C. § 552(b)(4)**
Defining coronavirus lipidomic response
The goal of this project is to characterize the lipid response to coronavirus infection.

Foreign component funded by grant: No

There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

PENDING

Not Applicable

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

On January 6, 2020 Dr. Sims began a new position at Pacific Northwest National Laboratory (PNNL) in Richland, Washington. Dr. Sims will continue to collaborate with Drs. Sheahan and Schaefer at the University of North Carolina at Chapel Hill (UNC) to meet the goals of this funded project. Funds for Year 1 have been appropriately distributed between the PNNL and UNC to allow work to continue at both sites. Prior to the start of Year 2, we anticipate petitioning NIH/NIAID/UNC to transition the award to PNNL allowing Dr. Sims to resume as Principle Investigator. Funds would then be distributed to UNC via subcontract to continue the collaboration and to ensure forward progress on the proposed work.

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

No

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: University of North Carolina at Chapel Hill	608195277	NC-004	104 Airport Drive, Suite 2200, CB 1350 Chapel Hill NC 275991350
Pacific Northwest National Laboratory	032987476	WA-004	902 Battelle Boulevard P.O. Box 999, MSIN J4-02 Richland WA 993520999

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Mon 6/8/2020 3:25:38 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: A little help please

It is no problem at all…just glad others are doing what they need to do to get the ball rolling for you!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 8, 2020 6:25 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: A little help please

You're a miracle worker!! Thank you very much! I think I owe you a boon!

I was thinking a gift card or would you prefer flowers? Your call! Thank you very much! Amy

---

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Monday, June 8, 2020 at 3:22 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: A little help please

FYI: See attachment!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 8, 2020 5:51 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: A little help please

Hi Chandra,

I hate to bug you again but one more thing please!

The report that you sent to me still says "draft" at the top of each page of the pdf. Do you have another pdf that does not have draft on it?

Thank you, Amy

PS. I hope you are doing well! ACS

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Thursday, May 28, 2020 at 3:04 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: A little help please

Hi Amy,

Attached is the progress report. However, you can't go by the amount that is on the progress report since the notice of award was issued to UNC before the relinquish statement was submitted. Therefore, they had to include the

amount for your year 2 award along with the remaining balance from year 1.

You will have to ask Carol for the info since she completed the relinquish statement and shared it with Vicki to get her approval before sending it to OSR to submit and process.

Thanks,
Chandra

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, May 28, 2020 5:58 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: A little help please

Hi Chandra,
Is it possible for you to tell me exactly how much carry forward UNC reported to the NIH for the R21 that is being relinquished? We are working on that paperwork and I am not sure of the exact dollar amount that was left over.

If it is easier and contained within the progress report you can just send me that!

I hope you are doing well and that life is getting a little easier at UNC. I hope you got to do something fun over the long weekend. Thank you very much! Amy

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Mon 6/8/2020 3:42:42 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: A little help please

That's fine since there is always something that can be ordered!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 8, 2020 6:42 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: A little help please

I appreciate it. If you leave me to my own devices it will be Amazon as they have a little bit of everything. Thank you, Amy

---

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Monday, June 8, 2020 at 3:25 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: A little help please

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Date: Monday, June 8, 2020 at 3:22 PM
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Subject: RE: A little help please

FYI: See attachment!

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not have draft on it?

Thank you, Amy

PS. I hope you are doing well! ACS

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Thursday, May 28, 2020 at 3:04 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: A little help please

Hi Amy,

Attached is the progress report. However, you can't go by the amount that is on the progress report since the notice of award was issued to UNC before the relinquish statement was submitted. Therefore, they had to include the amount for your year 2 award along with the remaining balance from year 1.

You will have to ask Carol for the info since she completed the relinquish statement and shared it with Vicki to get her approval before sending it to OSR to submit and process.

Thanks,
Chandra

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, May 28, 2020 5:58 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: A little help please

Hi Chandra,
Is it possible for you to tell me exactly how much carry forward UNC reported to the NIH for the R21 that is being relinquished? We are working on that paperwork and I am not sure of the exact dollar amount that was left over.

If it is easier and contained within the progress report you can just send me that!

I hope you are doing well and that life is getting a little easier at UNC. I hope you got to do something fun over the long weekend. Thank you very much! Amy

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Mon 6/8/2020 3:51:06 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: A little help please

You are just TOO much!! I just received it. Thank you very much since it may go towards a neck massager after dealing with your former colleague – who are now starting to realize EVERYTHING you did!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 8, 2020 6:49 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: A little help please

Cool. You should get it soon!

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Monday, June 8, 2020 at 3:42 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: A little help please

That's fine since there is always something that can be ordered!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 8, 2020 6:42 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: A little help please

I appreciate it. If you leave me to my own devices it will be Amazon as they have a little bit of everything. Thank you, Amy

---

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Monday, June 8, 2020 at 3:25 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: A little help please

It is no problem at all…just glad others are doing what they need to do to get the ball rolling for you!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 8, 2020 6:25 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: A little help please

You're a miracle worker!! Thank you very much! I think I owe you a boon!

I was thinking a gift card or would you prefer flowers? Your call! Thank you very much! Amy

---

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Monday, June 8, 2020 at 3:22 PM

To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: A little help please

FYI: See attachment!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 8, 2020 5:51 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: A little help please

Hi Chandra,

I hate to bug you again but one more thing please!

The report that you sent to me still says “draft” at the top of each page of the pdf. Do you have another pdf that does not have draft on it?

Thank you, Amy

PS. I hope you are doing well! ACS

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Thursday, May 28, 2020 at 3:04 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: A little help please

Hi Amy,

Attached is the progress report. However, you can’t go by the amount that is on the progress report since the notice of award was issued to UNC before the relinquish statement was submitted. Therefore, they had to include the amount for your year 2 award along with the remaining balance from year 1.

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I hope you are doing well and that life is getting a little easier at UNC. I hope you got to do something fun over the long weekend. Thank you very much! Amy

From: Fulcher, Leslie[leslie_fulcher@med.unc.edu]
Sent: Wed 6/10/2020 3:03:35 AM (UTC-07:00)
To: Ames, Amber A[Amber.Ames@pnnl.gov]; Koltz, Diane M[dkoltz@email.unc.edu]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Fulcher, Leslie[leslie_fulcher@med.unc.edu]
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form
Attachment: PNNL MLI Order Form Oct2019 (002).docx

Good Morning Amber,
Yes, once the contract is executed, Amy will be able to order as needed up to the dollar amount on the contract and during the 1 year period. I am including our contract specialist who can look at your suggested changes and she will be in touch with you soon.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 9:02 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Thanks, Leslie. The project would like to be able to order up to 10 ALI medium and 26 Normal HBE Cells from now until September 30, 2021. Are they able to order on an as-needed basis? I can incorporate a signed version of the attached into the PO for the project to use? Once I sign it, they won't be able to edit it. Perhaps we need to do a purchase order per order?

I note I provided redlines on the attached. Please advise if UNCC is able to work with the redlines.

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
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To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,
Thanks for emailing back, but to complete the contract, I need the agreement signed and returned to me prior to ordering. As for payment options, a check is fine, but we do have an account that funds could be wired. If that works for you, I can share that information.
Thank you,
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Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

Attached please find Purchase Order No. 521567 to purchase up to the quantities I had listed below. Per the PO, we will place orders via the ordering website. There is no need to sign the PO—if you can acknowledge receipt and that this will work for ordering/payment purposes, that would be helpful.

I'm guessing the MLI Tissue Procurement and Cell Culture Core Facility will want a paper check mailed to the 125 Mason Farm Road address instead of paid by ACH to UNCC's main Bank of America account?

Amy, the shipping address in PES is 331 Building, Room 70. Even if a different shipping address is input in the UNCC online ordering system, any orders associated with PO 521567 will ship to 331/70. If you need a different ship to, let me know.

Thanks!

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 12:36 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,

As long as the contract is signed, the dollar amount is entered, and the period is in place there will be no rate increase.
You don't need to select the quantity of any item, but if your project you will use the quantity listed below, entering in the dollar amount is sufficient. I may suggest adding a little wiggle room in the dollar amount because once the dollar amount is reached, even before the term is up, we will need to renew the contract.

Also, once the contract is executed, you would just log onto our ordering website and order what you need.
Please let me know if you have any questions.

Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>

Sent: Tuesday, June 9, 2020 1:19 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

I have a requisition to issue a Purchase Order to UNCC for a fixed unit rate contract for the following:

Description	Price	Maximum Quantity Expected	Extended Price
BEGM MEDIUM	(b) (4)		
ALI MEDIUM			
VALI MEDIUM			
Normal HBE Cells			
Diseased HBE Cells			
Cystic Fibrosis HBE Cells			
Normal Microvascular Cells			
Normal Fibroblast Cells			
Total Not to Exceed Amount			(b) (4)

The project would like to use the purchase order for payment of requirements on an as-needed basis through September 30, 2021.

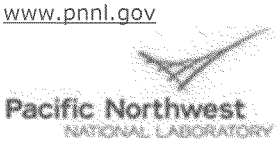
My question is how long the pricing in Exhibit A of the attached is valid? Are the prices updated annually?

Do you have any concerns with this approach?

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.

Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov



The University of North Carolina at Chapel Hill

MLI Tissue Procurement and Cell
Culture Core Facility
Recharge Core Agreement

The University of North Carolina at Chapel Hill
MLI Tissue Procurement and Cell Culture Core Facility
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Road
Room 1119 Marsico Hall, CB 7248
Chapel Hill, NC 27599-7361

Make checks payable to: The University of North Carolina at Chapel Hill

Remit payment to:
University of North Carolina - Chapel Hill
MLI Tissue Procurement and Cell Culture Core Facility
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Road
Room 1119 Marsico Hall, CB 7248
Tax ID#: 56-600-1393

Payment Terms: Net 30 days upon receipt of invoice

Not to Exceed Cost: $ _____

Start Date:_____End Date: _____

Payment Method: PO_____Credit Card _____

Client
Client Name: _____Contact Name: _____

Mailing Address: _____
_____
_____
_____

Phone Number: _____
Contact E-mail Address:_____

Send Invoice to: (if different from above):
Name:_____Email

Address:
_____
_____

Description of Services):
Specialized services related to provision of human primary lung cells and custom media in accordance with Exhibit A attached hereto.

Terms and Conditions

1) Services. The University of North Carolina at Chapel Hill ("University") possesses expertise and related technologies and equipment through its MLI Tissue Procurement and Cell Culture Core Facility ("Facility"). Client has instructed University to undertake the specific services described above (the "Services"). In consideration of Client's payment to the Facility in accordance with the terms stated herein, the Facility shall perform the Services.

2) Reports. Facility shall provide Client with a report regarding the data obtained in the course of the Services. The report shall be maintained as confidential pursuant to Section 3 below. Client recognizes that the results of the Services which do not disclose Confidential Information provided hereunder may be deemed publishable by University, and that the University employees engaged in the Services shall be free to publish these results, consistent with the obligations imposed in Section 3 of this Agreement.

3) Confidentiality. Any confidential or proprietary information disclosed by Client to University ("Confidential Information") shall be disclosed in writing and designated as confidential and/or proprietary, or if disclosed orally, shall be confirmed in writing and designated confidential and/or proprietary within thirty (30) days of such disclosure. University shall use the Confidential Information only for the purpose of this Agreement and further agrees that it will not disclose or publish such Confidential Information except that the foregoing restrictions shall not apply to: (a) Confidential Information which is or becomes publicly known through no breach of this agreement by University; (b) Confidential Information learned from a third party entitled to disclose such information; (c) Confidential Information already known to or developed by University prior to receipt hereunder, or information independently developed at any time by University personnel not privy to the Confidential Information, as shown by University's written records; or (d) Confidential Information required to be disclosed by operation of law (including, but not limited to, the North Carolina Public Records Act) or court order. The obligation of confidentiality imposed by this Section shall expire three (3) years following the expiration or termination of this Agreement. University will use a reasonable degree of care to prevent the inadvertent, accidental, unauthorized, or mistaken disclosure or use by its employees of Confidential Information. For avoidance of doubt, data, information, results, materials, or products of the Services shall be considered Confidential Information for the purposes of this Agreement.

4) Intellectual Property. It is not anticipated that intellectual property will arise in University's performance of the Services. However, in the event of an invention by at least one employee of University the intellectual property shall be owned as follows: a) Inventions which involve the use of, composition of, or improvement to Client-provided materials or information, or a derivative, analogue thereof shall belong to Client; and b) Inventions which cover a scientific or analytical measurement process, technique, procedure, medium, device or other process which is not unique to characterizing, testing, or fabricating Client's proprietary materials or does not derive from Client-provided materials or Client's Confidential Information shall be owned by University.

5) Publicity. Neither party will use the name of the other party in any publicity, advertising, or news release without the prior written approval of the authorized representative of the other party.

6) Termination. Either party may terminate this Agreement upon prior written notice to the other party. All reasonable costs and non-cancelable obligations incurred by University at the time of said termination shall be reimbursed by Client. At the request of Client, all unused Client-provided materials at the time of termination shall either be returned to Client or destroyed by University as negotiated with the Client.

7) Independent Contractor. In the performance of the Services, University shall be deemed to be and shall be an independent contractor.

8) No Warranties and Indemnity. University makes no warranties, express or implied, regarding the quality of product produced under this Agreement. University shall use its reasonable efforts to perform the Services. University does not warrant or guarantee any results from a given project. University shall not be liable for Client's use of the report or other information provided by University.

9) Export Control. University will not accept export-controlled materials or technical information under this Agreement. Client hereby represents and warrants that materials and technical information provided to University do not require any license from the U.S. government before being exported.

10) Hazardous Materials. All materials provided by Client must be accompanied by the appropriate environmental and safety information for those materials as required by law.

11) Governing Law. This Agreement shall be governed and construed in accordance with the laws of the State of North Carolina.

12) Entire Agreement. The terms and conditions of Purchase Order No. 521567 supplement this agreement.

Check one:

_____No Client employees will work in University facilities in connection with this Agreement

_____Client employees will be performing work related to this Agreement in University facilities.

By Authorized Official of The University of North Carolina at Chapel Hill	By Authorized Official of Client
By:_____	By: _____
Name: acting on behalf of Terry Magnuson, PhD	Name: _____
Title: Vice Chancellor for Research	Title: _____
Date: _____	Date: _____

EXHIBIT A

MARSICO LUNG INSTITUTE

Tissue Procurement and Cell Culture Core

EXTERNAL PRICING

MEDIA	
BEGM MEDIUM	(b) (4)
ALI MEDIUM	(b) (4)
VALI MEDIUM	(b) (4)
HUMAN BRONCHIAL EPITHELIAL CELLS	
Normal HBE Cells	(b) (4)
Diseased HBE Cells	(b) (4)
Cystic Fibrosis HBE Cells	(b) (4)
OTHER HUMAN LUNG CELLS	
Normal Microvascular Cells	(b) (4)
Normal Fibroblast Cells	(b) (4)

DESCRIPTIONS

MEDIA	
BEGM MEDIUM	Bronchial epithelial growth media for expansion of cells on plastic
ALI MEDIUM	Air-Liquid interface media for differentiation of cells on porous supports
VALI MEDIUM	Vertex-ALI for differentiation of cells on porous supports (contains Ultroser G)

HUMAN BRONCHIAL EPITHELIAL CELLS	
Normal Donors	No history of prior chronic lung disease, smoker or non-smoker
Diseased Donors	History of prior chronic lung disease— (COPD, asthma)
Cystic Fibrosis Donors	Homozygous severe CFTR mutation— (F508del/F508del)
Cystic Fibrosis Donors	Heterozygous F508del/second severe CFTR mutation— (F508del/Other)
Cystic Fibrosis Donors	Non F508del CFTR mutations— (Other CF/Other CF)

OTHER HUMAN LUNG CELLS	
Normal Microvascular Cells	No history of prior chronic lung disease
Normal Fibroblast Cells	No history of prior chronic lung disease

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 6/17/2020 8:14:03 AM (UTC-07:00)
To: Schaefer, Alexandra[aschaefe@email.unc.edu]
Subject: FW: QIAGEN account manager

Alex,

I finally got an answer from Qiagen and you are not going to like it. They have discontinued the kit you were using and Qiagen is not offering any alternatives.

Let me know how I can assist in finding another product. I hate to bring you bad news but I guess this happens sometimes.

I hope you are doing well otherwise. Thank you, Amy

From: Terrie Wright - QIAGEN <Terrie.Wright@qiagen.com>
Date: Wednesday, June 17, 2020 at 7:38 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: QIAGEN account manager

Hi Amy,
I have an unfortunate update. It looks like this has been fully discontinued. I also reached out to Technical Support to see if we have any alternatives and there aren't. I apologize.
Terrie

From: Sims, Amy C [mailto:amy.sims@pnnl.gov]
Sent: Tuesday, June 16, 2020 11:06 AM
To: Terrie Wright - QIAGEN <Terrie.Wright@qiagen.com>
Subject: Re: QIAGEN account manager

Caution: This email originated from outside QIAGEN. If you believe it to be suspicious, please report it using the 'Report Message' button in Outlook or via the QIAGEN Service Portal.

Hi Terrie,

That is great news. The catalog number is EpiTect ChIP OneDay Kit, Qiagen # 334471

If you can follow up with me on availability I will loop in the UNC group in the next round of emails. Thank you very much! Amy

PS. The lack of communication has been going on for most of 2020.

From: Terrie Wright - QIAGEN <Terrie.Wright@qiagen.com>
Date: Tuesday, June 16, 2020 at 8:51 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: QIAGEN account manager

Hi Amy,

Can you confirm the catalog number, just to be on the safe side that we are speaking of the same kit?
My apologies for the UNC account manager. Are there specific people that need follow up? I can help facilitate. Jeremy usually is good with follow up though I know his wife just had twins recently so that might be causing delays.

Kind regards,
Terrie

From: Sims, Amy C [mailto:amy.sims@pnnl.gov]
Sent: Monday, June 15, 2020 3:06 PM
To: Terrie Wright - QIAGEN <Terrie.Wright@qiagen.com>
Subject: Re: QIAGEN account manager

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Hi Terrie,

That is great news. I have a collaborative project with UNC Chapel Hill and they are having a really hard time obtaining Qiagen products and their representative has been hard to communicate with.

My colleagues need several EpiTect ChIP OneDay kits. Can you please tell me if they are in stock and if so how many are available. If they are not in stock when does Qiagen expect to have them again?

Thank you very much for your assistance. Best wishes, Amy

From: Terrie Wright - QIAGEN <Terrie.Wright@qiagen.com>
Date: Monday, June 15, 2020 at 12:52 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: QIAGEN account manager

Hi Dr. Sims,
I received your message and am happy to help!

Terrie Wright
Senior Customer Solutions Manager, Transitional Accounts SE, NW

QIAGEN - Sample to Insight
QIAGEN Inc.
Life Science Sales

Direct Phone: 1.240.686.7545
Phone: 1.800.426.8157 ext 67545
Mobile : 1.850.206.1796
Fax: 1.240.686.3844

Terrie.Wright@qiagen.com
www.QIAGEN.com



Automation improves workflow efficiency and quality of results. Explore this link to see which automation solution is right for you and contact us for more information or a personalized demo.

www.qiagen.com/automateme

From: Ames, Amber A[Amber.Ames@pnnl.gov]
Sent: Thur 6/18/2020 9:58:11 AM (UTC-07:00)
To: Fulcher, Leslie[leslie_fulcher@med.unc.edu]; Koltz, Diane M[dkoltz@email.unc.edu]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form
Attachment: PNNL MLI Order Form Oct2019 (002).docx

Just checking in to see if there is a response to our requested changes to the order form terms.

Thanks so much!

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Wednesday, June 10, 2020 3:04 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Koltz, Diane M <dkoltz@email.unc.edu>
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Battelle Memorial Institute
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902 Battelle Blvd.
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Tel: (509) 371-7050
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Pacific Northwest
NATIONAL LABORATORY

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Dear Leslie,

I have a requisition to issue a Purchase Order to UNCC for a fixed unit rate contract for the following:

Description	Price	Maximum Quantity Expected	Extended Price
BEGM MEDIUM			
ALI MEDIUM			
VALI MEDIUM			
Normal HBE Cells			
Diseased HBE Cells			
Cystic Fibrosis HBE Cells			
Normal Microvascular Cells			
Normal Fibroblast Cells			
Total Not to Exceed Amount			(b) (4)

(b) (4)

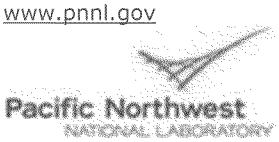
The project would like to use the purchase order for payment of requirements on an as-needed basis through September 30, 2021.

My question is how long the pricing in Exhibit A of the attached is valid? Are the prices updated annually?

Do you have any concerns with this approach?

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov



The University of North Carolina at Chapel Hill

MLI Tissue Procurement and Cell
Culture Core Facility
Recharge Core Agreement

The University of North Carolina at Chapel Hill
MLI Tissue Procurement and Cell Culture Core Facility
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Road
Room 1119 Marsico Hall, CB 7248
Chapel Hill, NC 27599-7361

Make checks payable to: The University of North Carolina at Chapel Hill

Remit payment to:
University of North Carolina - Chapel Hill
MLI Tissue Procurement and Cell Culture Core Facility
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Road
Room 1119 Marsico Hall, CB 7248
Tax ID#: 56-600-1393

Payment Terms: Net 30 days upon receipt of invoice

Not to Exceed Cost: $ _____

Start Date:_____End Date: _____

Payment Method: PO_____Credit Card _____

Client
Client Name: _____Contact Name: _____

Mailing Address: _____
_____
_____
_____

Phone Number: _____
Contact E-mail Address:_____

Send Invoice to: (if different from above):
Name:_____Email

Address:
_____
_____

Description of Services):
Specialized services related to provision of human primary lung cells and custom media in accordance with Exhibit A attached hereto.

Terms and Conditions

1) Services. The University of North Carolina at Chapel Hill ("University") possesses expertise and related technologies and equipment through its MLI Tissue Procurement and Cell Culture Core Facility ("Facility"). Client has instructed University to undertake the specific services described above (the "Services"). In consideration of Client's payment to the Facility in accordance with the terms stated herein, the Facility shall perform the Services.

2) Reports. Facility shall provide Client with a report regarding the data obtained in the course of the Services. The report shall be maintained as confidential pursuant to Section 3 below. Client recognizes that the results of the Services which do not disclose Confidential Information provided hereunder may be deemed publishable by University, and that the University employees engaged in the Services shall be free to publish these results, consistent with the obligations imposed in Section 3 of this Agreement.

3) Confidentiality. Any confidential or proprietary information disclosed by Client to University ("Confidential Information") shall be disclosed in writing and designated as confidential and/or proprietary, or if disclosed orally, shall be confirmed in writing and designated confidential and/or proprietary within thirty (30) days of such disclosure. University shall use the Confidential Information only for the purpose of this Agreement and further agrees that it will not disclose or publish such Confidential Information except that the foregoing restrictions shall not apply to: (a) Confidential Information which is or becomes publicly known through no breach of this agreement by University; (b) Confidential Information learned from a third party entitled to disclose such information; (c) Confidential Information already known to or developed by University prior to receipt hereunder, or information independently developed at any time by University personnel not privy to the Confidential Information, as shown by University's written records; or (d) Confidential Information required to be disclosed by operation of law (including, but not limited to, the North Carolina Public Records Act) or court order. The obligation of confidentiality imposed by this Section shall expire three (3) years following the expiration or termination of this Agreement. University will use a reasonable degree of care to prevent the inadvertent, accidental, unauthorized, or mistaken disclosure or use by its employees of Confidential Information. For avoidance of doubt, data, information, results, materials, or products of the Services shall be considered Confidential Information for the purposes of this Agreement.

4) Intellectual Property. It is not anticipated that intellectual property will arise in University's performance of the Services. However, in the event of an invention by at least one employee of University the intellectual property shall be owned as follows: a) Inventions which involve the use of, composition of, or improvement to Client-provided materials or information, or a derivative, analogue thereof shall belong to Client; and b) Inventions which cover a scientific or analytical measurement process, technique, procedure, medium, device or other process which is not unique to characterizing, testing, or fabricating Client's proprietary materials or does not derive from Client-provided materials or Client's Confidential Information shall be owned by University.

5) Publicity. Neither party will use the name of the other party in any publicity, advertising, or news release without the prior written approval of the authorized representative of the other party.

6) Termination. Either party may terminate this Agreement upon prior written notice to the other party. All reasonable costs and non-cancelable obligations incurred by University at the time of said termination shall be reimbursed by Client. At the request of Client, all unused Client-provided materials at the time of termination shall either be returned to Client or destroyed by University as negotiated with the Client.

7) Independent Contractor. In the performance of the Services, University shall be deemed to be and shall be an independent contractor.

8) No Warranties and Indemnity. University makes no warranties, express or implied, regarding the quality of product produced under this Agreement. University shall use its reasonable efforts to perform the Services. University does not warrant or guarantee any results from a given project. University shall not be liable for Client's use of the report or other information provided by University.

9) Export Control. University will not accept export-controlled materials or technical information under this Agreement. Client hereby represents and warrants that materials and technical information provided to University do not require any license from the U.S. government before being exported.

10) Hazardous Materials. All materials provided by Client must be accompanied by the appropriate environmental and safety information for those materials as required by law.

11) Governing Law. This Agreement shall be governed and construed in accordance with the laws of the State of North Carolina.

12) Entire Agreement. The terms and conditions of Purchase Order No. 521567 supplement this agreement.

Check one:

_____No Client employees will work in University facilities in connection with this Agreement

_____Client employees will be performing work related to this Agreement in University facilities.

By Authorized Official of The University of North Carolina at Chapel Hill	By Authorized Official of Client
By:_____	By: _____
Name: acting on behalf of Terry Magnuson, PhD	Name: _____
Title: Vice Chancellor for Research	Title: _____
Date: _____	Date: _____

EXHIBIT A

MARSICO LUNG INSTITUTE

Tissue Procurement and Cell Culture Core

EXTERNAL PRICING

MEDIA	
BEGM MEDIUM	$360/Liter
ALI MEDIUM	$360/Liter
VALI MEDIUM	$525/Liter
HUMAN BRONCHIAL EPITHELIAL CELLS	
Normal HBE Cells	$800/Million
Diseased HBE Cells	$800/Million
Cystic Fibrosis HBE Cells	$2225/Million
OTHER HUMAN LUNG CELLS	
Normal Microvascular Cells	$800/Million
Normal Fibroblast Cells	$800/Million

DESCRIPTIONS

MEDIA	
BEGM MEDIUM	Bronchial epithelial growth media for expansion of cells on plastic
ALI MEDIUM	Air-Liquid interface media for differentiation of cells on porous supports
VALI MEDIUM	Vertex-ALI for differentiation of cells on porous supports (contains Ultroser G)

HUMAN BRONCHIAL EPITHELIAL CELLS	
Normal Donors	No history of prior chronic lung disease, smoker or non-smoker
Diseased Donors	History of prior chronic lung disease— (COPD, asthma)
Cystic Fibrosis Donors	Homozygous severe CFTR mutation— (F508del/F508del)
Cystic Fibrosis Donors	Heterozygous F508del/second severe CFTR mutation— (F508del/Other)
Cystic Fibrosis Donors	Non F508del CFTR mutations— (Other CF/Other CF)

OTHER HUMAN LUNG CELLS	
Normal Microvascular Cells	No history of prior chronic lung disease
Normal Fibroblast Cells	No history of prior chronic lung disease

From: Koltz, Diane M[dkoltz@email.unc.edu]
Sent: Thur 6/18/2020 11:05:34 AM (UTC-07:00)
To: Ames, Amber A[Amber.Ames@pnnl.gov]; Fulcher, Leslie[leslie_fulcher@med.unc.edu]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I received your changes for review and upon a first look, UNC cannot agree to all of the supplemental terms contained in the online documents you want to include. As a state institution, we are somewhat limited. The order form contains the minimal terms UNC requires in its contracts and we typically do not agree to changes. Is there any possibility that we could make UNC's agreement control, or not reference the terms at all, since much of what is contained in the online "purchase agreements" won't apply to what we are providing. If this is not possible, please provide me word versions of the online agreements so I can outline our requested edits and comments. Also, please note that review of the documents will take time.

Thanks,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Thursday, June 18, 2020 12:58 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Just checking in to see if there is a response to our requested changes to the order form terms.

Thanks so much!

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Wednesday, June 10, 2020 3:04 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Good Morning Amber,
Yes, once the contract is executed, Amy will be able to order as needed up to the dollar amount on the contract and during the 1 year period. I am including our contract specialist who can look at your suggested changes and she will be in touch with you soon.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 9:02 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C

<amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Thanks, Leslie. The project would like to be able to order up to 10 ALI medium and 26 Normal HBE Cells from now until September 30, 2021. Are they able to order on an as-needed basis? I can incorporate a signed version of the attached into the PO for the project to use? Once I sign it, they won't be able to edit it. Perhaps we need to do a purchase order per order?

I note I provided redlines on the attached. Please advise if UNCC is able to work with the redlines.

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 5:29 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,
Thanks for emailing back, but to complete the contract, I need the agreement signed and returned to me prior to ordering. As for payment options, a check is fine, but we do have an account that funds could be wired. If that works for you, I can share that information.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 5:09 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

Attached please find Purchase Order No. 521567 to purchase up to the quantities I had listed below. Per the PO, we will place orders via the ordering website. There is no need to sign the PO—if you can acknowledge receipt and that this will work for ordering/payment purposes, that would be helpful.

I'm guessing the MLI Tissue Procurement and Cell Culture Core Facility will want a paper check mailed to the 125 Mason Farm Road address instead of paid by ACH to UNCC's main Bank of America account?

Amy, the shipping address in PES is 331 Building, Room 70. Even if a different shipping address is input in the UNCC online ordering system, any orders associated with PO 521567 will ship to 331/70. If you need a different ship to, let me know.

Thanks!

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050

amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 12:36 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,

As long as the contract is signed, the dollar amount is entered, and the period is in place there will be no rate increase.
You don't need to select the quantity of any item, but if your project you will use the quantity listed below, entering in the dollar amount is sufficient. I may suggest adding a little wiggle room in the dollar amount because once the dollar amount is reached, even before the term is up, we will need to renew the contract.

Also, once the contract is executed, you would just log onto our ordering website and order what you need.
Please let me know if you have any questions.

Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 9, 2020 1:19 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

I have a requisition to issue a Purchase Order to UNCC for a fixed unit rate contract for the following:

Description	Price	Maximum Quantity Expected	Extended Price
BEGM MEDIUM	(b) (4)	[redacted]	[redacted]
ALI MEDIUM	(b) (4)	[redacted]	[redacted]
VALI MEDIUM	(b) (4)	[redacted]	[redacted]
Normal HBE	(b) (4)	[redacted]	[redacted]

Cells			
Diseased HBE Cells	(b) (4)	[redacted]	[redacted]
Cystic Fibrosis HBE Cells	(b) (4)	[redacted]	[redacted]
Normal Microvascular Cells	(b) (4)	[redacted]	[redacted]
Normal Fibroblast Cells	(b) (4)	[redacted]	[redacted]
Total Not to Exceed Amount			(b) (4)

The project would like to use the purchase order for payment of requirements on an as-needed basis through September 30, 2021.

My question is how long the pricing in Exhibit A of the attached is valid? Are the prices updated annually?

Do you have any concerns with this approach?

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Sorensen, Kerstin[sorensen@email.unc.edu]
Sent: Fri 6/19/2020 11:21:43 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: FW: MPH@UNC - EPID 795

From: "Sorensen, Kerstin" <sorensen@email.unc.edu>
Date: Friday, June 19, 2020 at 1:56 PM
To: "Sims, Amy C" <sims0018@email.unc.edu>, "Thomas, Jim" <jim.thomas@unc.edu>
Cc: "Gihlstorf, Catherine M" <catherine_gihlstorf@unc.edu>
Subject: MPH@UNC - EPID 795

Good afternoon,

I'm reaching out about the EPID 795 Data in Public Health course that you are currently developing for the MPH@UNC online program. We are planning the teaching assignments for the January 2021 term, and I understand that your course will be rolled out then. Will you be teaching the course? Or will you need an adjunct to teach it?

The schedule for the January 2021 term is currently being prepared, so *if* you will be teaching the course do you have a preferred day and time? All classes in the MPH@UNC program are taught Monday-Thursday at night, at or after 6pm.

Kind regards,
Kerstin

Kerstin Sorensen, Ph.D.
Adjunct Faculty Coordinator for MPH@UNC
UNC Gillings School of Global Public Health
1121 McGavran-Greenberg Hall
Chapel Hill, NC 27599
(919) 962-7310
sorensen@email.unc.edu

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Fri 6/19/2020 11:27:18 AM (UTC-07:00)
To: Sorensen, Kerstin[sorensen@email.unc.edu]
Subject: Re: MPH@UNC - EPID 795

Hi Kerstin,

I am a little confused. Do you have a few minutes to chat later today? My number is 509-372-6496. Thank you, Amy

---

From: "Sorensen, Kerstin" <sorensen@email.unc.edu>
Date: Friday, June 19, 2020 at 11:22 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: FW: MPH@UNC - EPID 795

From: "Sorensen, Kerstin" <sorensen@email.unc.edu>
Date: Friday, June 19, 2020 at 1:56 PM
To: "Sims, Amy C" <sims0018@email.unc.edu>, "Thomas, Jim" <jim.thomas@unc.edu>
Cc: "Gihlstorf, Catherine M" <catherine_gihlstorf@unc.edu>
Subject: MPH@UNC - EPID 795

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Kerstin

Kerstin Sorensen, Ph.D.
Adjunct Faculty Coordinator for MPH@UNC
UNC Gillings School of Global Public Health
1121 McGavran-Greenberg Hall
Chapel Hill, NC 27599
(919) 962-7310
sorensen@email.unc.edu

From: Sorensen, Kerstin[sorensen@email.unc.edu]
Sent: Fri 6/19/2020 11:28:53 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: MPH@UNC - EPID 795

Sure, I will call you in about 10 minutes.

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Friday, June 19, 2020 at 2:27 PM
To: "Sorensen, Kerstin" <sorensen@email.unc.edu>
Subject: Re: MPH@UNC - EPID 795

Hi Kerstin,

I am a little confused. Do you have a few minutes to chat later today? My number is 509-372-6496. Thank you, Amy

---

From: "Sorensen, Kerstin" <sorensen@email.unc.edu>
Date: Friday, June 19, 2020 at 11:22 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: FW: MPH@UNC - EPID 795

From: "Sorensen, Kerstin" <sorensen@email.unc.edu>
Date: Friday, June 19, 2020 at 1:56 PM
To: "Sims, Amy C" <sims0018@email.unc.edu>, "Thomas, Jim" <jim.thomas@unc.edu>
Cc: "Gihlstorf, Catherine M" <catherine_gihlstorf@unc.edu>
Subject: MPH@UNC - EPID 795

Good afternoon,

I'm reaching out about the EPID 795 Data in Public Health course that you are currently developing for the MPH@UNC online program. We are planning the teaching assignments for the January 2021 term, and I understand that your course will be rolled out then. Will you be teaching the course? Or will you need an adjunct to teach it?

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Kind regards,
Kerstin

Kerstin Sorensen, Ph.D.

Adjunct Faculty Coordinator for MPH@UNC
UNC Gillings School of Global Public Health
1121 McGavran-Greenberg Hall
Chapel Hill, NC 27599
(919) 962-7310
sorensen@email.unc.edu

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 6/22/2020 8:30:22 AM
To: Caldwell, Chandra [ccaldwel@email.unc.edu]
Subject: Help with Sheahan other support please

Importance: High

Hi Chandra,

Tim has two NIH grants on his other support that he did not give the grant numbers.

Can you please help me find them? Thank you very much! Amy

1. R01 (PI: Meshnick) 04/01/20-03/31/25 0.36 cal months (3%)
NIH $(b) (4)
Molecular epidemiology of arboviruses in the Democratic Republic of the Congo

2. R21 (PI: Sheahan) 07/01/20-06/30/22 0.90 cal months (7.5%)
NIH $(b) (4)

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Mon 6/22/2020 10:05:49 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Help with Sheahan other support please

Hi Amy,

The grant number was not given since it had not been assigned given that they were under council review. NIH hasn't had a problem with the grant being listed this way under pending grants on the other support.

Thanks,
C.

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 22, 2020 11:30 AM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Help with Sheahan other support please
Importance: High

Hi Chandra,

Tim has two NIH grants on his other support that he did not give the grant numbers.
Can you please help me find them? Thank you very much! Amy

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Molecular epidemiology of arboviruses in the Democratic Republic of the Congo

2. R21 (PI: Sheahan) 07/01/20-06/30/22 0.90 cal months (7.5%)
NIH $(b) (4)

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 6/22/2020 10:10:10 AM
To: Caldwell, Chandra [ccaldwel@email.unc.edu]
Subject: Re: Help with Sheahan other support please

Okay. Thank you! I think we have a VERY new Grants manager and she asked for this information. For some reason I thought that the NIH was assigning numbers at the time of submission but I could have made that up.

Thank you very much! I really appreciate it. I hope you are doing well! Amy

---

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Monday, June 22, 2020 at 10:06 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Help with Sheahan other support please

Hi Amy,

The grant number was not given since it had not been assigned given that they were under council review. NIH hasn't had a problem with the grant being listed this way under pending grants on the other support.

Thanks,
C.

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 22, 2020 11:30 AM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Help with Sheahan other support please
Importance: High

Hi Chandra,

Tim has two NIH grants on his other support that he did not give the grant numbers.

Can you please help me find them? Thank you very much! Amy

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NIH $(b) (4)
Molecular epidemiology of arboviruses in the Democratic Republic of the Congo

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NIH $(b) (4)

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 6/23/2020 8:41:34 AM
To: Caldwell, Chandra [ccaldwel@email.unc.edu]
Subject: Re: Help with Sheahan other support please

Importance: High

Hi Chandra,

Here is what the NIH said to us. (in italics)
If the grant is under council review, it has a grant number. From a quick QVR search, "Characterization of hepacivirus pathogenesis, viral adaptation and the mapping of host susceptibility alleles in the Collaborative Cross" (the last NIH pending grant listed), the grant number is 1 R21 AI152558-01. I would also like to note that the current grant status for that grant is "Pending Award." The grant that is "Pending Council Review" is actually not included in Dr. Sheahan's Other Support at all (1 R21AI15607-01, "In vitro and in vivo models of nCoV-2019 pathogenesis for the evaluation of medical countermeasures"). I cannot speak to anything previously done. Any NIH grant reported (active or pending) must have a full NIH grant number. The only exception to this are grant applications that were very recently submitted. Please resubmit the Other Support to include the appropriate information for Dr. Sheahan (as a pdf attachment).

Can you please help me with an updated other support for Tim? If you are busy who else should I ask? Thank you very much! Amy

---

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Monday, June 22, 2020 at 10:06 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Help with Sheahan other support please

Hi Amy,

The grant number was not given since it had not been assigned given that they were under council review. NIH hasn't had a problem with the grant being listed this way under pending grants on the other support.

Thanks,
C.

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, June 22, 2020 11:30 AM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Help with Sheahan other support please
Importance: High

Hi Chandra,

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Can you please help me find them? Thank you very much! Amy

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Molecular epidemiology of arboviruses in the Democratic Republic of the Congo

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From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Tue 6/23/2020 8:51:32 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Help with Sheahan other support please

Hi Amy,
Send me the other support that you have for Tim.

Thanks,
Chandra

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, June 23, 2020 11:42 AM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: Help with Sheahan other support please
Importance: High

Hi Chandra,

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If the grant is under council review, it has a grant number. From a quick QVR search, "Characterization of hepacivirus pathogenesis, viral adaptation and the mapping of host susceptibility alleles in the Collaborative Cross" (the last NIH pending grant listed), the grant number is 1 R21 AI152558-01. I would also like to note that the current grant status for that grant is "Pending Award." The grant that is "Pending Council Review" is actually not included in Dr. Sheahan's Other Support at all (1 R21AI15607-01, "In vitro and in vivo models of nCoV-2019 pathogenesis for the evaluation of medical countermeasures"). I cannot speak to anything previously done. Any NIH grant reported (active or pending) must have a full NIH grant number. The only exception to this are grant applications that were very recently submitted. Please resubmit the Other Support to include the appropriate information for Dr. Sheahan (as a pdf attachment).

Can you please help me with an updated other support for Tim? If you are busy who else should I ask? Thank you very much! Amy

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Hi Amy,

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Thanks,
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Sent: Monday, June 22, 2020 11:30 AM

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Subject: Help with Sheahan other support please
Importance: High

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NIH $(b) (4)
Molecular epidemiology of arboviruses in the Democratic Republic of the Congo

2. R21 (PI: Sheahan) 07/01/20-06/30/22 0.90 cal months (7.5%)
NIH $(b) (4)

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 6/23/2020 8:59:52 AM
To: Caldwell, Chandra [ccaldwel@email.unc.edu]
Subject: Re: Help with Sheahan other support please
Attachments: 76382_othersupport_V2REV.docx

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NIH $(b) (4)

OTHER SUPPORT FORMAT PAGE

SIMS, AMY
ACTIVE

R21AI146872 (Sims/Sheahan) 06/05/19-05/31/21 1.9 cal months
UNC Chapel Hill/NIH 5 U.S.C. § 552(b)(6)
How MERS-CoV regulates the innate immune response
The major goal of the project is to determine if primary human lung cells infected with Middle Eastr espiratory syndrome coronavirus (MERS-CoV) use epigenetic mechanisms to regulate the expression of interferon stimulated genes.
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

LDRD (Sims) 03/07/20-09/30/21 4.4 cal months
Pacific Northwest National Laboratory 5 U.S.C. § 552(b)(6)
Defining coronavirus lipidomic response
The goal of this project is to characterize the lipid response to coronavirus infection.
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

PENDING
Not Applicable

SHEAHAN, TIMOTHY
ACTIVE

R21AI146872 (PI: Sheahan/Sims) 06/05/19-05/30/21 0.60 cal months (5%
NIH **{THIS GRANT}** 5 U.S.C. § 552(b)(6)
How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
This proposal will build on foundational studies performed in continuous human lung cell lines and define ways that MERS-CoV regulates innate immunity in primary human lung fibroblasts and microvascular endothelial cells.
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

U19AI142759 CETR (PI: Whitley) 03/01/14-02/28/24 3.6 cal months (30%)
UAB/NIH/NIAID 5 U.S.C. § 552(b)(6)
Antiviral Drug Discovery and Development Center
The specific aims of the proposal will identify small molecule inhibitors of CoV fidelity and RNA capping, define their mechanism of action, and determine their efficacy against SARS-CoV and across CoV families using in vivo mouse models of acute and persistent CoV disease.
Role: Investigator
Foreign component funded by grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01 AI131688-01 (PI: Rice) 03/15/17-02/281/22 1.8 cal months (15%)
Rockefeller/NIH 5 U.S.C. § 552(b)(6)
Analysis of immunity, viral adaptation and pathogenesis in a new mouse model of HCV-related rodent hepacivirus infection

Mechanisms that contribute to the persistence of hepatotropic viruses, such as HCV, are not well understood. We have recently established the first immune-competent mouse model of an HCV-related virus. With this new model, we propose to systematically study immunity and host-virus interactions during a hepatotropic RNA virus infection in vivo.
Role: Subcontract PI
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01 AI132178-01 (MPI: Sheahan/Baric) 08/09/17-07/31/22 2.4 cal months (20%)
NIH 5 U.S.C. § 552(b)(6)
Broad-spectrum antiviral GS-5734 to treat MERS-CoV and related emerging CoV
In partnership with Gilead Sciences, we aim to accelerate the preclinical development of GS-5734 and promote IND licensure. We define the pharmacokinetics, pharmacodynamics, resistance profile, efficacy breadth and mechanism of action of GS-5734 against MERS-CoV and related emerging CoV.
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

R01AI108197-06 (MPI: Baric/Denison) 03/01/18-02/28/23 1.8 cal months (15%)
Vanderbilt/NIH 5 U.S.C. § 552(b)(6)
Determinants of Coronavirus Fidelity in Replication and Pathogenesis
To identify common and unique determinants of CoV nsp14-ExoN functions CoV replication, fidelity and IFN sensitivity across CoVs; To determine pathways of adaptation to loss of nsp14-ExoN activity in vitro and in vivo; and to define mechanisms of ExoN-regulated CoV sensitivity to the innate antiviral immune response.
Role: Co-Investigator
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

U01AI149644 (PI: Baric) 04/19/19-03/31/24 1.8 cal months (15%)
NIH 5 U.S.C. § 552(b)(6)
Respiratory Virus Vaccine and Adjuvant Exploration
Vaccination is one of the most effective public health measures for protecting against infectious disease, and the proposed studies will identify adjuvants and adjuvant combinations that safely elicit long lived protective immunity against emerging pathogens in at risk populations.
Role: Investigator
Foreign component funded by this grant: No
There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

PENDING:
R01 (PI: Meshnick) 04/01/20-03/31/25 0.36 cal months (3%)
NIH 5 U.S.C. § 552(b)(6)
Molecular epidemiology of arboviruses in the Democratic Republic of the Congo
The grant is innovative in its multidisciplinarity, combining epidemiological, entomological, serological, phylogenetic and basic sciences approaches. Together, this research will, for the first time, provide data on the incidence, types, sources, and genomic traits of this important group of viruses in Central Africa.
Foreign component funded by this grant: Yes
Foreign investigators: Antoinette Tshefu, University of Kinshasa (Congo, Democratic Republic)
Supplied by foreign site: Patient Samples
Technology transfer to foreign site: No

R21 (PI: Sheahan) 07/01/20-06/30/22 0.90 cal months (7.5%)

NIH 5 U.S.C. § 552(b)(6)

Characterization of hepacivirus pathogenesis, viral adaptation and the mapping of host susceptibility alleles in the Collaborative Cross

The goals of this proposal are to: 1) phenotype the kinetics of virus replication/adaptation, pathogenesis and the host response in CC lines with delayed clearance and chronic infection and 2) to map the genetic determinants driving virus titer, viral evolution, clearance, weight loss, blood leukocyte modulation, and chronic infection

Foreign component funded by this grant: No

There are no Domestic/Foreign gifts, appointments, lab or office space, scientific materials, affiliations, and/or foreign faculty/scholars/scientists/post-docs for this grant.

Not Assigned (PI: Baric) 07/01/20-06/30/25 0.36 cal months (3%)

EcoHealth Alliance 5 U.S.C. § 552(b)(6)

US-China Collab: Spillover, co-infection, and control of bat-origin livestock coronaviruses

To develop an economic model of farm profit maximization linked to the compartmental epidemiological model of co-infection disease. *Foreign component funded by this grant: No*

OVERLAP: If any of the pending awards are funded, Dr. Sheahan will reduce is effort accordingly to not exceed 12 calendar months.

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Tue 6/23/2020 11:51:35 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Help with Sheahan other support please
Attachment: Sheahan Other Support_AS grant.docx

FYI: See attachment.

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, June 23, 2020 12:00 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re: Help with Sheahan other support please

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Sent: Tue 6/23/2020 12:02:21 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Help with Sheahan other support please

No problem at all since each NIH PO is different!

From: Sims, Amy C <amy.sims@pnnl.gov>
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NIH $(b) (4)

From: Fulcher, Leslie [leslie_fulcher@med.unc.edu]
Sent: 6/25/2020 2:18:24 PM
To: Allen, Devon Grace [allendg@live.unc.edu]; Williams, Allison Blair [ablair05@email.unc.edu]; Lopez, Christopher [christopher_lopez@med.unc.edu]; Zimmer, Hannah [hvzimmer@med.unc.edu]; Galiger, Jacob Ryan [jgaliger@ad.unc.edu]; Lam, Mariam [mariam_lam@med.unc.edu]; Fulcher, Leslie [leslie_fulcher@med.unc.edu]; Lopes, Emma [emmar0se@live.unc.edu]; Bowen, Marisa Ann [marisa_bowen@med.unc.edu]; Dong, Weizhen [valerie_dong@med.unc.edu]
CC: Sims, Amy C [amy.sims@pnnl.gov]
Subject: Update on Amy Sims Pilot project

Importance: High
Flag: Follow Up

Team
Easy thing first:

The coolboxes should arrive tomorrow and I would like to send Amy 1 -12 well containing a few extra Tclears that Marisa and Valerie have and Allison and Chris have extra millicells which I would also like to test with the shipping protocol.

Please plan to ship 2-4 millicells, and 2- Tclears in 12 well plate following the gel protocol which is now located in the protocol section.

Shipping Address:
Attn: Amy Sims, 331/70
Battlelle for US DOE
790 6th Street
Richland, WA 99353 USA
5 U.S.C. § 552(b)(6)
Amy, please confirm address and we will use our Fedex account for this pilot shipment but you can share your account for the near future projects.

Amy would like to test P3 cells to confirm they work before her massive studies begin.

On June 26th, please thaw -1 vial of each. The goal is to seed 6 Tclears at P3 ~250K/well (Total =1.5Mp3 cells)

DD044L	2	D Star	EwokE	20	orange	7/14/2015

This code needs Full QC. You should have plenty of cells to accomplish this.

DD068K	2	Garden	Tulip L	13	red	10/20/2014

DD063K	2	D Star	LeiaD	13	pink	9/26/2014

June 28th: W/F plastic (Emma? If she is not available, I need someone to come in)
June 29th: Day 3 W/F plastic

June 30th: Day 4: Pass and replate

If yield is 2-3M, seed 2M P150 and freeze 1 vial of extra

If yield is 1-2M, seed P100 and P60s

Remember 44L needs QC.

July 1st: W/F (day 1)

July 2nd: W/F (day 2)

July 5th: If student/technician can w/f great, if not have 2 ml of extra BEGM on July 2nd feed.

July 6th: Seed 6 Tclears for each code. I would like to target 250K for P3 cells. (If you think there are not 1.5M cells in the dish, please feed and pass the following day)

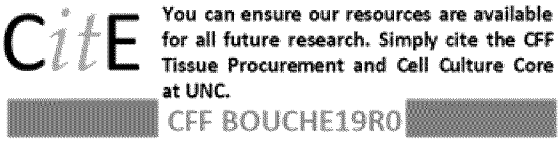
Regular MWF maintenance and we will ship out ~day 28 to Amy to test.

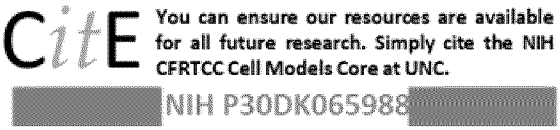
Please email me asap if questions

Thank you,

Leslie

Leslie Fulcher
Laboratory Manager
UNC CF Tissue Procurement and Cell Culture Core
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Rd.
Rm. 1119 Marsico Hall, CB 7248
Chapel Hill, NC 27599
919-966-7055
MLI Tissue Procurement and Cell Culture Core Ordering: https://infoporte.unc.edu/cores/buy.php
https://www.med.unc.edu/mlicellcore/





From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 6/26/2020 9:21:47 AM
To: Moore, Victoria L [victoria_moore@unc.edu]; Caldwell, Chandra [ccaldwel@email.unc.edu]
Subject: !!Continuing Amy's R21 saga!!

Importance: High

Hi ladies,

I hope you are doing well. The trauma and drama of transferring my R21 continues.

We finally had everything in to the NIH and I thought we were making progress when things ground to a halt again.

Apparently in a transfer the direct costs calculation for a prime and subcontract is the following: prime direct dollars + subcontract total dollars! We spoke with the NIH grants manager today and yes this is really the case.

This put us over by **5 U.S.C. § 552(b)(4)**

We are going to have to do some budget reductions/rearrangements to allow enough funds to be able to do the work.

I hate to ask for help again but I am not sure I have much choice. I will send you revised budgets and documents as soon as possible. I need to chat with Tim first.

Please let me know if you have any questions. Thank you very much. Amy

From: Zimmer, Hannah[hvzimmer@med.unc.edu]
Sent: Fri 6/26/2020 10:15:11 AM (UTC-07:00)
To: Fulcher, Leslie[leslie_fulcher@med.unc.edu]; Allen, Devon Grace[allendg@live.unc.edu]; Williams, Allison Blair[ablair05@email.unc.edu]; Lopez, Christopher[christopher_lopez@med.unc.edu]; Galiger, Jacob Ryan[jgaliger@ad.unc.edu]; Lam, Mariam[mariam_lam@med.unc.edu]; Lopes, Emma[emmar0se@live.unc.edu]; Bowen, Marisa Ann[marisa_bowen@med.unc.edu]; Dong, Weizhen[valerie_dong@med.unc.edu]
Cc: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Update on Amy Sims Pilot project

Just to keep everyone on the same page, I have thawed the vials and will maintain the cultures until they are ready to be shipped. Also, I spoke with Amy to verify when she would want the extra millis/t clears shipped and she said she doesn't want anything shipped until July 6th.

-Hannah

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Thursday, June 25, 2020 5:18 PM
To: Allen, Devon Grace <allendg@live.unc.edu>; Williams, Allison Blair <ablair05@email.unc.edu>; Lopez, Christopher <christopher_lopez@med.unc.edu>; Zimmer, Hannah <hvzimmer@med.unc.edu>; Galiger, Jacob Ryan <jgaliger@ad.unc.edu>; Lam, Mariam <mariam_lam@med.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Lopes, Emma <emmar0se@live.unc.edu>; Bowen, Marisa Ann <marisa_bowen@med.unc.edu>; Dong, Weizhen <valerie_dong@med.unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>
Subject: Update on Amy Sims Pilot project

Team
Easy thing first:

The coolboxes should arrive tomorrow and I would like to send Amy 1 -12 well containing a few extra Tclears that Marisa and Valerie have and Allison and Chris have extra millicells which I would also like to test with the shipping protocol.

Please plan to ship 2-4 millicells, and 2- Tclears in 12 well plate following the gel protocol which is now located in the protocol section.

Shipping Address:
Attn: Amy Sims, 331/70
Battlelle for US DOE
790 6th Street
Richland, WA 99353 USA
(b) (6) [redacted]
Amy, please confirm address and we will use our Fedex account for this pilot shipment but you can share your account for the near future projects.

Amy would like to test P3 cells to confirm they work before her massive studies begin.

On June 26th, please thaw -1 vial of each. The goal is to seed 6 Tclears at P3 ~250K/well (Total =1.5Mp3 cells)

DD044L	2	D Star	EwokE	20	orange	7/14/2015

This code needs Full QC. You should have plenty of cells to accomplish this.

DD068K	2	Garden	Tulip L	13	red	10/20/2014

DD063K	2	D Star	LeiaD	13	pink	9/26/2014

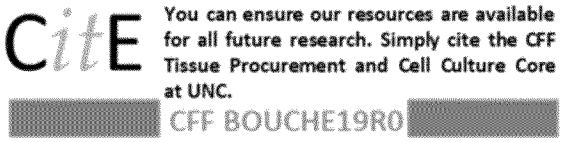
June 28th: W/F plastic (Emma? If she is not available, I need someone to come in)
June 29th: Day 3 W/F plastic
June 30th: Day 4: Pass and replate
    If yield is 2-3M, seed 2M P150 and freeze 1 vial of extra
    If yield is 1-2M, seed P100 and P60s
    Remember 44L needs QC.
July 1st: W/F (day 1)
July 2nd: W/F (day 2)
July 5th: If student/technician can w/f great, if not have 2 ml of extra BEGM on July 2nd feed.
July 6th: Seed 6 Tclears for each code. I would like to target 250K for P3 cells. (If you think there are not 1.5M cells in the dish, please feed and pass the following day)
Regular MWF maintenance and we will ship out ~day 28 to Amy to test.

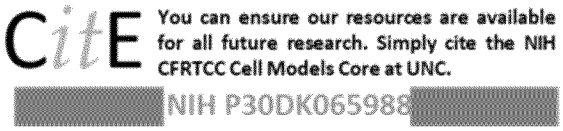
Please email me asap if questions
Thank you,

Leslie

Leslie Fulcher
Laboratory Manager
UNC CF Tissue Procurement and Cell Culture Core
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Rd.
Rm. 1119 Marsico Hall, CB 7248
Chapel Hill, NC 27599
919-966-7055
MLI Tissue Procurement and Cell Culture Core Ordering: https://infoporte.unc.edu/cores/buy.php

https://www.med.unc.edu/mlicellcore/


CitE
You can ensure our resources are available for all future research. Simply cite the CFF Tissue Procurement and Cell Culture Core at UNC.
CFF BOUCHE19R0


CitE
You can ensure our resources are available for all future research. Simply cite the NIH CFRTCC Cell Models Core at UNC.
NIH P30DK065988

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Fri 6/26/2020 10:19:21 AM (UTC-07:00)
To: Zimmer, Hannah[hvzimmer@med.unc.edu]; Fulcher, Leslie[leslie_fulcher@med.unc.edu]; Allen, Devon Grace[allendg@live.unc.edu]; Williams, Allison Blair[ablair05@email.unc.edu]; Lopez, Christopher[christopher_lopez@med.unc.edu]; Galiger, Jacob Ryan[jgaliger@ad.unc.edu]; Lam, Mariam[mariam_lam@med.unc.edu]; Lopes, Emma[emmar0se@live.unc.edu]; Bowen, Marisa Ann[marisa_bowen@med.unc.edu]; Dong, Weizhen[valerie_dong@med.unc.edu]
Subject: Re: Update on Amy Sims Pilot project

Thank you! I appreciate it. Next week is a holiday week and I wanted to make there were no issues with the shipment. Thank you again, Amy

---

From: "Zimmer, Hannah" <hvzimmer@med.unc.edu>
Date: Friday, June 26, 2020 at 10:15 AM
To: "Fulcher, Leslie" <leslie_fulcher@med.unc.edu>, "Allen, Devon Grace" <allendg@live.unc.edu>, "Williams, Allison Blair" <ablair05@email.unc.edu>, "Lopez, Christopher" <christopher_lopez@med.unc.edu>, "Galiger, Jacob Ryan" <jgaliger@ad.unc.edu>, "Lam, Mariam" <mariam_lam@med.unc.edu>, "Lopes, Emma" <emmar0se@live.unc.edu>, "Bowen, Marisa Ann" <marisa_bowen@med.unc.edu>, "Dong, Weizhen" <valerie_dong@med.unc.edu>
Cc: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Update on Amy Sims Pilot project

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To: Allen, Devon Grace <allendg@live.unc.edu>; Williams, Allison Blair <ablair05@email.unc.edu>; Lopez, Christopher <christopher_lopez@med.unc.edu>; Zimmer, Hannah <hvzimmer@med.unc.edu>; Galiger, Jacob Ryan <jgaliger@ad.unc.edu>; Lam, Mariam <mariam_lam@med.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Lopes, Emma <emmar0se@live.unc.edu>; Bowen, Marisa Ann <marisa_bowen@med.unc.edu>; Dong, Weizhen <valerie_dong@med.unc.edu>
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Attn: Amy Sims, 331/70
Battlelle for US DOE
790 6th Street
Richland, WA 99353 USA
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If yield is 2-3M, seed 2M P150 and freeze 1 vial of extra
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Remember 44L needs QC.
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July 2nd: W/F (day 2)
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Regular MWF maintenance and we will ship out ~day 28 to Amy to test.

Please email me asap if questions
Thank you,

Leslie

Leslie Fulcher
Laboratory Manager
UNC CF Tissue Procurement and Cell Culture Core
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125 Mason Farm Rd.

Rm. 1119 Marsico Hall, CB 7248
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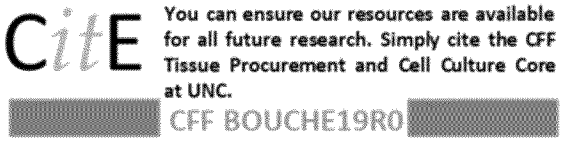
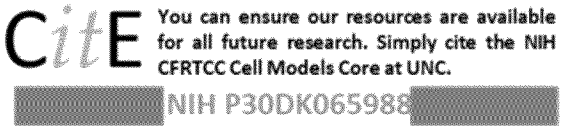
919-966-7055
MLI Tissue Procurement and Cell Culture Core Ordering: https://infoporte.unc.edu/cores/buy.php

https://www.med.unc.edu/mlicellcore/





From: Ames, Amber A[Amber.Ames@pnnl.gov]
Sent: Mon 6/29/2020 10:24:30 AM (UTC-07:00)
To: Koltz, Diane M[dkoltz@email.unc.edu]; Fulcher, Leslie[leslie_fulcher@med.unc.edu]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form
Attachment: PO 521567.xml
Attachment: GP-A-409.24-FP_October 2019.pdf
Attachment: MLI Order Form Oct2019 (002).docx

Dear Diane,

I have been advised that we would like to pursue UNC as the source of the HBE cells. I have attached our purchase order template in word. We do not customize the General Provisions so those are a .pdf. All changes will be listed in the purchase order as an alteration to the GPs—sample below. We have a long history of contracting with UNC so I have copied the Alterations we have negotiated for previous awards. Unfortunately, as a DOE M&O contractor we are also very limited on what we can negotiate. DOE requires their terms control. We understand universities cannot grant indemnity and we are confident we will be able to negotiate changes that will be acceptable to UNC and DOE.

Alterations to General Provisions
1. Permits and Responsibilities (cl. 358—Nov 1991) is hereby deleted and replaced with:
"The Contractor is an independent contractor, not an agent or employee of Battelle. The Contractor shall, without additional expense to Battelle or the Government, be responsible for obtaining any necessary licenses and permits, and for complying with any Federal, State, and municipal laws, codes, and regulations applicable to the performance of the work. The Contractor shall also be responsible for all damages to persons or property that occurs as a result of the Contractor's fault or negligence only in the manner and to the extent permitted under North Carolina law, including but not limited to the NC Tort Claims Act, GS 143-291, et seq., and without waiver of its sovereign immunity."
2. Insurance—Liability to Third Persons (cl. 378b—Mar 1996) is hereby deleted and replaced with:
"University of North Carolina is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."
3. Disputes (cl. 331—Nov 2014)
Delete in its entirety.
4. Insurance Requirements (cl. 378—Nov 2014) is hereby deleted and replaced with:
"University of North Carolina is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."

I note I have been advised we will have another order with a budget of 5 U.S.C. § 552(b)(4) so it is critical we resolve the terms and conditions.

Thank you for your assistance with this matter.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Thursday, June 18, 2020 11:06 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I received your changes for review and upon a first look, UNC cannot agree to all of the supplemental terms contained in the online documents you want to include. As a state institution, we are somewhat limited. The order form contains the minimal terms UNC requires in its contracts and we typically do not agree to changes. Is there any possibility that we could make UNC's agreement control, or not reference the terms at all, since much of what is contained in the online "purchase agreements" won't apply to what we are providing. If this is not possible, please provide me word versions of the online agreements so I can outline our requested edits and comments. Also, please note that review of the documents will take time.

Thanks,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Thursday, June 18, 2020 12:58 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Just checking in to see if there is a response to our requested changes to the order form terms.

Thanks so much!

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Wednesday, June 10, 2020 3:04 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Good Morning Amber,
Yes, once the contract is executed, Amy will be able to order as needed up to the dollar amount on the contract and during the 1 year period. I am including our contract specialist who can look at your suggested changes and she will be in touch with you soon.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>

Sent: Tuesday, June 09, 2020 9:02 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Thanks, Leslie. The project would like to be able to order up to 10 ALI medium and 26 Normal HBE Cells from now until September 30, 2021. Are they able to order on an as-needed basis? I can incorporate a signed version of the attached into the PO for the project to use? Once I sign it, they won't be able to edit it. Perhaps we need to do a purchase order per order?

I note I provided redlines on the attached. Please advise if UNCC is able to work with the redlines.

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 5:29 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,
Thanks for emailing back, but to complete the contract, I need the agreement signed and returned to me prior to ordering. As for payment options, a check is fine, but we do have an account that funds could be wired. If that works for you, I can share that information.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 5:09 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

Attached please find Purchase Order No. 521567 to purchase up to the quantities I had listed below. Per the PO, we will place orders via the ordering website. There is no need to sign the PO—if you can acknowledge receipt and that this will work for ordering/payment purposes, that would be helpful.

I'm guessing the MLI Tissue Procurement and Cell Culture Core Facility will want a paper check mailed to the 125 Mason Farm Road address instead of paid by ACH to UNCC's main Bank of America account?

Amy, the shipping address in PES is 331 Building, Room 70. Even if a different shipping address is input in the UNCC online ordering system, any orders associated with PO 521567 will ship to 331/70. If you need a different ship to, let me know.

Thanks!

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute

Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 12:36 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,

As long as the contract is signed, the dollar amount is entered, and the period is in place there will be no rate increase.
You don't need to select the quantity of any item, but if your project you will use the quantity listed below, entering in the dollar amount is sufficient. I may suggest adding a little wiggle room in the dollar amount because once the dollar amount is reached, even before the term is up, we will need to renew the contract.

Also, once the contract is executed, you would just log onto our ordering website and order what you need.
Please let me know if you have any questions.

Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 9, 2020 1:19 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

I have a requisition to issue a Purchase Order to UNCC for a fixed unit rate contract for the following:

Description	Price	Maximum Quantity Expected	Extended Price
BEGM MEDIUM	5 U.S.C. § 552(b)(4)	0	5 U.S.C. § 552(b)(4)
ALI MEDIUM	5 U.S.C. § 552(b)(4)	10	5 U.S.C. § 552(b)(4)

VALI MEDIUM	5 U.S.C. § 552(b)(4)	0	
Normal HBE Cells	5 U.S.C. § 552(b)(4)	26	5 U.S.C. § 552(b)(4)
Diseased HBE Cells	5 U.S.C. § 552(b)(4)	0	
Cystic Fibrosis HBE Cells	5 U.S.C. § 552(b)(4)	0	5 U.S.C. § 552(b)(4)
Normal Microvascular Cells	5 U.S.C. § 552(b)(4)	0	
Normal Fibroblast Cells	5 U.S.C. § 552(b)(4)	0	
Total Not to Exceed Amount			5 U.S.C. § 552(b)(4)

The project would like to use the purchase order for payment of requirements on an as-needed basis through September 30, 2021.

My question is how long the pricing in Exhibit A of the attached is valid? Are the prices updated annually?

Do you have any concerns with this approach?

Kind regards,

Amber A. Ames
Senior Contracts Specialist
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Tel: (509) 371-7050
amber.ames@pnnl.gov
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Pacific Northwest
NATIONAL LABORATORY

From: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Sent: Tue 6/30/2020 6:58:55 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Cc: michael waldholz 5 U.S.C. § 552(b)(6)
Subject: Re: EIDD-2801

Hi Amy,

How are you?

I just got off the phone with Michael (CC'd above), a journalist that most recently wrote a story about remdesivir in Scientific American, and he was wondering if he would talk to you about our work together on remdesivir and EIDD-2801 for a deeper dive in the coronavirus drug work.

He's already talked to Denison and Baric. I know you are busy but I thought your input would be valuable for this story given that we were partners in this work and you got into this before I even came back to UNC.

I hope you are well.

Tim

From: michael waldholz 5 U.S.C. § 552(b)(6)
Date: Friday, June 19, 2020 at 5:53 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: EIDD-2801

Dear Tim,
Hope this finds you doing well.
I'm sorry I didn't have the time to get to you when I reported about remdesivir and EIDD-2801 research for my Scientific American article that ran online and in the June issue Scientific American. I
I received the press release that EIDD-2801 is going into the next phase of clinical testing.
I have a publication interested in a more in-depth discovery story about the drug, and I hope to speak with you sometime soon if you can be available.
Until then, please keep me in mind if you can about any updates or details you think I should know, or might be valuable to my reporting.
Best regards,
Michael

MICHAEL WALDHOLZ
5 U.S.C. § 552(b)(6)

From: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Sent: Tue 6/30/2020 7:00:38 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Vero E6 USA

Hi Amy,

Were Vero E6 USAMRIID ever sorted for high ACE2 expression? Ralph mentioned this the other day but perhaps we were getting this confused with Calu-3?

Sup?!!!!!!!

Tim

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 6/30/2020 9:49:40 AM (UTC-07:00)
To: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Subject: Re: Vero E6 USA

Howdy! Sorry weird morning. Our older dog is having lots of issues with his stomach and we don't get to sleep as much as we would like.

So, all I can tell you is that the Vero USAMRIID aka E6 cells used by the Baric lab are a) magical as they seem to do really well with SARS-CoV, b) came from the Jarhling group when we made the virus SARS-CoV 2003 stocks (pretty sure) and c) the cells used by the lab at large are not sorted to my knowledge.

Calu3 2B4 are for sure sorted but I don't know if Boyd sorted the US Vero cells or not. I would ask Boyd as he would know more than me. I never did any FACS experiments in the Baric lab or ever for that matter.

Ralph often convinces himself of things that did not happen. I am not saying this is the case with vero cell sorting but it might be. Good luck!! Amy

---

From: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Date: Tuesday, June 30, 2020 at 7:02 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Vero E6 USA

Hi Amy,

Were Vero E6 USAMRIID ever sorted for high ACE2 expression? Ralph mentioned this the other day but perhaps we were getting this confused with Calu-3?

Sup?!!!!!!!

Tim

From: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Sent: Tue 6/30/2020 12:05:15 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Vero E6 USA

Sorry to hear about the pupper!

Yea. I think I convinced Ralph that the sorting did not happen and that the cells are just magical! Boyd has no memory of sorting either!

Thanks!
T

From: Amy Sims <amy.sims@pnnl.gov>
Date: Tuesday, June 30, 2020 at 12:50 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: Re: Vero E6 USA

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So, all I can tell you is that the Vero USAMRIID aka E6 cells used by the Baric lab are a) magical as they seem to do really well with SARS-CoV, b) came from the Jarhling group when we made the virus SARS-CoV 2003 stocks (pretty sure) and c) the cells used by the lab at large are not sorted to my knowledge.

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Ralph often convinces himself of things that did not happen. I am not saying this is the case with vero cell sorting but it might be. Good luck!! Amy

---

From: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Date: Tuesday, June 30, 2020 at 7:02 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Vero E6 USA

Hi Amy,

Were Vero E6 USAMRIID ever sorted for high ACE2 expression? Ralph mentioned this the other day but perhaps we were getting this confused with Calu-3?

Sup?!!!!!!!

Tim

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 6/30/2020 12:22:22 PM (UTC-07:00)
To: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Subject: Re: Vero E6 USA

Welcome! One other piece of news.

So when funds are transferred to another institution it turns out that the following is true.

The total direct (spendable dollars) becomes the direct dollars from the prime + the direct and indirect dollars (aka total costs) from the subcontract. I did not know this and so this makes our budget over by more than $30K.

I am doing what I can to minimize and spread out the funds but there will be a reduction in UNC's overall available dollars. One thing I did that is helping is to move the funds for sequencing costs to PNNL's side. This means the bill will just come to me instead of you guys paying it and I will work with Alex on this when the time comes.

If you have major concerns or if you want to talk about this please let me know. Vicki will send you the revised budget once all of the changes have been made. Thank you very much! I hope you and the ladies Sheahan are doing well in these crazy times!!

Amy

From: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Date: Tuesday, June 30, 2020 at 12:07 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Vero E6 USA

Sorry to hear about the pupper!

Yea. I think I convinced Ralph that the sorting did not happen and that the cells are just magical! Boyd has no memory of sorting either!

Thanks!
T

From: Amy Sims <amy.sims@pnnl.gov>
Date: Tuesday, June 30, 2020 at 12:50 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: Re: Vero E6 USA

Howdy! Sorry weird morning. Our older dog is having lots of issues with his stomach and we don't get to sleep as much as we would like.

So, all I can tell you is that the Vero USAMRIID aka E6 cells used by the Baric lab are a) magical as they seem to do really well with SARS-CoV, b) came from the Jarhling group when we made the virus SARS-CoV 2003 stocks (pretty sure) and c) the cells used by the lab at large are not sorted to my knowledge.

Calu3 2B4 are for sure sorted but I don't know if Boyd sorted the US Vero cells or not. I would ask Boyd as he would know more than me. I never did any FACS experiments in the Baric lab or ever for that matter.

Ralph often convinces himself of things that did not happen. I am not saying this is the case with vero cell sorting but it might be. Good luck!! Amy

---

From: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Date: Tuesday, June 30, 2020 at 7:02 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Vero E6 USA

Hi Amy,

Were Vero E6 USAMRIID ever sorted for high ACE2 expression? Ralph mentioned this the other day but perhaps we were getting this confused with Calu-3?

Sup?!!!!!!!

Tim

From: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Sent: Tue 6/30/2020 12:38:56 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Vero E6 USA

That's fine about the budget. As long as Alex/Vicki/Kalyn know what we have for spending in relation to the science that needs to be done, we should be fine.

Thanks!

T

From: Amy Sims <amy.sims@pnnl.gov>
Date: Tuesday, June 30, 2020 at 3:22 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: Re: Vero E6 USA

Welcome! One other piece of news.

So when funds are transferred to another institution it turns out that the following is true.

The total direct (spendable dollars) becomes the direct dollars from the prime + the direct and indirect dollars (aka total costs) from the subcontract. I did not know this and so this makes our budget over by more than $30K.

I am doing what I can to minimize and spread out the funds but there will be a reduction in UNC's overall available dollars. One thing I did that is helping is to move the funds for sequencing costs to PNNL's side. This means the bill will just come to me instead of you guys paying it and I will work with Alex on this when the time comes.

If you have major concerns or if you want to talk about this please let me know. Vicki will send you the revised budget once all of the changes have been made. Thank you very much! I hope you and the ladies Sheahan are doing well in these crazy times!!

Amy

From: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Date: Tuesday, June 30, 2020 at 12:07 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Vero E6 USA

Sorry to hear about the pupper!

Yea. I think I convinced Ralph that the sorting did not happen and that the cells are just magical! Boyd has no memory of sorting either!

Thanks!
T

From: Amy Sims <amy.sims@pnnl.gov>
Date: Tuesday, June 30, 2020 at 12:50 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Subject: Re: Vero E6 USA

Howdy! Sorry weird morning. Our older dog is having lots of issues with his stomach and we don't get to sleep as much as we would like.

So, all I can tell you is that the Vero USAMRIID aka E6 cells used by the Baric lab are a) magical as they seem to do really well with SARS-CoV, b) came from the Jarhling group when we made the virus SARS-CoV 2003 stocks (pretty sure) and c) the cells used by the lab at large are not sorted to my knowledge.

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Ralph often convinces himself of things that did not happen. I am not saying this is the case with vero cell sorting but it might be. Good luck!! Amy

---

From: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>
Date: Tuesday, June 30, 2020 at 7:02 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Vero E6 USA

Hi Amy,

Were Vero E6 USAMRIID ever sorted for high ACE2 expression? Ralph mentioned this the other day but perhaps we were getting this confused with Calu-3?

Sup?!!!!!!!

Tim

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 6/30/2020 4:53:52 PM
To: Moore, Victoria L [victoria_moore@unc.edu]
CC: Caldwell, Chandra [ccaldwel@email.unc.edu]
Subject: Re:
Attachments: 2_6_30_2020_Sims_R21_Yr2_UNC_Subcontact_vm.xlsx

Vicki,

UNC's new total dollar amount for the Sims Sheahan R21 is going to be 5 U.S.C. § 552(b)(4)

This is the best I could do. Attached are my recommendation but of course you guys can do whatever you want.

I increased Sheahan's effort to 5% again so that it matched what we indicated in his other support document. I moved the 5 U.S.C. § 552(b)(4) RNA sequencing costs to PNNL and removed the travel costs in case that helps with the budget justification.

PNNL would like another signed face page but we are not in a rush to get it.

Please let me know if you have any questions. Thank you very much! Amy

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Mon 7/6/2020 10:51:22 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE:
Attachment: Signed Revised LOI.pdf

FYI: Revised LOI attached!

Best,
Chandra

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, June 30, 2020 7:54 PM
To: Moore, Victoria L <victoria_moore@unc.edu>
Cc: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re:

Vicki,

UNC's new total dollar amount for the Sims Sheahan R21 is going to be 5 U.S.C. § 552(b)(4)

This is the best I could do. Attached are my recommendation but of course you guys can do whatever you want.

I increased Sheahan's effort to [redacted] again so that it matched what we indicated in his other support document. I moved the 5 U.S.C. § 552(b)(4) in RNA sequencing costs to PNNL and removed the travel costs in case that helps with the budget justification.

PNNL would like another signed face page but we are not in a rush to get it.

Please let me know if you have any questions. Thank you very much! Amy

UNC RESEARCH

Subrecipient Letter of Intent To University of North Carolina at Chapel Hill

To be completed by UNC-CH Project Team

SUBRECIPIENT	SPONSOR
Legal Name: The University of North Carolina at Chapel Hill	Legal Name: Battelle-PNWD, Operator of PNNL for US DOE
DUNS: 608195277	
Lead PI: Dr. Timothy Sheahan	Lead PI: Dr. Amy Sims
Subrecipient Administrative Contact:	***Sponsor Administrative Contact:***
Name/Title: David Paul/Associate Vice Chancellor	Name/Title: Barb Hays, Contracting Professional
Address: 104 Airport Dr., Suite 2200, CB 1350 Chapel Hill, NC, 27599	Address: 902 Battelle Blvd. - PO Box 999 Richland, WA 99352-0999
Phone: 919-966-3411	Phone: 509-372-4008
Email: ResAdminOSR@unc.edu	Email: barb.hays@pnnl.gov

GENERAL INFORMATION

Project Title: How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells

Prime Awarding Agency: NIH

RFA/RFP: PA-18-489

Project Period: Start 06/01/2020 End 05/31/2021

UNC-CH Proposal Number: 20-5613

BUDGET INFORMATION

Choose appropriate F&A Type:

(•) Federal Rate ( ) Sponsor Rate ( ) Other

Applicable F&A Rate: 5 U.S.C. § 552(b)(4) %

Direct Costs: 5 U.S.C. § 552(b)(4)

Indirect Costs: 5 U.S.C. § 552(b)(4)

Total Request: 5 U.S.C. § 552(b)(4)

COMPLIANCE INFORMATION

Human Subjects: ( ) Yes (•) No

Animal Subjects: ( ) Yes (•) No

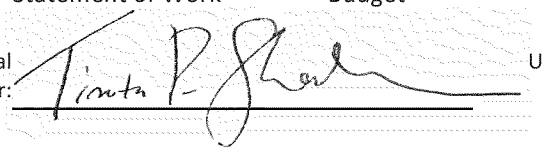
UNC-CH is a Federal Demonstration Partnership (FDP) Pilot Participant.

This LETTER OF INTENT confirms the appropriate program and administrative personnel at UNC-CH have reviewed and approve the above referenced Solicitation/RFP/RFA. Further, UNC-CH and its Principal Investigator certify that:

Information submitted within this application is true, complete, and accurate to the best of UNC-CH's and PI's knowledge; any false, fictitious, or fraudulent statements or claims may subject the UNC-CH and PI to criminal, civil, or administrative penalties; PI agrees to accept responsibility for the scientific conduct of the project and to provide the required progress reports if an award is made and a mutually agreeable subcontract is executed as a result of UNC-CH's application.

Further, UNC-CH confirms it maintains an active and enforced conflict of interest policy meeting the requirements of 42 CFR Part 5. Subpart F, and 45 CFR Part 94.

Included: Statement of Work Budget Budget Justification Other:

UNC-CH Principal Investigator: 

Date: 07/01/2020

UNC-CH Authorized Official: Alexie Mina Digitally signed by Alexie Mina Date: 2020.07.06 13:41:59 -04'00'

Date:

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 7/6/2020 11:37:26 AM
To: Caldwell, Chandra [ccaldwel@email.unc.edu]
Subject: Re:

Thank you very much! I really appreciate it. Amy

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Monday, July 6, 2020 at 10:53 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE:

FYI: Revised LOI attached!

Best,
Chandra

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, June 30, 2020 7:54 PM
To: Moore, Victoria L <victoria_moore@unc.edu>
Cc: Caldwell, Chandra <ccaldwel@email.unc.edu>
Subject: Re:

Vicki,

UNC's new total dollar amount for the Sims Sheahan R21 is going to be 5 U.S.C. § 552(b)(4)

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I increased Sheahan's effort to 5% again so that it matched what we indicated in his other support document. I moved the 5 U.S.C. § 552(b)(4) RNA sequencing costs to PNNL and removed the travel costs in case that helps with the budget justification.

PNNL would like another signed face page but we are not in a rush to get it.

Please let me know if you have any questions. Thank you very much! Amy

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 7/7/2020 2:32:16 PM
To: Schaefer, Alexandra [aschaefe@email.unc.edu]; Sheahan, Timothy Patrick [sheahan@email.unc.edu]
CC: Baric, Ralph S [rbaric@email.unc.edu]
Subject: Year 2 for R21

Dear Alex and Tim,

I hope you are both doing well and finding a little down time in your crazy days.

I wanted to update you on the year 2 funds for the R21. The good news is that we finally got a revised notice of award for the R21 from the NIH and the subcontract should be in the works very soon.

The bad news is that our grants manager held PNNL to a rule that is often not enforced and that changed the amount of funds UNC (and PNNL) is going to receive.

When funds are transferred the NIH has the option to hold the direct (also know as spendable dollars) to the following: total direct dollars (5 U.S.C. § 552(b)(4)) = direct dollars for the new institution + TOTAL costs (direct plus indirect costs) for the subcontract

This meant that the budget we originally sent to the NIH for Year 2 had to be reduced by 5 U.S.C. § 552(b)(4)

One of the things I did to try to salvage as much money as possible was to move 5 U.S.C. § 552(b)(4) or so for the ChIP RNA Seq analysis to PNNL so that we could keep that total dollar amount. Alex, this basically means whenever you submit those samples for analysis that the bill needs to come to PNNL instead of being paid by UNC.

Please let me know if you have any questions and I will do my best to find the answer.

I will let you know when UNC has the subcontract for review.

Best wishes, Amy

PS. Alex I wasn't sure if you had a chance to find an alternative kit for looking at the fibroblasts. Please let me know how that is going and how I can help. Thank you, Amy

From: Ames, Amber A[Amber.Ames@pnnl.gov]
Sent: Wed 7/8/2020 10:21:37 AM (UTC-07:00)
To: Koltz, Diane M[dkoltz@email.unc.edu]; Fulcher, Leslie[leslie_fulcher@med.unc.edu]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form
Attachment: PO 521567.xml
Attachment: GP-A-409.24-FP_October 2019.pdf
Attachment: MLI Order Form Oct2019 (002).docx

Dear Diane,

Just checking in for a status update.

Kind regards,

Amber

From: Ames, Amber A
Sent: Monday, June 29, 2020 10:25 AM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

I have been advised that we would like to pursue UNC as the source of the HBE cells. I have attached our purchase order template in word. We do not customize the General Provisions so those are a .pdf. All changes will be listed in the purchase order as an alteration to the GPs—sample below. We have a long history of contracting with UNC so I have copied the Alterations we have negotiated for previous awards. Unfortunately, as a DOE M&O contractor we are also very limited on what we can negotiate. DOE requires their terms control. We understand universities cannot grant indemnity and we are confident we will be able to negotiate changes that will be acceptable to UNC and DOE.

Alterations to General Provisions

1. Permits and Responsibilities (cl. 358—Nov 1991) is hereby deleted and replaced with:
"The Contractor is an independent contractor, not an agent or employee of Battelle. The Contractor shall, without additional expense to Battelle or the Government, be responsible for obtaining any necessary licenses and permits, and for complying with any Federal, State, and municipal laws, codes, and regulations applicable to the performance of the work. The Contractor shall also be responsible for all damages to persons or property that occurs as a result of the Contractor's fault or negligence only in the manner and to the extent permitted under North Carolina law, including but not limited to the NC Tort Claims Act, GS 143-291, et seq., and without waiver of its sovereign immunity."

2. Insurance—Liability to Third Persons (cl. 378b—Mar 1996) is hereby deleted and replaced with:
"University of North Carolina is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."

3. Disputes (cl. 331—Nov 2014)
Delete in its entirety.

4. Insurance Requirements (cl. 378—Nov 2014) is hereby deleted and replaced with:
"University of North Carolina is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."

I note I have been advised we will have another order with a budget of 5 U.S.C. § 552(b)(4) so it is critical we resolve the terms and conditions.

Thank you for your assistance with this matter.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Thursday, June 18, 2020 11:06 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I received your changes for review and upon a first look, UNC cannot agree to all of the supplemental terms contained in the online documents you want to include. As a state institution, we are somewhat limited. The order form contains the minimal terms UNC requires in its contracts and we typically do not agree to changes. Is there any possibility that we could make UNC's agreement control, or not reference the terms at all, since much of what is contained in the online "purchase agreements" won't apply to what we are providing. If this is not possible, please provide me word versions of the online agreements so I can outline our requested edits and comments. Also, please note that review of the documents will take time.

Thanks,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Thursday, June 18, 2020 12:58 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Just checking in to see if there is a response to our requested changes to the order form terms.

Thanks so much!

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Wednesday, June 10, 2020 3:04 AM

To: Ames, Amber A <Amber.Ames@pnnl.gov>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Good Morning Amber,
Yes, once the contract is executed, Amy will be able to order as needed up to the dollar amount on the contract and during the 1 year period. I am including our contract specialist who can look at your suggested changes and she will be in touch with you soon.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 9:02 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Thanks, Leslie. The project would like to be able to order up to 10 ALI medium and 26 Normal HBE Cells from now until September 30, 2021. Are they able to order on an as-needed basis? I can incorporate a signed version of the attached into the PO for the project to use? Once I sign it, they won't be able to edit it. Perhaps we need to do a purchase order per order?

I note I provided redlines on the attached. Please advise if UNCC is able to work with the redlines.

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 5:29 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,
Thanks for emailing back, but to complete the contract, I need the agreement signed and returned to me prior to ordering. As for payment options, a check is fine, but we do have an account that funds could be wired. If that works for you, I can share that information.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 5:09 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

Attached please find Purchase Order No. 521567 to purchase up to the quantities I had listed below. Per the PO, we

will place orders via the ordering website. There is no need to sign the PO—if you can acknowledge receipt and that this will work for ordering/payment purposes, that would be helpful.

I'm guessing the MLI Tissue Procurement and Cell Culture Core Facility will want a paper check mailed to the 125 Mason Farm Road address instead of paid by ACH to UNCC's main Bank of America account?

Amy, the shipping address in PES is 331 Building, Room 70. Even if a different shipping address is input in the UNCC online ordering system, any orders associated with PO 521567 will ship to 331/70. If you need a different ship to, let me know.

Thanks!

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 12:36 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,

As long as the contract is signed, the dollar amount is entered, and the period is in place there will be no rate increase.
You don't need to select the quantity of any item, but if your project you will use the quantity listed below, entering in the dollar amount is sufficient. I may suggest adding a little wiggle room in the dollar amount because once the dollar amount is reached, even before the term is up, we will need to renew the contract.

Also, once the contract is executed, you would just log onto our ordering website and order what you need.
Please let me know if you have any questions.

Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 9, 2020 1:19 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

I have a requisition to issue a Purchase Order to UNCC for a fixed unit rate contract for the following:

Description	Price	Maximum Quantity Expected	Extended Price
BEGM MEDIUM	5 U.S.C. § 552(b)(4)	0	5 U.S.C. § 552(b)(4)
ALI MEDIUM		10	
VALI MEDIUM		0	
Normal HBE Cells		26	
Diseased HBE Cells		0	
Cystic Fibrosis HBE Cells		0	
Normal Microvascular Cells		0	
Normal Fibroblast Cells		0	
Total Not to Exceed Amount			

The project would like to use the purchase order for payment of requirements on an as-needed basis through September 30, 2021.

My question is how long the pricing in Exhibit A of the attached is valid? Are the prices updated annually?

Do you have any concerns with this approach?

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov


Pacific Northwest
NATIONAL LABORATORY

From: Schaefer, Alexandra[aschaefe@email.unc.edu]
Sent: Sun 7/12/2020 8:09:35 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Year 2 for R21

Hi Amy,

thanks for the update!

sorry, I have been quiet in the last weeks--
but especially the last 3-4 weeks, we have had a crazy mouse workload in the BSL3.....
now, there is light at the end of the tunnel again (at least a glimpse of it)

hmmmm 5 U.S.C. § 552(b)(4) -- that sucks

I have finished the ChIPs for STAT1 in the MEVS and will finish those most likely within the next couple of weeks

It's a bummer that we can't get the Qiagen kits anymore, especially with the money constraint, since the others are so much more expensive, however, the invitrogen ones (with magnetic beads) are way more specific, and super sensitive, sop that will help in the end
----- I have been using those for years now, and they are super reliable, and easy to use, and work for our stuff--
so, I will probably use them from now on for all the experiments

Talk to you soon again,
Alex

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, July 7, 2020 5:32 PM
To: Schaefer, Alexandra <aschaefe@email.unc.edu>; Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Cc: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Year 2 for R21

Dear Alex and Tim,

I hope you are both doing well and finding a little down time in your crazy days.

I wanted to update you on the year 2 funds for the R21. The good news is that we finally got a revised notice of award for the R21 from the NIH and the subcontract should be in the works very soon.

The bad news is that our grants manager held PNNL to a rule that is often not enforced and that changed the amount of funds UNC (and PNNL) is going to receive.

When funds are transferred the NIH has the option to hold the direct (also know as spendable dollars) to the following: total direct dollars (could not exceed 5 U.S.C. § 552(b)(4) for us) = direct dollars for the new institution + TOTAL costs (direct plus indirect costs) for the subcontract

This meant that the budget we originally sent to the NIH for Year 2 had to be reduced by over 5 U.S.C. § 552(b)(4).

One of the things I did to try to salvage as much money as possible was to move the 5 U.S.C. § 552(b)(4) or so for the ChIP RNA Seq analysis to PNNL so that we could keep that total dollar amount. Alex, this basically means whenever you submit those samples for analysis that the bill needs to come to PNNL instead of being paid by UNC.

Please let me know if you have any questions and I will do my best to find the answer.

I will let you know when UNC has the subcontract for review.

Best wishes, Amy

PS. Alex I wasn't sure if you had a chance to find an alternative kit for looking at the fibroblasts. Please let me know how that is going and how I can help. Thank you, Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 7/13/2020 12:18:50 PM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]; Baric, Ralph S[rbaric@email.unc.edu]
Subject: Shipment of cell stocks this week or next?

Hi Ben,

I hope you are doing well and that you and your family are staying safe in these super crazy times.

Would it be possible for you to send me some stocks of different tissue culture lines at some point over the next two weeks? I would really appreciate it.

Can you please send me the following??

1. Vero cells E6 aka USAMRIID
2. Vero cells CC81 aka WHO
3. MDCK cells
4. LLCMK2 cells
5. Calu3 cells

I really appreciate it. Please let me know if you have any questions. Thank you very much! Amy

PS. I will send you the address and anything else you need in the next round of emails.

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Mon 7/13/2020 12:20:48 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]; Baric, Ralph S[rbaric@email.unc.edu]
Subject: RE: Shipment of cell stocks this week or next?

Shouldn't be a problem. Do any of these need an MTA? And/or are they already listed on that big MTA we did a while back? I can check if you don't know off the top of your head.

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From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, July 13, 2020 3:19 PM
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From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 7/13/2020 1:13:18 PM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]; Baric, Ralph S[rbaric@email.unc.edu]
Subject: Re: Shipment of cell stocks this week or next?

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From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Tue 7/14/2020 6:52:46 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Shipment of cell stocks this week or next?

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Sent: Monday, July 13, 2020 4:13 PM
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From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 7/14/2020 8:42:18 AM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]
Subject: Re: Shipment of cell stocks this week or next?

Thank you. I appreciate it. Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
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From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Tue 7/14/2020 8:43:22 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Shipment of cell stocks this week or next?

From what I can gather (from Rachel and Lisa), it sounds like our version of LLCMK2 is probably fine to share without an MTA. Thoughts?

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, July 14, 2020 11:42 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: Shipment of cell stocks this week or next?

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Date: Tuesday, July 14, 2020 at 6:53 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Shipment of cell stocks this week or next?

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From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 7/14/2020 8:44:57 AM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]
Subject: Re: Shipment of cell stocks this week or next?

I think we got them from a collaborator in 2006 and that most likely no one really cares where they came from anymore. I am fine if you guys are. Thank you, Amy

---

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
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To: McGlaughon, Ben <benmcg@email.unc.edu>
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PS. I will send you the address and anything else you need in the next round of emails.

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Tue 7/14/2020 8:46:45 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Shipment of cell stocks this week or next?

Works for me! I'll start the process of figuring out our stock situation with all of these so that I can start sending them your way once you're ready.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, July 14, 2020 11:45 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: Shipment of cell stocks this week or next?

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From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 7/14/2020 8:55:14 AM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]
Subject: Re: Shipment of cell stocks this week or next?

Consider me ready any time now. Thank you, Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, July 14, 2020 at 8:47 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Shipment of cell stocks this week or next?

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From: Ames, Amber A[Amber.Ames@pnnl.gov]
Sent: Thur 7/16/2020 1:25:43 PM (UTC-07:00)
To: Koltz, Diane M[dkoltz@email.unc.edu]
Cc: Fulcher, Leslie[leslie_fulcher@med.unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Diana,

Just checking in to see if you have an update.

Kind regards,

Amber

From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Wednesday, July 08, 2020 11:03 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I am working with my manager on reviewing the General Terms and Conditions and hope to be back with you by the end of the week.
Thanks for your patience,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Wednesday, July 8, 2020 1:22 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

Just checking in for a status update.

Kind regards,

Amber

From: Ames, Amber A
Sent: Monday, June 29, 2020 10:25 AM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

I have been advised that we would like to pursue UNC as the source of the HBE cells. I have attached our purchase order template in word. We do not customize the General Provisions so those are a .pdf. All changes will be listed in the purchase order as an alteration to the GPs—sample below. We have a long history of contracting with UNC so I have copied the Alterations we have negotiated for previous awards. Unfortunately, as a DOE M&O contractor we are also very limited on what we can negotiate. DOE requires their terms control. We understand universities cannot grant indemnity and we are confident we will be able to negotiate changes that will be acceptable to UNC and DOE.

Alterations to General Provisions

1. Permits and Responsibilities (cl. 358—Nov 1991) is hereby deleted and replaced with:
"The Contractor is an independent contractor, not an agent or employee of Battelle. The Contractor shall, without additional expense to Battelle or the Government, be responsible for obtaining any necessary licenses and permits, and for complying with any Federal, State, and municipal laws, codes, and regulations applicable to the performance of the work. The Contractor shall also be responsible for all damages to persons or property that occurs as a result of the Contractor's fault or negligence only in the manner and to the extent permitted under North Carolina law, including but not limited to the NC Tort Claims Act, GS 143-291, et seq., and without waiver of its sovereign immunity."

2. Insurance—Liability to Third Persons (cl. 378b—Mar 1996) is hereby deleted and replaced with:
"University of North Carolina is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."

3. Disputes (cl. 331—Nov 2014)
Delete in its entirety.

4. Insurance Requirements (cl. 378—Nov 2014) is hereby deleted and replaced with:
"University of North Carolina is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."

I note I have been advised we will have another order with a budget of 5 U.S.C. § 552(b)(4) so it is critical we resolve the terms and conditions.

Thank you for your assistance with this matter.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov



From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Thursday, June 18, 2020 11:06 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I received your changes for review and upon a first look, UNC cannot agree to all of the supplemental terms contained

in the online documents you want to include. As a state institution, we are somewhat limited. The order form contains the minimal terms UNC requires in its contracts and we typically do not agree to changes. Is there any possibility that we could make UNC's agreement control, or not reference the terms at all, since much of what is contained in the online "purchase agreements" won't apply to what we are providing. If this is not possible, please provide me word versions of the online agreements so I can outline our requested edits and comments. Also, please note that review of the documents will take time.

Thanks,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Thursday, June 18, 2020 12:58 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Just checking in to see if there is a response to our requested changes to the order form terms.

Thanks so much!

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Wednesday, June 10, 2020 3:04 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Good Morning Amber,
Yes, once the contract is executed, Amy will be able to order as needed up to the dollar amount on the contract and during the 1 year period. I am including our contract specialist who can look at your suggested changes and she will be in touch with you soon.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 9:02 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Thanks, Leslie. The project would like to be able to order up to 10 ALI medium and 26 Normal HBE Cells from now until September 30, 2021. Are they able to order on an as-needed basis? I can incorporate a signed version of the attached into the PO for the project to use? Once I sign it, they won't be able to edit it. Perhaps we need to do a purchase order per order?

I note I provided redlines on the attached. Please advise if UNCC is able to work with the redlines.

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 5:29 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,
Thanks for emailing back, but to complete the contract, I need the agreement signed and returned to me prior to ordering. As for payment options, a check is fine, but we do have an account that funds could be wired. If that works for you, I can share that information.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 5:09 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

Attached please find Purchase Order No. 521567 to purchase up to the quantities I had listed below. Per the PO, we will place orders via the ordering website. There is no need to sign the PO—if you can acknowledge receipt and that this will work for ordering/payment purposes, that would be helpful.

I'm guessing the MLI Tissue Procurement and Cell Culture Core Facility will want a paper check mailed to the 125 Mason Farm Road address instead of paid by ACH to UNCC's main Bank of America account?

Amy, the shipping address in PES is 331 Building, Room 70. Even if a different shipping address is input in the UNCC online ordering system, any orders associated with PO 521567 will ship to 331/70. If you need a different ship to, let me know.

Thanks!

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 12:36 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,

As long as the contract is signed, the dollar amount is entered, and the period is in place there will be no rate increase.
You don't need to select the quantity of any item, but if your project you will use the quantity listed below, entering in the dollar amount is sufficient. I may suggest adding a little wiggle room in the dollar amount because once the dollar amount is reached, even before the term is up, we will need to renew the contract.

Also, once the contract is executed, you would just log onto our ordering website and order what you need.
Please let me know if you have any questions.

Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 9, 2020 1:19 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

I have a requisition to issue a Purchase Order to UNCC for a fixed unit rate contract for the following:

Description	Price	Maximum Quantity Expected	Extended Price
BEGM MEDIUM	5 U.S.C. § 552(b)(4)	(b) (4)	5 U.S.C. § 552(b)(4)
ALI MEDIUM			
VALI MEDIUM			
Normal HBE Cells			
Diseased HBE Cells			
Cystic Fibrosis HBE Cells			
Normal Microvascular			

Cells			
Normal Fibroblast Cells	5 U.S.C. § 552(b)(4)	(b) (4)	5 U.S.C. § 552(b)(4)
Total Not to Exceed Amount			

The project would like to use the purchase order for payment of requirements on an as-needed basis through September 30, 2021.

My question is how long the pricing in Exhibit A of the attached is valid? Are the prices updated annually?

Do you have any concerns with this approach?

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 7/16/2020 3:49:42 PM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]
Subject: Re: Shipment of cell stocks this week or next?

Hi Ben,

I am trying to plan some experiments in the near future and it would be really helpful to know when the cells might arrive.

Thank you, Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, July 14, 2020 at 8:47 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Shipment of cell stocks this week or next?

Works for me! I'll start the process of figuring out our stock situation with all of these so that I can start sending them your way once you're ready.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, July 14, 2020 11:45 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: Shipment of cell stocks this week or next?

I think we got them from a collaborator in 2006 and that most likely no one really cares where they came from anymore. I am fine if you guys are. Thank you, Amy

---

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, July 14, 2020 at 8:43 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Shipment of cell stocks this week or next?

From what I can gather (from Rachel and Lisa), it sounds like our version of LLCMK2 is probably fine to share without an MTA. Thoughts?

Ben

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Sent: Tuesday, July 14, 2020 11:42 AM
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Subject: Re: Shipment of cell stocks this week or next?

Thank you. I appreciate it. Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, July 14, 2020 at 6:53 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>

Subject: RE: Shipment of cell stocks this week or next?

They're all covered in the MTA except for the LLCMK2 cells, you're right. I will check with the MTA office and see if it's easier to amend the current MTA or just file a new one. I'll let you know what I find out.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, July 13, 2020 4:13 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>; Baric, Ralph S <rbaric@email.unc.edu>
Subject: Re: Shipment of cell stocks this week or next?

Hi Ben,

I believe I asked for all of the cell lines below except for the LLCMK2 cells in the big MTA. Please check and make sure I didn't miss one. Let me know if the existing MTA can be modified and/or how we should proceed.

Thank you very much! Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Monday, July 13, 2020 at 12:22 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: RE: Shipment of cell stocks this week or next?

Shouldn't be a problem. Do any of these need an MTA? And/or are they already listed on that big MTA we did a while back? I can check if you don't know off the top of your head.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, July 13, 2020 3:19 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>; Baric, Ralph S <rbaric@email.unc.edu>
Subject: Shipment of cell stocks this week or next?

Hi Ben,

I hope you are doing well and that you and your family are staying safe in these super crazy times.

Would it be possible for you to send me some stocks of different tissue culture lines at some point over the next two weeks? I would really appreciate it.

Can you please send me the following??

1. Vero cells E6 aka USAMRIID
2. Vero cells CC81 aka WHO
3. MDCK cells
4. LLCMK2 cells
5. Calu3 cells

I really appreciate it. Please let me know if you have any questions. Thank you very much! Amy

PS. I will send you the address and anything else you need in the next round of emails.

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Thur 7/16/2020 3:57:00 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Shipment of cell stocks this week or next?

I've tracked down both types of Vero cells, still waiting to hear back about the rest. I'll ask again tomorrow and let you know what I hear.

Ben

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Sent: Thur 7/16/2020 4:00:42 PM (UTC-07:00)
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I really appreciate it. Please let me know if you have any questions. Thank you very much! Amy

PS. I will send you the address and anything else you need in the next round of emails.

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 7/21/2020 11:27:50 AM
To: Schaefer, Alexandra [aschaefe@email.unc.edu]
Subject: Re: Year 2 for R21

Hi Alex,

I am very sorry it has taken me so long to get back in touch with you. I am very excited to hear that you have finished the STAT1 ChIPs for the MVE that is great news. I am also relieved to know that the Invitrogen kits will work in place of the ones from Qiagen. I really hate when products are discontinued without notice.

I am hoping that the subcontract for UNC will be established soon. Remember that in addition to UNC's direct costs I am holding 5 U.S.C. § 552(b)(4) or you to do RNA Seq with when the samples are ready.

I hope things are improving on your end. I will be in touch in August so we can have a meeting and catch up. Thank you, Amy

---

From: "Schaefer, Alexandra" <aschaefe@email.unc.edu>
Date: Sunday, July 12, 2020 at 8:09 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Year 2 for R21

Hi Amy,

thanks for the update!

sorry, I have been quiet in the last weeks--
but especially the last 3-4 weeks, we have had a crazy mouse workload in the BSL3.....
now, there is light at the end of the tunnel again (at least a glimpse of it)

hmmmm 5 U.S.C. § 552(b)(4) that sucks

I have finished the ChIPs for STAT1 in the MEVS and will finish those most likely within the next couple of weeks

It's a bummer that we can't get the Qiagen kits anymore, especially with the money constraint, since the others are so much more expensive, however, the invitrogen ones (with magnetic beads) are way more specific, and super sensitive, sop that will help in the end
----- I have been using those for years now, and they are super reliable, and easy to use, and work for our stuff--
so, I will probably use them from now on for all the experiments

Talk to you soon again,
Alex

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, July 7, 2020 5:32 PM

To: Schaefer, Alexandra <aschaefe@email.unc.edu>; Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Cc: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Year 2 for R21

Dear Alex and Tim,

I hope you are both doing well and finding a little down time in your crazy days.

I wanted to update you on the year 2 funds for the R21. The good news is that we finally got a revised notice of award for the R21 from the NIH and the subcontract should be in the works very soon.

The bad news is that our grants manager held PNNL to a rule that is often not enforced and that changed the amount of funds UNC (and PNNL) is going to receive.

When funds are transferred the NIH has the option to hold the direct (also know as spendable dollars) to the following: total direct dollars (5 U.S.C. § 552(b)(4)) = direct dollars for the new institution + TOTAL costs (direct plus indirect costs) for the subcontract

This meant that the budget we originally sent to the NIH for Year 2 had to be reduced by over 5 U.S.C. § 552(b)(4)

One of the things I did to try to salvage as much money as possible was to move the 5 U.S.C. § 552(b)(4) or so for the ChIP RNA Seq analysis to PNNL so that we could keep that total dollar amount. Alex, this basically means whenever you submit those samples for analysis that the bill needs to come to PNNL instead of being paid by UNC.

Please let me know if you have any questions and I will do my best to find the answer.

I will let you know when UNC has the subcontract for review.

Best wishes, Amy

PS. Alex I wasn't sure if you had a chance to find an alternative kit for looking at the fibroblasts. Please let me know how that is going and how I can help. Thank you, Amy

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Tue 7/21/2020 12:49:35 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Shipment of cell stocks this week or next?

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>
> **From:** "McGlaughon, Ben" <benmcg@email.unc.edu>
> **Date:** Tuesday, July 14, 2020 at 8:47 AM
> **To:** "Sims, Amy C" <amy.sims@pnnl.gov>
> **Subject:** RE: Shipment of cell stocks this week or next?
>
> Works for me! I'll start the process of figuring out our stock situation with all of these so that I can start sending them your way once you're ready.
>
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>
> ---
>
> **From:** Sims, Amy C <amy.sims@pnnl.gov>
> **Sent:** Tuesday, July 14, 2020 11:45 AM
> **To:** McGlaughon, Ben <benmcg@email.unc.edu>
> **Subject:** Re: Shipment of cell stocks this week or next?
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> **Date:** Tuesday, July 14, 2020 at 8:43 AM
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> **Subject:** RE: Shipment of cell stocks this week or next?
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>
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From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, July 14, 2020 11:42 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: Shipment of cell stocks this week or next?

Thank you. I appreciate it. Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, July 14, 2020 at 6:53 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Shipment of cell stocks this week or next?

They're all covered in the MTA except for the LLCMK2 cells, you're right. I will check with the MTA office and see if it's easier to amend the current MTA or just file a new one. I'll let you know what I find out.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, July 13, 2020 4:13 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>; Baric, Ralph S <rbaric@email.unc.edu>
Subject: Re: Shipment of cell stocks this week or next?

Hi Ben,

I believe I asked for all of the cell lines below except for the LLCMK2 cells in the big MTA. Please check and make sure I didn't miss one. Let me know if the existing MTA can be modified and/or how we should proceed.

Thank you very much! Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Monday, July 13, 2020 at 12:22 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: RE: Shipment of cell stocks this week or next?

Shouldn't be a problem. Do any of these need an MTA? And/or are they already listed on that big MTA we did a while back? I can check if you don't know off the top of your head.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, July 13, 2020 3:19 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>; Baric, Ralph S <rbaric@email.unc.edu>
Subject: Shipment of cell stocks this week or next?

Hi Ben,

I hope you are doing well and that you and your family are staying safe in these super crazy times.

Would it be possible for you to send me some stocks of different tissue culture lines at some point over

the next two weeks? I would really appreciate it.

Can you please send me the following??

1. Vero cells E6 aka USAMRIID
2. Vero cells CC81 aka WHO
3. MDCK cells
4. LLCMK2 cells
5. Calu3 cells

I really appreciate it. Please let me know if you have any questions. Thank you very much! Amy

PS. I will send you the address and anything else you need in the next round of emails.

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 7/22/2020 8:17:27 AM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]
Subject: Re: Shipment of cell stocks this week or next?

Perfect. Thank you very much! Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Wednesday, July 22, 2020 at 8:16 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Shipment of cell stocks this week or next?

FedEx tracking # 771059935827

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, July 22, 2020 9:59 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: Shipment of cell stocks this week or next?

Ship what you can today. That would be really great. Then take next week to find the rest if possible. Let's wait to ship until the first week of August as I will be out of town for work next week. Thank you very much.
Amy

Get Outlook for iOS

From: McGlaughon, Ben <benmcg@email.unc.edu>
Sent: Wednesday, July 22, 2020 5:49 AM
To: Sims, Amy C
Subject: RE: Shipment of cell stocks this week or next?

That's fine, and if it doesn't work we can just cover shipping and it won't be an issue. I'm making an effort to get at least some of these shipped out today, but with everybody being so busy it has been hard to find the cells. If not today then I will make sure they are ready by Monday or Tuesday of next week. Does all that work for you?

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, July 21, 2020 7:40 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: Shipment of cell stocks this week or next?

Hi Ben,

Thank you. I appreciate it. I know it's a pain to track all of these down. I am trying to figure out if there is a fedex number for PNNL or if the best thing to do is to use your account number and select bill recipient and then make sure to add the "Request ID" number below to the PO number space on the Fedex form. This should allow me to be billed instead of the Baric lab. Will that work?

Please add everything I listed below on the side of the box as we have a central receiving for all packages and this information will expedite my receipt of the box.

Thank you very much! Amy

Battelle for the US DOE
Attn: Amy Sims/331/70
(b) (6) [redacted]
Collaborator samples, no PO
790 6th Street
Richland, WA 99354

Request Id: RCV10114

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, July 21, 2020 at 12:50 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Shipment of cell stocks this week or next?

Still working on tracking all these down, but can you get me an address, phone number, and FedEx number (if you have one) so that when I have everything ready I can ship?

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, July 16, 2020 7:01 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: Shipment of cell stocks this week or next?

Awesome. Thank you, Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Thursday, July 16, 2020 at 3:58 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Shipment of cell stocks this week or next?

I've tracked down both types of Vero cells, still waiting to hear back about the rest. I'll ask again tomorrow and let you know what I hear.

Ben

> On Jul 16, 2020, at 6:49 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:
>
> Hi Ben,
>
> I am trying to plan some experiments in the near future and it would be really helpful to know when the cells might arrive.
>
> Thank you, Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>

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2. Vero cells CC81 aka WHO
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4. LLCMK2 cells
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PS. I will send you the address and anything else you need in the next round of emails.

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Thur 7/23/2020 11:20:27 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: FedEx Shipment 771059935827: Your package has been delivered

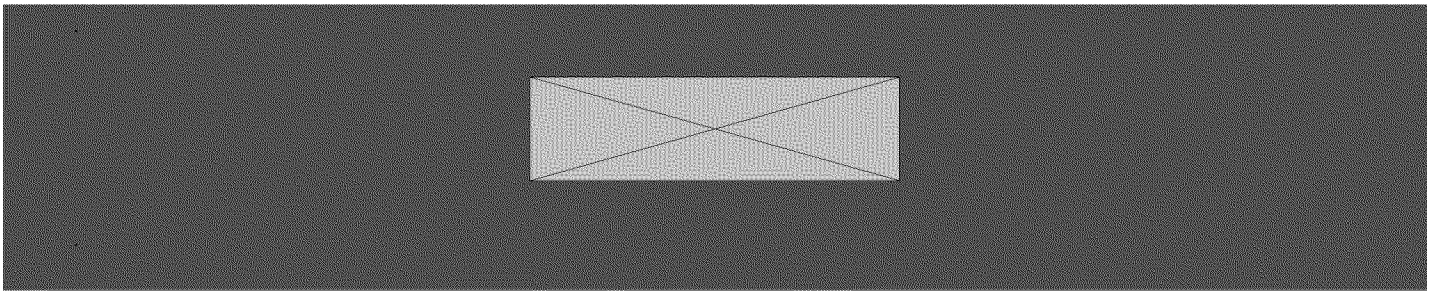
Great! Glad it made it.

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, July 23, 2020 2:12 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: FW: FedEx Shipment 771059935827: Your package has been delivered

Thank you, Ben. The package made it to the clearing house! I really appreciate it. Amy

---

From: "TrackingUpdates@fedex.com" <TrackingUpdates@fedex.com>
Reply-To: "trackingmail@fedex.com" <trackingmail@fedex.com>
Date: Thursday, July 23, 2020 at 10:36 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: FedEx Shipment 771059935827: Your package has been delivered



Hi. Your package was delivered Thu, 07/23/2020 at 10:23am.



Delivered to 790 6TH ST, RICHLAND, WA 99354

Received by I.HARRIS

OBTAIN PROOF OF DELIVERY

TRACKING NUMBER 771059935827

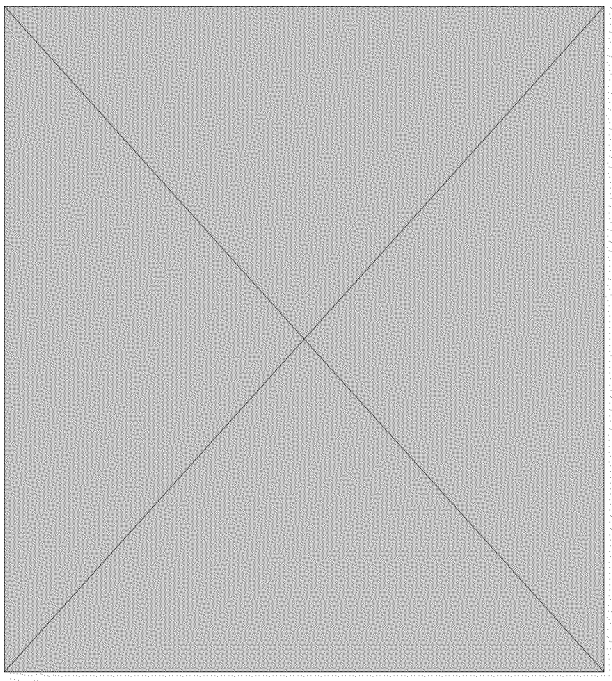
FROM
Benjamin McGlaughon
3205 Hooker Research Bldg
135 Dauer Drive
Chapel Hill, NC, US, 27599

TO
Attn: Amy Sims
790 6th Street
Request Id: RCV10114
RICHLAND, WA, US, 99354

REFERENCE 5116594

SHIPPER REFERENCE	**5116594**
SHIP DATE	Wed 7/22/2020 12:42 PM
DELIVERED TO	Shipping/Receiving
PACKAGING TYPE	Your Packaging
ORIGIN	Chapel Hill, NC, US, 27599
DESTINATION	RICHLAND, WA, US, 99354
SPECIAL HANDLING	Adult Signature Required
NUMBER OF PIECES	1
TOTAL SHIPMENT WEIGHT	15.00 LB
SERVICE TYPE	FedEx Priority Overnight

Download the



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Thank you for your business.

From: Ames, Amber A[Amber.Ames@pnnl.gov]
Sent: Thur 7/23/2020 5:02:44 PM (UTC-07:00)
To: sheahan@email.unc.edu[sheahan@email.unc.edu]; ResAdminOSR@unc.edu[ResAdminOSR@unc.edu]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]
Subject: Request for Proposal No. 596021
Attachment: PR 596021 RFP.pdf
Attachment: PR 596021 SOW.pdf
Attachment: REPRESENTATIONS AND CERTIFICATIONS final track changes 3-10-20 FORM (3).pdf
Attachment: GP-A-409.25-EDNP_October 2019.pdf
Attachment: R21_Yr2_UNC_Subcontact_Costs.pdf

Dear Dr. Sheahan,

Attached please find a request for proposal for the University of North Carolina at Chapel Hill and Principal Investigator Timothy Sheahan to support the "How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells" project, per the attached Statement of Work dated July 14, 2020.

This will confirm I am in receipt of the attached budget. If the cost elements have not changed (salary, fringe) the attached budget is sufficient for award. If you have a budget justification that explains the fringe rates and how the supplies were estimated, that would be helpful. The only other document I need to make the award is the completed Representations and Certifications.

In support of the RFP, please find:

- RFP instructions
- Statement of Work
- Representations and Certifications (required for all actions over $25K)
- General Provisions

As noted in the attached, your response is requested by COB **Friday, July 31, 2020.**

As a Federally Research and Development center we operate under a standard set of terms and conditions defined by DOE which outline how we can receive and how we must spend monies coming to the laboratory. This enables us to receive sponsor funds directly, but also provides a standard set of DOE terms under which we must place our all of subcontracts. We do not have authority to award grants. All subawards will be in the form of a subcontract subject to the applicable General Provisions for the applicable subcontract type. **There is no authorization to begin work and costs are not allowable until the contract is issued. If it is urgent for to start work, I can award a Precontract Authorization to cover costs while we finalize this contract. In the absence of this, costs are not allowable until a precontract authorization is issued or the contract is issued.**

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov


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With the U.S. Department of Energy
Operating the Pacific Northwest National Laboratory (PNNL) (www.pnnl.gov)

Request for Proposal No. 596021	
Issued by: Battelle Battelle Boulevard, K9-15 P.O. Box 999 Richland, WA 99352-0999 USA	**Contracts Specialist:** Name: Amber Ames Telephone Number: (509) 371-7050 E-mail: amber.ames@pnnl.gov
Proposal Due Date: COB Friday, July 31, 2020	**Period of Performance:** Date of contract award through May 31, 2021
Payment Terms: Net 30	**Anticipated Contract Type:** Cost Reimbursement

This is a Request for Proposal for University of North Carolina at Chapel Hill and Principal Investigator Timothy Sheahan to support the "How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells" project, per the attached Statement of Work dated July 14, 2020.

Contract Contents

The resulting contract will include the following generation provisions:

- The General Provisions Applicable for Educational Institutions and Nonprofit Organizations, Form A-409.25-Ed/NP dated October 2019, apply and may be viewed at http://www.pnnl.gov/contracts/contractdocuments.aspx.

Battelle Contracts Representative

The Battelle Contracts Representative, Amber Ames, is the sole point of contact for any communications or questions regarding this acquisition.

Solicitation Provisions

In addition to the requirements outlined herein, the Solicitation Provisions, Form A-609-SP (November 2014), available at http://www.pnnl.gov/contracts/contractdocuments.aspx apply to this Request for Proposal.

Submission of Proposals

The proposal submitted should include:

A. Completed Representation - Certification form found at:
http://www.pnnl.gov/contracts/contractdocuments.aspx
   - The NAICS code for section A.1 of the Representations and Certifications is 611310
   - The size standard for section A.2 is $30 million.

B. A budget with budget justification for each cost element identified, including:
   - **Direct Labor**: provide the labor category of the listed individuals and their credentials, i.e., payroll register, education, and experience. Identify all foreign nationals, and nationality that are expected to work on this project. If possible, provide salary backup to substantiate rates proposed. Provide breakdown of rate and quantity, whether it is rate x hours or monthly salary x FTE months.
   - **Other Direct Costs**: list materials, supplies, equipment, etc. including pricing support obtained such as quotes.
   - **Approved Rate Agreement**, including **Fringe** and **Indirect Rates** or link to rate agreement.

- **Travel** include breakdown of estimate including airfare, lodging, meals, transportation, etc. Identify all travelers expected to travel to foreign locations.

If helpful, you may use the Contract Pricing Proposal form CR Contracts with Universities located at http://www.pnnl.gov/contracts/contractdocuments.aspx.

Proposals shall be delivered to Battelle on or before **COB Friday, July 31, 2020** and shall be valid for a minimum of 60 days.

Proposals are preferred to be submitted via Email to amber.ames@pnnl.gov with a subject line that includes the words "Proposal to RFP 596021".

Funding is not fully obligated for this action. Contract award is subject to Availability of Funds at the time of award.

Ombudsman Program

Offeror is hereby notified that issues/concerns relative to this solicitation and/or any resulting contract award that are not resolved by the Battelle Contracts Representative identified herein shall be resolved through Battelle's Ombudsman Program by email at acquisitionombudsman@pnnl.gov. Any issue/concern shall be submitted, in writing, no later than 30 calendar days after contract award to be considered for review.

Statement of Work
How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
University of North Carolina at Chapel Hill, Principal Investigator Timothy Sheahan
July 16, 2020

I. Background

The molecular mechanisms regulating emerging highly pathogenic human respiratory coronavirus pathogenesis are complex and include dampening of the host innate immune response allowing higher viral titers immediately following entry. Previous studies tracking the expression of interferon stimulated gene (ISG) expression in Middle East respiratory syndrome coronavirus (MERS-CoV) infected continuous human lung epithelial cells demonstrated that specific ISG expression patterns could be detected and these patterns could be used to determine how CoV were modulating the innate immune response. Epigenetic/chromatin remodeling mechanisms were found to be important regulators of host chromatin remodeling that altered host expression ISG patterns. This proposal will build on these foundational studies performed in continuous human lung cell lines and define ways that MERS-CoV regulates innate immunity in primary human lung fibroblasts and microvascular endothelial cells.

II. Scope

University of North Carolina at Chapel Hill will analyze the fibroblast ChIP PCR samples collected in 2019 and discuss data with PNNL to determine next steps. University of North Carolina at Chapel Hill will perform ChIP Seq analysis of MERS-CoV infected microvascular endothelial cells at a single time point for three donors. University of North Carolina at Chapel Hill will perform BioRad Primer PCR Pathway Arrays on MERS-CoV infected microvascular endothelial cells and fibroblasts. Drs Sheahan and Schaefer will work in close collaboration with PNNL to analyze datasets to determine how MERS-CoV regulates ISG expression in human lung microvascular endothelial cells and fibroblasts.

III. Deliverables

- Evaluate project results and direction, in collaboration with PNNL
- Collaborate on experiment direction and identify alternatives for experiments
- Participate in meetings to discuss project status/progress, findings, and trouble shoot as needed
- Write and submit progress report and manuscript draft in collaboration with PNNL

Start Date: July 1, 2020-June 30, 2021

NAME	TITLE	SALARY	EFFORT	12 Cal Months	SALARY	FRINGE	TOTAL
Sheahan, Timothy	PI		5%	0.60			
Schaefer, Alexandra	Staff Scientist		20%	2.40			
TBD	Research Specialist	5 U.S.C. § 552(b)(4)	0%	0.00	5 U.S.C. § 552(b)(4)		
TBD	Research Specialist		-	0.00			
TOTALS:			0.25				

			0
SUPPLIES			
	Cell Culture, Serum and Media	5 U.S.C. § 552(b)(4)	
	BSL3 gear PAPR		
	Tissue culture reagents		
	Enymes, kits and reagents		
	Misc.		
	Computer Supplies		
Total Supplies		$	
EQUIPMENT (Itemize)			
OTHER (Itemize by category)			
Sequencing Reactions		$0	
Animal Cost		$0	
Animal per diem		$0	
		$0	
TOTAL OTHER:		$0	
TRAVEL			
	International	$0	
	Domestic	$0	
TOTAL COST:			$
CONSORTIUM DIRECT			
SUBTOTAL DIRECT COST FOR BUDGET PERIOD			$
CONSORTIUM F & A			
TOTAL DIRECT COSTS			$
UNC-CH F & A @ 55.5% MOD		$(b) (4)	$
TOTAL COST			$

5 U.S.C. § 552(b)(4)

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 7/23/2020 5:15:04 PM
To: Moore, Victoria L [victoria_moore@unc.edu]; Caldwell, Chandra [ccaldwel@email.unc.edu]; Burkhart, Carol J. [carol_burkhart@unc.edu]; Parrish, Kalyn [klparrish@unc.edu]
CC: Sheahan, Timothy Patrick [sheahan@email.unc.edu]
Subject: FW: Request for Proposal No. 596021
Attachments: PR 596021 RFP.pdf; PR 596021 SOW.pdf; REPRESENTATIONS AND CERTIFICATIONS final track changes 3-10-20 FORM (3).pdf; GP-A-409.25-EDNP_October 2019.pdf; R21_Yr2_UNC_Subcontact_Costs.pdf

Trying to keep everyone in the loop. Please let me know if I can assist.

Thank you, Amy

From: "Ames, Amber A" <Amber.Ames@pnnl.gov>
Date: Thursday, July 23, 2020 at 5:02 PM
To: "sheahan@email.unc.edu" <sheahan@email.unc.edu>, "ResAdminOSR@unc.edu" <ResAdminOSR@unc.edu>
Cc: "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>, "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Request for Proposal No. 596021

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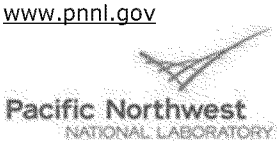

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With the U.S. Department of Energy
Operating the Pacific Northwest National Laboratory (PNNL) (www.pnnl.gov)

Request for Proposal No. 596021	
Issued by: Battelle Battelle Boulevard, K9-15 P.O. Box 999 Richland, WA 99352-0999 USA	**Contracts Specialist:** Name: Amber Ames Telephone Number: (509) 371-7050 E-mail: amber.ames@pnnl.gov
Proposal Due Date: COB Friday, July 31, 2020	**Period of Performance:** Date of contract award through May 31, 2021
Payment Terms: Net 30	**Anticipated Contract Type:** Cost Reimbursement

This is a Request for Proposal for University of North Carolina at Chapel Hill and Principal Investigator Timothy Sheahan to support the "How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells" project, per the attached Statement of Work dated July 14, 2020.

Contract Contents

The resulting contract will include the following generation provisions:

- The General Provisions Applicable for Educational Institutions and Nonprofit Organizations, Form A-409.25-Ed/NP dated October 2019, apply and may be viewed at http://www.pnnl.gov/contracts/contractdocuments.aspx.

Battelle Contracts Representative

The Battelle Contracts Representative, Amber Ames, is the sole point of contact for any communications or questions regarding this acquisition.

Solicitation Provisions

In addition to the requirements outlined herein, the Solicitation Provisions, Form A-609-SP (November 2014), available at http://www.pnnl.gov/contracts/contractdocuments.aspx apply to this Request for Proposal.

Submission of Proposals

The proposal submitted should include:

A. Completed Representation - Certification form found at:
http://www.pnnl.gov/contracts/contractdocuments.aspx
   - The NAICS code for section A.1 of the Representations and Certifications is 611310
   - The size standard for section A.2 is $30 million.

B. A budget with budget justification for each cost element identified, including:
   - **Direct Labor**: provide the labor category of the listed individuals and their credentials, i.e., payroll register, education, and experience. Identify all foreign nationals, and nationality that are expected to work on this project. If possible, provide salary backup to substantiate rates proposed. Provide breakdown of rate and quantity, whether it is rate x hours or monthly salary x FTE months.
   - **Other Direct Costs**: list materials, supplies, equipment, etc. including pricing support obtained such as quotes.
   - **Approved Rate Agreement**, including **Fringe** and **Indirect Rates** or link to rate agreement.

- **Travel** include breakdown of estimate including airfare, lodging, meals, transportation, etc. Identify all travelers expected to travel to foreign locations.

If helpful, you may use the Contract Pricing Proposal form CR Contracts with Universities located at http://www.pnnl.gov/contracts/contractdocuments.aspx.

Proposals shall be delivered to Battelle on or before **COB Friday, July 31, 2020** and shall be valid for a minimum of 60 days.

Proposals are preferred to be submitted via Email to amber.ames@pnnl.gov with a subject line that includes the words "Proposal to RFP 596021".

Funding is not fully obligated for this action. Contract award is subject to Availability of Funds at the time of award.

Ombudsman Program

Offeror is hereby notified that issues/concerns relative to this solicitation and/or any resulting contract award that are not resolved by the Battelle Contracts Representative identified herein shall be resolved through Battelle's Ombudsman Program by email at acquisitionombudsman@pnnl.gov. Any issue/concern shall be submitted, in writing, no later than 30 calendar days after contract award to be considered for review.

Statement of Work
How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
University of North Carolina at Chapel Hill, Principal Investigator Timothy Sheahan
July 16, 2020

I. Background

The molecular mechanisms regulating emerging highly pathogenic human respiratory coronavirus pathogenesis are complex and include dampening of the host innate immune response allowing higher viral titers immediately following entry. Previous studies tracking the expression of interferon stimulated gene (ISG) expression in Middle East respiratory syndrome coronavirus (MERS-CoV) infected continuous human lung epithelial cells demonstrated that specific ISG expression patterns could be detected and these patterns could be used to determine how CoV were modulating the innate immune response. Epigenetic/chromatin remodeling mechanisms were found to be important regulators of host chromatin remodeling that altered host expression ISG patterns. This proposal will build on these foundational studies performed in continuous human lung cell lines and define ways that MERS-CoV regulates innate immunity in primary human lung fibroblasts and microvascular endothelial cells.

II. Scope

University of North Carolina at Chapel Hill will analyze the fibroblast ChIP PCR samples collected in 2019 and discuss data with PNNL to determine next steps. University of North Carolina at Chapel Hill will perform ChIP Seq analysis of MERS-CoV infected microvascular endothelial cells at a single time point for three donors. University of North Carolina at Chapel Hill will perform BioRad Primer PCR Pathway Arrays on MERS-CoV infected microvascular endothelial cells and fibroblasts. Drs Sheahan and Schaefer will work in close collaboration with PNNL to analyze datasets to determine how MERS-CoV regulates ISG expression in human lung microvascular endothelial cells and fibroblasts.

III. Deliverables

- Evaluate project results and direction, in collaboration with PNNL
- Collaborate on experiment direction and identify alternatives for experiments
- Participate in meetings to discuss project status/progress, findings, and trouble shoot as needed
- Write and submit progress report and manuscript draft in collaboration with PNNL

From: Caldwell, Chandra[ccaldwel@email.unc.edu]
Sent: Fri 7/24/2020 8:59:15 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Request for Proposal No. 596021
Attachment: BGJUNC_Budget_Justification_RV_6.docx

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Trying to keep everyone in the loop. Please let me know if I can assist.

Thank you, Amy

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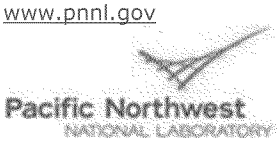

UNC Budget Justification

Personnel:

Timothy Sheahan Ph.D., Principal Investigator (5% effort, 0.60 cal months). Dr. Sheahan has extensive (>15 years) select agent/BSL3 experience primarily working with in vitro an in vivo models of human coronavirus infection to better understand highly pathogenic human respiratory virus pathogenicity and pathogen host interactions. Dr. Sheahan will oversee all work performed at UNC Chapel Hill and work closely with Drs. Sims and Dr. Schaefer to ensure steady progress on meeting the goals of the project. He will interact closely with Dr. Schaefer and Mr. Scobey to ensure steady progress during the course of the proposal, evaluate results and propose alternative experiments. Dr. Sheahan will manage fiscal matters associated with the work performed at UNC Chapel Hill.

Alexandra Schaefer, Ph.D., Co-Investigator (20% effort, 2.4 cal months). Dr. Schaefer pioneered the use of ChIP-RT PCR/Seq in the laboratory and will be critical for examining the relationships between histone modifications, DNA methylation and ISG expression control. Dr. Schaefer has extensive experience working under BSL3 conditions and will perform all primary human lung cell epigenetic experiments. She will work closely with Drs. Sims and Sheahan to plan, execute, and trouble shoot the proposed studies. She will meet with Drs. Sims and Sheahan frequently to discuss and trouble shoot experimental results and issues. Dr. Schaefer will assist with the preparation of all reports and manuscripts.

Fringe Benefits: Faculty/Staff: 24.863% Social Security and Retirement 5 U.S.C. § 552(b)(4) TE Health Insurance.

Supplies:

BL3 Protective Gear 5 U.S.C. § 552(b)(4) **Year 2)** Personnel wear powered air purifying HEPA filtered breathing apparatuses, wear tyvek suits, tyvek aprons, hoods, booties and are double gloved when entering the BSL3 facility. These materials are expensive as the HEPA, organic chemical filters and even batteries must be replaced every ~6 months, and the tyvek suits are disposable. Moreover, the PAPR (powered air breathing apparatus) are expensive and must be replaced every ~2 years from normal wear and tear, and daily contact with EPA disinfectants. Personnel use high quantities of disinfectants like ethanol, Clorox and other EPA approved disinfectants in maintaining a safe working environment in the BSL3. Personnel spray down tyvek suits, etc. with alcohol or related disinfectants in the process of deconing and leaving the BSL3 facility. All materials that leave the BSL3 must be disinfected, packaged in disinfected, sealed containers, which are disinfected prior to removal from the BSL3 facility. In addition, funds are requested to help defray costs associated with the decontamination and maintenance of the BSL3 laboratory each year.

Miscellaneous 5 U.S.C. § 552(b)(4) **in Year 2)** Monies are requested to purchase glassware, pipettes, etc. used in day to day virologic and cell culture procedures as well as in growing, titering and characterizing virus growth in vitro. Funds are also requested to purchase chemicals, reagents, micropipetors, autoclave supplies, plastic tips, water baths, and other small equipment items that typically have short half lives in laboratory settings.

Kits and Reagents 5 U.S.C. § 552(b)(4) **in Year 2)** Funds are requested to purchase the wide variety of kits required to perform the proposed epigenetic experiments. For ChIP Seq experiments we will need the MAGnify Chromatin Immunoprecipitation system and the histone specific antisera required for pull down are obtained by purchasing the EpiTect ChIP Antibody kit and pre-sequencing PCR requires CyberGreen kits and general PCR reagents. For detecting methylated DNA, we will require the MethylMiner Methylated DNA Enrichment Kit as well as running addition general PCR reactions using the reagents listed above.

Tissue Culture Reagents 5 U.S.C. § 552(b)(4) **in Year 2)** We are requesting funds to purchase cell culture supplies and plastic ware to perform cell passage and viral plaque assays to determine viral titers.

Indirect Costs (Facilities and Administration): In accordance with the University's F&A Cost Rate Agreement dated November 23, 2016, the University's predetermined F&A rate is 55.50%. This rate remains in effect through June 30, 2020. The base for calculating Facilities and Administrative cost (indirect cost) is modified total direct costs (MTDC), consisting of all salaries and wages, fringe benefits, materials and supplies, and services.

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 7/24/2020 9:21:20 AM
To: Caldwell, Chandra [ccaldwel@email.unc.edu]
Subject: Re: Request for Proposal No. 596021

Yes m'am. I would be happy to. Always lots of moving parts. I hope you are doing well! Thank you, Amy

---

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Friday, July 24, 2020 at 9:20 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
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Cc: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
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Trying to keep everyone in the loop. Please let me know if I can assist.

Thank you, Amy

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Cc: "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>, "Sims, Amy C" <amy.sims@pnnl.gov>
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NATIONAL LABORATORY

From: Ames, Amber A[Amber.Ames@pnnl.gov]
Sent: Fri 7/24/2020 11:44:58 AM (UTC-07:00)
To: sheahan@email.unc.edu[sheahan@email.unc.edu]; ResAdminOSR@unc.edu[ResAdminOSR@unc.edu]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]
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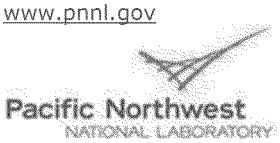

Attachment 0598

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Transmitted via e-mail to: sheahan@email.unc.edu

July 24, 2020

Timothy Sheahan, PhD
University of North Carolina at Chapel Hill
Department of Epidemiology
3302 Michael Hooker Research Building
CB #7435
Chapel Hill, NC 27599

Dear Dr. Sheahan:

SUBJECT: PROPOSED CONTRACT NO. 528372

Battelle is in the process of preparing the subject contract to be finalized with you in accordance with the negotiations to be concluded no later than August 31, 2020.

To facilitate commencement of work under Contract No. 528372 as recognized during contract negotiations, Battelle proposes to include a clause in the contract to the effect that precontract costs in the amount d[5 U.S.C. § 552(b)(4)], incurred from July 27, 2020, but prior to the award date of Contract No. 528372, will be allowable to the extent that they would have been allowable if incurred after the date of Contract No. 528372. Precontract costs will not include costs of preparing bid/proposals or of participating in contract negotiations.

It is understood that the commencement of work by University of North Carolina at Chapel Hill, prior to the date of Contract No. 528372, is entirely at its own risk. Invoices for reimbursement for precontract costs will not be paid until after execution of Contract No. 528372 by both parties. Work efforts charged as precontract costs shall be limited to the following activities: "How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells" Statement of Work dated July 16, 2020. All work shall be conducted with strict adherence to the Statement of Work and any specified Quality Assurance requirements.

Please acknowledge your acceptance of these conditions by signing below and returning to my attention.

Sincerely,

Digitally signed by Amber A. Ames
Date: 2020.07.24 10:59:15 -07'00'

Amber A. Ames
Senior Contracts Specialist

Acknowledge: University of North Carolina at Chapel Hill

By: (signature and printed name) Date:

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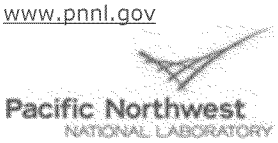

From: Ames, Amber A
Sent: Thursday, July 23, 2020 5:03 PM
To: sheahan@email.unc.edu; ResAdminOSR@unc.edu
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: Request for Proposal No. 596021

Dear Dr. Sheahan,

Attached please find a request for proposal for the University of North Carolina at Chapel Hill and Principal Investigator Timothy Sheahan to support the "How MERS-CoV Regulates Innate Immunity in Primary Human Lung

Cells" project, per the attached Statement of Work dated July 14, 2020.

This will confirm I am in receipt of the attached budget. If the cost elements have not changed (salary, fringe) the attached budget is sufficient for award. If you have a budget justification that explains the fringe rates and how the supplies were estimated, that would be helpful. The only other document I need to make the award is the completed Representations and Certifications.

In support of the RFP, please find:

- RFP instructions
- Statement of Work
- Representations and Certifications (required for all actions over $25K)
- General Provisions

As noted in the attached, your response is requested by COB **Friday, July 31, 2020.**

As a Federally Research and Development center we operate under a standard set of terms and conditions defined by DOE which outline how we can receive and how we must spend monies coming to the laboratory. This enables us to receive sponsor funds directly, but also provides a standard set of DOE terms under which we must place our all of subcontracts. We do not have authority to award grants. All subawards will be in the form of a subcontract subject to the applicable General Provisions for the applicable subcontract type. **There is no authorization to begin work and costs are not allowable until the contract is issued. If it is urgent for to start work, I can award a Precontract Authorization to cover costs while we finalize this contract. In the absence of this, costs are not allowable until a precontract authorization is issued or the contract is issued.**

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 7/24/2020 1:04:02 PM
To: Caldwell, Chandra [ccaldwel@email.unc.edu]
Subject: Re: Request for Proposal No. 596021

Thank you. I haven't worked with Amber before and she doesn't seem to check in with Norma and I like Barb does. Still trying to get it all worked out! Thank you again, Amy

---

From: "Caldwell, Chandra" <ccaldwel@email.unc.edu>
Date: Friday, July 24, 2020 at 1:03 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 596021

Got it...thanks!

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Friday, July 24, 2020 3:52 PM
To: Caldwell, Chandra <ccaldwel@email.unc.edu>; Moore, Victoria L <victoria_moore@unc.edu>; Burkhart, Carol J. <carol_burkhart@unc.edu>
Cc: Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Subject: FW: Request for Proposal No. 596021

Here is the latest update from PNNL. Thank you, Amy

From: "Ames, Amber A" <Amber.Ames@pnnl.gov>
Date: Friday, July 24, 2020 at 11:45 AM
To: "sheahan@email.unc.edu" <sheahan@email.unc.edu>, "ResAdminOSR@unc.edu" <ResAdminOSR@unc.edu>
Cc: "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>, "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 596021

Dear Dr. Sheahan,

Attached please find a Precontract Cost Authorization Letter which authorizes work to begin Monday, July 27, 2020. I have been advised by the project it is critical to get work underway to continue ongoing research. This will need to be signed by someone at UNCC with signature authority. It will be incorporated into the contract.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
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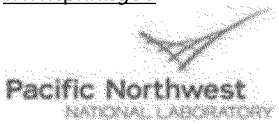

From: Ames, Amber A
Sent: Thursday, July 23, 2020 5:03 PM
To: sheahan@email.unc.edu; ResAdminOSR@unc.edu
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: Request for Proposal No. 596021

Dear Dr. Sheahan,

Attached please find a request for proposal for the University of North Carolina at Chapel Hill and Principal Investigator Timothy Sheahan to support the "How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells" project, per the attached Statement of Work dated July 14, 2020.

This will confirm I am in receipt of the attached budget. If the cost elements have not changed (salary, fringe) the attached budget is sufficient for award. If you have a budget justification that explains the fringe rates and how the supplies were estimated, that would be helpful. The only other document I need to make the award is the completed Representations and Certifications.

In support of the RFP, please find:

- RFP instructions
- Statement of Work
- Representations and Certifications (required for all actions over $25K)
- General Provisions

As noted in the attached, your response is requested by COB **Friday, July 31, 2020.**

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Kind regards,

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amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Ames, Amber A [Amber.Ames@pnnl.gov]
Sent: 7/24/2020 3:27:31 PM
To: Koltz, Diane M [dkoltz@email.unc.edu]
CC: Fulcher, Leslie [leslie_fulcher@med.unc.edu]; Sandoval, Norma I [Norma.Sandoval@pnnl.gov]; Sims, Amy C [amy.sims@pnnl.gov]; Kinsey, Pamela M [Pamela.Kinsey@pnnl.gov]
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form
Attachments: GP-A-409.24-FP_October 2019.pdf; MLI Order Form Oct2019 (002).docx; PO 521567.xml

Dear Diane,

Thank you in advance for any update you can provide.

Kind regards,

Amber A. Ames
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Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Ames, Amber A
Sent: Thursday, July 16, 2020 1:26 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Diane,

Just checking in to see if you have an update.

Kind regards,

Amber

From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Wednesday, July 08, 2020 11:03 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I am working with my manager on reviewing the General Terms and Conditions and hope to be back with you by the end of the week.

Thanks for your patience,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Wednesday, July 8, 2020 1:22 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

Just checking in for a status update.

Kind regards,

Amber

From: Ames, Amber A
Sent: Monday, June 29, 2020 10:25 AM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

I have been advised that we would like to pursue UNC as the source of the HBE cells. I have attached our purchase order template in word. We do not customize the General Provisions so those are a .pdf. All changes will be listed in the purchase order as an alteration to the GPs—sample below. We have a long history of contracting with UNC so I have copied the Alterations we have negotiated for previous awards. Unfortunately, as a DOE M&O contractor we are also very limited on what we can negotiate. DOE requires their terms control. We understand universities cannot grant indemnity and we are confident we will be able to negotiate changes that will be acceptable to UNC and DOE.

Alterations to General Provisions

1. Permits and Responsibilities (cl. 358—Nov 1991) is hereby deleted and replaced with:
"The Contractor is an independent contractor, not an agent or employee of Battelle. The Contractor shall, without additional expense to Battelle or the Government, be responsible for obtaining any necessary licenses and permits, and for complying with any Federal, State, and municipal laws, codes, and regulations applicable to the performance of the work. The Contractor shall also be responsible for all damages to persons or property that occurs as a result of the Contractor's fault or negligence only in the manner and to the extent permitted under North Carolina law, including but not limited to the NC Tort Claims Act, GS 143-291, et seq., and without waiver of its sovereign immunity."

2. Insurance—Liability to Third Persons (cl. 378b—Mar 1996) is hereby deleted and replaced with:
"University of North Carolina is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."

3. Disputes (cl. 331—Nov 2014)
Delete in its entirety.

4. Insurance Requirements (cl. 378—Nov 2014) is hereby deleted and replaced with:
"University of North Carolina is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."

I note I have been advised we will have another order with a budget of 5 U.S.C. § 552(b)(4) so it is critical we resolve the terms and conditions.

Thank you for your assistance with this matter.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
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Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
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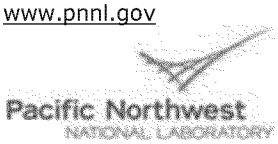

From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Thursday, June 18, 2020 11:06 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I received your changes for review and upon a first look, UNC cannot agree to all of the supplemental terms contained in the online documents you want to include. As a state institution, we are somewhat limited. The order form contains the minimal terms UNC requires in its contracts and we typically do not agree to changes. Is there any possibility that we could make UNC's agreement control, or not reference the terms at all, since much of what is contained in the online "purchase agreements" won't apply to what we are providing. If this is not possible, please provide me word versions of the online agreements so I can outline our requested edits and comments. Also, please note that review of the documents will take time.

Thanks,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Thursday, June 18, 2020 12:58 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Just checking in to see if there is a response to our requested changes to the order form terms.

Thanks so much!

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Wednesday, June 10, 2020 3:04 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Good Morning Amber,
Yes, once the contract is executed, Amy will be able to order as needed up to the dollar amount on the contract and during the 1 year period. I am including our contract specialist who can look at your suggested changes and she will be in touch with you soon.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 9:02 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Thanks, Leslie. The project would like to be able to order up to 10 ALI medium and 26 Normal HBE Cells from now until September 30, 2021. Are they able to order on an as-needed basis? I can incorporate a signed version of the attached into the PO for the project to use? Once I sign it, they won't be able to edit it. Perhaps we need to do a purchase order per order?

I note I provided redlines on the attached. Please advise if UNCC is able to work with the redlines.

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 5:29 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,
Thanks for emailing back, but to complete the contract, I need the agreement signed and returned to me prior to ordering. As for payment options, a check is fine, but we do have an account that funds could be wired. If that works for you, I can share that information.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 5:09 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

Attached please find Purchase Order No. 521567 to purchase up to the quantities I had listed below. Per the PO, we will place orders via the ordering website. There is no need to sign the PO—if you can acknowledge receipt and that this will work for ordering/payment purposes, that would be helpful.

I'm guessing the MLI Tissue Procurement and Cell Culture Core Facility will want a paper check mailed to the 125 Mason Farm Road address instead of paid by ACH to UNCC's main Bank of America account?

Amy, the shipping address in PES is 331 Building, Room 70. Even if a different shipping address is input in the UNCC online ordering system, any orders associated with PO 521567 will ship to 331/70. If you need a different ship to, let me know.

Thanks!

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 12:36 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,

As long as the contract is signed, the dollar amount is entered, and the period is in place there will be no rate increase.
You don't need to select the quantity of any item, but if your project you will use the quantity listed below, entering in the dollar amount is sufficient. I may suggest adding a little wiggle room in the dollar amount because once the dollar amount is reached, even before the term is up, we will need to renew the contract.

Also, once the contract is executed, you would just log onto our ordering website and order what you need.
Please let me know if you have any questions.

Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 9, 2020 1:19 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

I have a requisition to issue a Purchase Order to UNCC for a fixed unit rate contract for the following:

Description	Price	Maximum Quantity Expected	Extended Price
BEGM MEDIUM	5 U.S.C. § 552(b)(4)	0	5 U.S.C. § 552(b)(4)
ALI MEDIUM		10	
VALI MEDIUM		0	
Normal HBE Cells		26	
Diseased HBE Cells		0	
Cystic Fibrosis HBE Cells		0	
Normal Microvascular Cells		0	
Normal Fibroblast Cells		0	
Total Not to Exceed Amount			

The project would like to use the purchase order for payment of requirements on an as-needed basis through September 30, 2021.

My question is how long the pricing in Exhibit A of the attached is valid? Are the prices updated annually?

Do you have any concerns with this approach?

Kind regards,

Amber A. Ames
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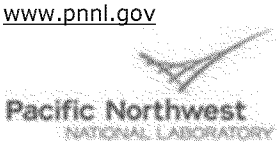

The University of North Carolina at Chapel Hill

MLI Tissue Procurement and Cell
Culture Core Facility
Recharge Core Agreement

The University of North Carolina at Chapel Hill
MLI Tissue Procurement and Cell Culture Core Facility
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Road
Room 1119 Marsico Hall, CB 7248
Chapel Hill, NC 27599-7361

Make checks payable to: The University of North Carolina at Chapel Hill

Remit payment to:
University of North Carolina - Chapel Hill
MLI Tissue Procurement and Cell Culture Core Facility
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Road
Room 1119 Marsico Hall, CB 7248
Tax ID#: 56-600-1393

Payment Terms: Net 30 days upon receipt of invoice

Not to Exceed Cost: $ _____

Start Date:_____End Date: _____

Payment Method: PO_____Credit Card _____

Client
Client Name: _____Contact Name: _____

Mailing Address: _____
_____
_____
_____

Phone Number: _____
Contact E-mail Address:_____

Send Invoice to: (if different from above):
Name:_____Email

Address:
_____
_____

Description of Services):
Specialized services related to provision of human primary lung cells and custom media in accordance with Exhibit A attached hereto.

Terms and Conditions

1) Services. The University of North Carolina at Chapel Hill ("University") possesses expertise and related technologies and equipment through its MLI Tissue Procurement and Cell Culture Core Facility ("Facility"). Client has instructed University to undertake the specific services described above (the "Services"). In consideration of Client's payment to the Facility in accordance with the terms stated herein, the Facility shall perform the Services.

2) Reports. Facility shall provide Client with a report regarding the data obtained in the course of the Services. The report shall be maintained as confidential pursuant to Section 3 below. Client recognizes that the results of the Services which do not disclose Confidential Information provided hereunder may be deemed publishable by University, and that the University employees engaged in the Services shall be free to publish these results, consistent with the obligations imposed in Section 3 of this Agreement.

3) Confidentiality. Any confidential or proprietary information disclosed by Client to University ("Confidential Information") shall be disclosed in writing and designated as confidential and/or proprietary, or if disclosed orally, shall be confirmed in writing and designated confidential and/or proprietary within thirty (30) days of such disclosure. University shall use the Confidential Information only for the purpose of this Agreement and further agrees that it will not disclose or publish such Confidential Information except that the foregoing restrictions shall not apply to: (a) Confidential Information which is or becomes publicly known through no breach of this agreement by University; (b) Confidential Information learned from a third party entitled to disclose such information; (c) Confidential Information already known to or developed by University prior to receipt hereunder, or information independently developed at any time by University personnel not privy to the Confidential Information, as shown by University's written records; or (d) Confidential Information required to be disclosed by operation of law (including, but not limited to, the North Carolina Public Records Act) or court order. The obligation of confidentiality imposed by this Section shall expire three (3) years following the expiration or termination of this Agreement. University will use a reasonable degree of care to prevent the inadvertent, accidental, unauthorized, or mistaken disclosure or use by its employees of Confidential Information. For avoidance of doubt, data, information, results, materials, or products of the Services shall be considered Confidential Information for the purposes of this Agreement.

4) Intellectual Property. It is not anticipated that intellectual property will arise in University's performance of the Services. However, in the event of an invention by at least one employee of University the intellectual property shall be owned as follows: a) Inventions which involve the use of, composition of, or improvement to Client-provided materials or information, or a derivative, analogue thereof shall belong to Client; and b) Inventions which cover a scientific or analytical measurement process, technique, procedure, medium, device or other process which is not unique to characterizing, testing, or fabricating Client's proprietary materials or does not derive from Client-provided materials or Client's Confidential Information shall be owned by University.

5) Publicity. Neither party will use the name of the other party in any publicity, advertising, or news release without the prior written approval of the authorized representative of the other party.

6) Termination. Either party may terminate this Agreement upon prior written notice to the other party. All reasonable costs and non-cancelable obligations incurred by University at the time of said termination shall be reimbursed by Client. At the request of Client, all unused Client-provided materials at the time of termination shall either be returned to Client or destroyed by University as negotiated with the Client.

7) Independent Contractor. In the performance of the Services, University shall be deemed to be and shall be an independent contractor.

8) No Warranties and Indemnity. University makes no warranties, express or implied, regarding the quality of product produced under this Agreement. University shall use its reasonable efforts to perform the Services. University does not warrant or guarantee any results from a given project. University shall not be liable for Client's use of the report or other information provided by University.

9) Export Control. University will not accept export-controlled materials or technical information under this Agreement. Client hereby represents and warrants that materials and technical information provided to University do not require any license from the U.S. government before being exported.

10) Hazardous Materials. All materials provided by Client must be accompanied by the appropriate environmental and safety information for those materials as required by law.

11) Governing Law. This Agreement shall be governed and construed in accordance with the laws of the State of North Carolina.

12) Entire Agreement. The terms and conditions of Purchase Order No. 521567 supplement this agreement.

Check one:

_____No Client employees will work in University facilities in connection with this Agreement

_____Client employees will be performing work related to this Agreement in University facilities.

By Authorized Official of The University of North Carolina at Chapel Hill	By Authorized Official of Client
By:_____	By: _____
Name: acting on behalf of Terry Magnuson, PhD	Name: _____
Title: Vice Chancellor for Research	Title: _____
Date: _____	Date: _____

EXHIBIT A

MARSICO LUNG INSTITUTE

Tissue Procurement and Cell Culture Core

EXTERNAL PRICING

MEDIA	
BEGM MEDIUM	(b) (4)
ALI MEDIUM	$269/Liter (b) (4)
VALI MEDIUM	(b) (4)
HUMAN BRONCHIAL EPITHELIAL CELLS	
Normal HBE Cells	(b) (4)
Diseased HBE Cells	(b) (4)
Cystic Fibrosis HBE Cells	(b) (4)
OTHER HUMAN LUNG CELLS	
Normal Microvascular Cells	(b) (4)
Normal Fibroblast Cells	(b) (4)

DESCRIPTIONS

MEDIA	
BEGM MEDIUM	Bronchial epithelial growth media for expansion of cells on plastic
ALI MEDIUM	Air-Liquid interface media for differentiation of cells on porous supports
VALI MEDIUM	Vertex-ALI for differentiation of cells on porous supports (contains Ultroser G)

HUMAN BRONCHIAL EPITHELIAL CELLS	
Normal Donors	No history of prior chronic lung disease, smoker or non-smoker
Diseased Donors	History of prior chronic lung disease— (COPD, asthma)
Cystic Fibrosis Donors	Homozygous severe CFTR mutation— (F508del/F508del)
Cystic Fibrosis Donors	Heterozygous F508del/second severe CFTR mutation— (F508del/Other)
Cystic Fibrosis Donors	Non F508del CFTR mutations— (Other CF/Other CF)

OTHER HUMAN LUNG CELLS	
Normal Microvascular Cells	No history of prior chronic lung disease
Normal Fibroblast Cells	No history of prior chronic lung disease

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 8/20/2020 9:34:36 AM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]
Cc: Baric, Ralph S[rbaric@email.unc.edu]
Subject: Adding NL63?

Ben,

I hope you are doing well and transitioning to working in the Baric laboratory in the weirdness of the pandemic.

Can you please talk to Ralph about adding human coronavirus NL63 to our existing MTA?

I would like both the current wild type strain (should contain a point mutation in spike following tissue culture adaptation) and the virus expressing green fluorescent protein GFP. Sarah Leist should have stocks of these at BSL2.

I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 8/20/2020 9:40:32 AM (UTC-07:00)
To: leist@email.unc.edu[leist@email.unc.edu]
Subject: Hello and a little help please

Hi Sarah!

I hope you and your kitty clan are doing well! I hope the boys transitioned to the US well and that everyone is getting along nicely! And that there is still somewhere for you to sleep in your apartment.

I know you are crazy busy but I am hoping you can help me with something that maybe won't take too long.

Could you help Ben with finding a few vials of the NL63 stocks from the experiment you and I worked on previously? I am asking to get the wild type (with the S point mutation) and the one with GFP. If you can't find these please let me know.
I really appreciate it as I know you are totally slammed. Congratulations on the publications! That is really great!

Thank you very much! I miss getting to catch up with you and I really hope you are getting a little down time to enjoy life! Amy

From: Baric, Ralph S[rbaric@email.unc.edu]
Sent: Thur 8/20/2020 10:14:00 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]; McGlaughon, Ben[benmcg@email.unc.edu]
Subject: RE: Adding NL63?

Hi Amy, no problem. Ben send Amy the viruses asap. Hope your doing well. We should chat sometime, likely need to revisit your paper and make sure we get it back out for review. I hope all are well and healthy in your family. Ralph

---

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, August 20, 2020 12:35 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Cc: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Adding NL63?

Ben,

I hope you are doing well and transitioning to working in the Baric laboratory in the weirdness of the pandemic.

Can you please talk to Ralph about adding human coronavirus NL63 to our existing MTA?

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I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: Purvine, Emilie[Emilie.Purvine@pnnl.gov]

Sent: Fri 8/21/2020 5:29:05 PM (UTC-07:00)

To: Feng, Song[song.feng@pnnl.gov]; Heath, Emily Jane Finnigan[eheath3@illinois.edu]; Jefferson, Brett A[brett.jefferson@pnnl.gov]; Joslyn, Cliff A[Cliff.Joslyn@pnnl.gov]; Kvinge, Henry J[henry.kvinge@pnnl.gov]; Mitchell, Hugh D[Hugh.Mitchell@pnnl.gov]; Praggastis, Brenda[Brenda.Praggastis@pnnl.gov]; Amie Eisfeld[amie.eisfeld@wisc.edu]; Sims, Amy C[amy.sims@pnnl.gov]; Thackray, Larissa[lthackray@wustl.edu]; shufang.fan@wisc.edu[shufang.fan@wisc.edu]; KEVIN B WALTERS[kevin.walters@wisc.edu]; Peter Halfmann[peter.halfmann@wisc.edu]; danielle.westhoffsmith@wisc.edu[danielle.westhoffsmith@wisc.edu]; qtan@pathology.wustl.edu[qtan@pathology.wustl.edu]; vimenach@utmb.edu[vimenach@utmb.edu]; sheahan@email.unc.edu[sheahan@email.unc.edu]; adam_cockrell@unc.edu[adam_cockrell@unc.edu]; jacob.kocher@unc.edu[jacob.kocher@unc.edu]; Stratton, Kelly G[kelly.stratton@pnnl.gov]; Heller, Natalie C[natalie.heller@pnnl.gov]; Bramer, Lisa M[Lisa.Bramer@pnnl.gov]; Diamond, Michael[mdiamond@wustl.edu]; Ralph Baric[rbaric@email.unc.edu]; Waters, Katrina M[Katrina.Waters@pnnl.gov]; YOSHIHIRO KAWAOKA[yoshihiro.kawaoka@wisc.edu]; Mcdermott, Jason E[Jason.McDermott@pnnl.gov]

Subject: hypergraphs paper ready to submit

Attachment: Hyperbio_centrality_paper.pdf

Hello all,

Thank you for your patience as my project team worked on revisions to the hypergraph paper you all saw back in January (wow has it been that long already?!). In our opinion we are ready to submit to BMC Bioinformatics but I am sending you all a copy now in case anybody has any final changes, acknowledgements, etc. that need to be included. In addition to anything in the content of the paper you wish to comment on, I ask that you please double check the following:

*) Your affiliation(s) - is this up to date? Any changes needed?
*) Author contributions - please make sure what I have listed for you is appropriate and adequate
*) Acknowledgements - please let me know what grants should be acknowledged for any of your experimental or analysis work

I will be submitting this for our internal approval process on Monday. Once that is approved, unless there are any objections, I will submit to the journal. Please try to get me comments before COB Friday, August 28. I hope to submit the following week.

Emilie Purvine, Ph.D.
Senior Data Scientist and Mathematician
Data Science and Analytics Group

Pacific Northwest National Laboratory
PNNL/Battelle Suite 500
1100 Dexter Ave. N
Seattle, WA 98109
Phone: 206-528-3461

METHODOLOGY

Hypergraph Models of Biological Networks to Identify Genes Critical to Pathogenic Viral Response

Song Feng[1], Emily Heath[3], Brett Jefferson[2], Cliff Joslyn[2,11], Henry Kvinge[2], Hugh D. Mitchell[1], Brenda Praggastis[2], Amie J. Eisfeld[5], Amy C. Sims[1], Larissa B. Thackray[7], Shufang Fan[5], Kevin B. Walters[5], Peter J. Halfmann[5], Danielle Westhoff-Smith[5], Qing Tan[7], Vineet D. Menachery[6], Timothy P. Sheahan[6], Adam S. Cockrell[6], Jacob F. Kocher[6], Kelly G. Stratton[2], Natalie C. Heller[2], Lisa M. Bramer[2], Michael S. Diamond[7], Ralph S. Baric[6], Katrina M. Waters[1], Yoshihiro Kawaoka[5,8,9,10], Jason E. McDermott[1,4] and Emilie Purvine[2*]

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Full list of author information is available at the end of the article

Abstract

Motivation: Representing biological networks as graphs is a powerful approach to reveal underlying patterns, signatures, and critical components from high-throughput biomolecular data. However, graphs do not natively capture the multi-way relationships present among genes and proteins in biological systems such as protein complexes, metabolic reactions, and signal transduction pathways. Hypergraphs are generalizations of graphs that naturally model multi-way interactions in data, and we therefore seek to understand how they can more faithfully identify, and potentially predict, complex relationships in genomic expression data sets.

Results: We compiled a novel data set of transcriptional host response to pathogenic viral infections and formulated relationships between genes as a hypergraph where hyperedges are differentially expressed genes and vertices represent conditions. We find that hypergraph betweenness centrality is a superior method for identification of genes important to viral response when compared with graph centrality. Our results demonstrate the utility of using hypergraphs to represent complex biological systems, and highlight potentially interesting biological results about host response to highly pathogenic viruses.

Keywords: Systems biology; Hypergraph; Viral infection; Biological networks; SARS; MERS; Inuenza; West Nile Virus; Host response; Viral pathogenesis

Background

Identifying molecular signatures critical to a biological process requires an accurate model of both that process and the biological system in which it occurs. Thus it is essential that such a model be able to represent its target with complexity commensurate with that of the system itself, rather than presenting only a simplified view. Commonly, biological systems and processes present as complex networks of interacting entities, for example within and between pathways and complexes. Graphs are frequently used to model these interactions, but since graphs can only capture interactions between pairs of entities, they fall short in many cases and are

not able to model the full complexity present in biological systems and processes in terms of higher order and multi-way interactions.

In this paper we investigate the role that hypergraph models, as mathematical generalizations of graph models, can play in providing the necessary complexity to capture multi-way interactions in biological systems. We assert that the complexity provided by hypergraphs more closely represents the systems being studied. In order to validate this assertion we provide a comparison between the use of graph and hypergraph centrality metrics to identify genes that are critical in host responses to viral infection. Our findings show that the genes identified using a hypergraph model align better with genes previously known to correlate with viral response than do genes identified using similar metrics from graphs or using average fold change for each gene across all conditions.

Network science for high-throughput data analysis

Modern biology has been transformed by the rapid growth of technologies to measure the abundance of large numbers of biological entities over many samples simultaneously. Such high-throughput methods like transcriptomics, proteomics, metabolomics, and lipidomics allow researchers to gain unparalleled scientific insight into the mechanisms underlying biological systems. A wide range of biological questions have been addressed using such systems biology approaches including questions related to cancer, microbiomes, and infectious disease. Analysis methods for high-throughput measurements are also varied, ranging from simple statistical tests for differential abundance (between control and experimental conditions, for example), to dimensionality reduction, to machine learning, all with the aim of extracting more relevant information from the high-dimensional and often noisy measurements.

A powerful approach for modeling systems using high-throughput data is network biology. Here biological networks are modeled as graphs, with molecular entities (genes, proteins, metabolites) represented as vertices, and relationships between molecules represented as edges connecting them. Relationships between molecules are generally determined from existing knowledge of protein-protein interactions, regulatory interactions, metabolic networks, or can be inferred from high-throughput systems biology data. We and others have used networks inferred from correlation or mutual information between abundance profiles of genes and proteins to identify critical entities [1, 2, 3], integrate different data types [4, 5, 6, 7], and represent and predict temporal dynamics in the system [8, 9, 10].

Hypergraphs for complex network models

While graph-based methods have been quite successful in the biological domain, their ability to model complex interactions amongst entities is necessarily limited. By construction, graphs model interactions (edges) between *pairs* of entities (vertices). But biological systems are replete with interactions among *many* entities, including protein complexes, transcription factor and microRNA regulation networks, lipid and metabolite enzyme-substrate interactions, metabolic networks, pathways, and protein function annotations. For example, the proteasome is a complex molecular machine involved in protein degradation, and composed of multiple subunits.

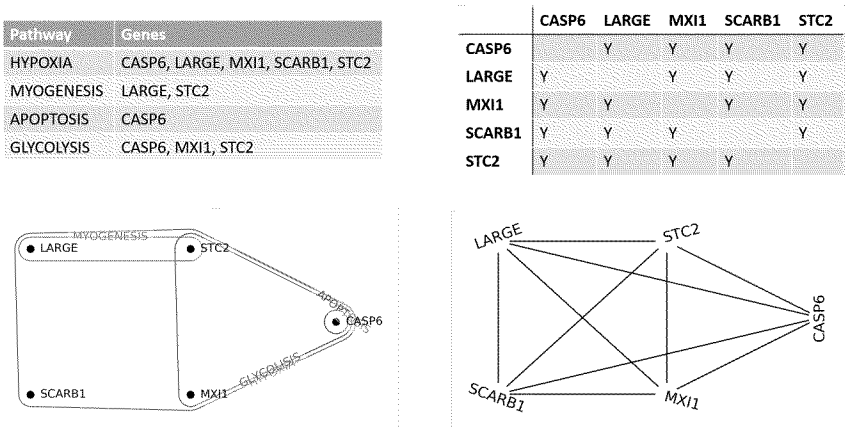
In a network model it would be represented as a collection of pairwise interactions between interacting subunits, but that would not fully represent how the different components of the complex interact with other regulatory proteins. Sometimes sets of interacting components are already understood, and sometimes they need to be discovered in data. In either event, a higher order mathematical model is needed.

A graph $G = \langle V, E \rangle$ comprises a set V of vertices connected by a set E of edges where each edge $e = \{u, v\}$ is a pair of distinct vertices. Representing *group* interactions is not possible natively in graphs, but rather requires more complex mathematical objects such as bipartite structures, frequently in conjunction with coding schemes such as semantic labels to identify different types of relationships and their components. The mathematical object that *natively* represents multi-way interactions in networks is called a "hypergraph". In contrast to a graph, in a hypergraph $H = \langle V, E \rangle$ those same vertices are connected generally in a set E of "hyperedges", where now each hyperedge e is an arbitrary subset of vertices, $e \subseteq V$. Thus every graph is a hypergraph where every hyperedge happens to have exactly two vertices, $|e| = 2$.

Although graphs and graph theory dominate network science applications and methods [11], hypergraphs are well-known objects in mathematics and computer science. They are closely related to bipartite graphs, that is, graphs with two distinct sets of nodes so that there are connections only between the two sets, and not within each set. Every hypergraph determines a bipartite graph with one part representing hypergraph vertices, and the other representing the hypergraph edges. And while conversely a bipartite graph also determines a unique hypergraph, it may also be the case that certain (disconnected) graphs have more than one bipartite separation, and thus could be consistent with multiple hypergraph representations [12]. While this mapping between hypergraphs and bipartite graphs is important for mathematical and algorithmic purposes, neither representation is generally sufficient by itself, and they each imply different considerations for modeling questions and applications. In this work, we treat these structures as hypergraphs only.

Hypergraphs have a history of use in a range of applications [13, 14, 15], and are seeing increasingly wide adoption [4, 16, 17, 18, 19]. A different form of hypergraph, called a *directed* hypergraph, may be more familiar to biological modelers. In a directed hypergraph (as used in e.g. [14]), each hyperedge $e = \{v_{j_1}, v_{j_2}, \ldots, v_{j_k}\} \in E$ is partitioned into two disjoint groups of vertices such that the first group are understood as inputs and the second as outputs. These are generalizations of directed graphs, and are used to model flow networks of different kinds, or inputs and outputs to reactions or processes. While directed hypergraphs are of interest to us, they are not the subject of the current work.

Hypergraph models are certainly more complicated than graphs, but the price paid allows for higher fidelity representation of data which may contain multi-way relationships. An example using a small subset of the gene set data from the Molecular Signatures Database (MSigDB) Hallmarks data set [20] is shown in Figure 1. On the upper left is a table showing a selection of four Hallmark gene sets that contain different collections of five genes (the gene sets contain more genes than these, we are taking a subset to illustrate our point). Its hypergraph is shown in the lower left. A typical approach to these same data would be to reduce the gene



Pathway	Genes
HYPOXIA	CASP6, LARGE, MXI1, SCARB1, STC2
MYOGENESIS	LARGE, STC2
APOPTOSIS	CASP6
GLYCOLYSIS	CASP6, MXI1, STC2

	CASP6	LARGE	MXI1	SCARB1	STC2
CASP6		Y	Y	Y	Y
LARGE	Y		Y	Y	Y
MXI1	Y	Y		Y	Y
SCARB1	Y	Y	Y		Y
STC2	Y	Y	Y	Y	

Figure 1: Hallmarks gene set example comparing graphs and hypergraphs. (Upper left) Lists of genes for a set of hallmark gene sets. (Lower left) Visualization of its hypergraph. (Upper right) Adjacency matrix of the underlying graph. (Lower right) Underlying gene interaction graph.

interaction structure to its underlying graph (not a proper hypergraph) of all and only the two-way interactions present between genes, whether in hyperedges with 2 vertices (like MYOGENESIS) or in larger hyperedges (as in HYPOXIA and GLYCOLYSIS). That gene interaction graph is shown in the lower right, represented by its adjacency matrix in the upper right. It can be seen that the reduced graph necessarily loses a great deal of information, boiling down the rich interaction structure that we know to be present to a fully connected graph on all five genes.

A challenge for scientists is to recognize the presence of hypergraph structure in their data, and to judge the relative value of representing them natively as hypergraphs or reducing them to these kinds of graph structures. In the literature we have seen hypergraphs used to model gene and protein interaction networks, pathways, and metabolic networks with multi-way interactions. In many of these cases the authors derive hypergraphs from an underlying graph, rather than directly from data. For example, Chitra built a hypergraph model based on an existing graph model of gene interaction networks [21]. They adapt the PageRank algorithm to hypergraphs in order to study disease-gene prioritization, and find that for monogenic diseases hypergraph PageRank noticeably outperforms graph PageRank. Protein-protein interaction networks are studied by Klamt *et al.* using graph algorithms to find sets of independent elements or tightly connected elements [14]. Tran studies protein function prediction building a graph from a similarity matrix derived from gene expression data [22] and then applying soft clustering to this graph to produce a hypergraph. Function prediction using this hypergraph is then shown to be superior to predictions based on graphs. In those three papers the authors infer a hypergraph from a graph structure rather than directly from data.

Ramadan *et al.* use hypergraphs to model the yeast proteome, where proteins are vertices and complexes are hyperedges [23], and apply an algorithm that finds tightly connected vertices to identify the core proteome. Finally, Zhou and Nakhleh study the claim that metabolic networks are hierarchical and small-world [24]. While this

claim comes from a graph model of the networks, Zhou and Nakleh instead model the metabolic networks of *E. coli* as a hypergraph and show that the claimed hierarchy and scaling properties are not supported. This result in particular conveys a critical message: when biological interactions are simplified into pairwise relationships and modeled using a graph, they can exhibit very different structure than when their true complexity is modeled using a hypergraph. Because of this structural variance, conclusions drawn based on the graph could provide misleading results. Although the data we consider are different, our method is similar to these last two papers in that we build hypergraphs directly from biological data rather than inferring a hypergraph from a standard graph model of the data.

Modeling host response in viral pathogenesis

Viral infection causes a response in the host cells in which the expression of a variety of cell systems are up- or down-regulated. The pathogenesis of the infection is reected in the signature of host responses elicited by each virus. Host response to viral infection has been extensively studied for decades, yet the root mechanisms of why some infections are severe and some are not remain poorly understood. However, high-throughput molecular approaches offer a way to discover novel host response genes, proteins, and pathways that contribute to the systems-level development of pathogenesis. A major advantage of such a systems biology approach to pathobiology is the ability to identify novel, key elements of a biological process, such as which regulators are involved in critical processes. High-throughput profiling methods (e.g. transcriptomics) provide powerful tools for examining how entire systems respond to different perturbations such as acute disease. Network reconstruction provides the opportunity to utilize all available data and is a critically important tool for representing complex sets of interactions [25]. In this paper we build and explore a *hypergraph* model of host response using transcriptomics data from viral infections in a number of biological systems.

Our contributions

We performed an analysis using transcriptomics data from host response to viral infection by five highly pathogenic viruses and found that gene rankings computed using hypergraph centrality were highly enriched for known immune and infection-related genes. While rankings derived from graphs constructed using other traditional computational biology techniques applied to the same infection data also resulted in rankings enriched for critical genes, we demonstrate that hypergraph-based metrics yield superior enrichment results. These results highlight the usefulness of hypergraphs for exploring mechanisms of virus pathobiology.

Methods

Data acquisition and processing

Microarray datasets collected from 2014 to 2017 and available from the Gene Expression Omnibus (GEO)[1] were gathered and processed. While details of experimental systems and conditions can be gathered from individual accessions from GEO, we list the infection conditions here:

[1]GEO accession IDs: GSE80059, GSE86533, GSE69027, GSE76600, GSE80697, GSE69945, GSE68945,GSE72008, GSE65575, GSE79458, GSE86528, GSE100496,

Ebola Virus: (Wild type and two mutants) in human hepatocyte cells.

Inuenza Virus: H7N9 (Wild type and two mutants) in human lung epithelial cells, H1N1 (wild type) in human lung epithelial cells, H1N1 (wild type) in mouse lung, H5N1 (wild type and one mutant) in mouse lung, H7N9 (wild type and two mutants) in mouse lung.

MERS-coronavirus: (Wild type and four mutants) in human lung epithelial cells, (wild type only) in *ex vivo* human epithelial cells, in *ex vivo* human lung fibroblasts, and *ex vivo* human lung microvascular endothelial cells.

SARS-coronavirus: (Wild type and four mutants) in human lung epithelial cells and mouse lung.

West Nile Virus: (Wild type and one mutant) in mouse cerebral cortex, mouse cerebellum and mouse lymph node.

Conversion from mouse to human gene symbols was done by capitalizing the mouse symbols. Quality control, background correction, quantile normalization, and differential expression analysis were performed in R using the limma package [26]. Replicates from each infection condition were compared to corresponding time-matched mock-infected samples to obtain $\log_2$-fold change values, as well as adjusted p-values.

Hypergraph representations and centrality metrics

A **hypergraph** is a structure $\langle V, E\rangle$, with $V = \{v_j\}_{j=1}^{n}$ a set of vertices, and $E = \{e_i\}_{i=1}^{m}$ a family of hyperedges with each $e_i \subseteq V$. Hyperedges can come in different sizes $|e_i|$ possibly ranging from the singleton $\{v\} \subseteq V$ (distinct from the element $v \in V$) to the entire vertex set V. A hyperedge $e = \{v_1, v_2\}$ with $|e| = 2$ is the same as a graph edge and so it follows that all graphs are hypergraphs. In the remainder of the paper where clear from context we may use the terms edge and hyperedge interchangeably.

Although frequently modeled using a graph, hypergraph structures are commonly found in biological data due to the abundance of complex interactions amongst biological entities. We have already shown an example in Figure 1 using gene set data from the MSigDB Hallmarks data set [20]. In this case the hypergraph has genes as vertices v_j, and gene sets as edges e_i identified simply as the collection of genes that are contained in that gene set.

While a gene set example serves as a simple way to illustrate the hypergraph concept for biological data, our work is concerned instead with the complexities of gene expression during viral infection as measured in the quantitative transcriptomics data described above. In this setting vertices v_j will represent individual biological "conditions" (e.g., mouse lung cells treated with a strain of Inuenza virus and sampled at 8 hours) and genes will now be represented as hyperedges e_i. Thus for us, a hyperedge e_i is a gene i, which includes a collection of conditions j as its vertices v_j. We recognize that our formulation is different from a typical graph approach to systems biology data where vertices represent genes and (graph) edges indicate some relationship between genes such as interaction or expression

GSE81909, GSE86530, GSE100504, GSE106523, GSE86529, GSE100509, GSE108594, GSE77193, GSE77160, GSE78888, GSE33267, GSE37827, GSE48142, GSE33266, GSE49262

correlation. Our motivation for making this change is pragmatic, for the sake of clarity in our description of hypergraph centrality measures below. However, as a technical matter, for each hypergraph H we can form a "dual" hypergraph H^{ff} determined exactly by swapping the roles of vertices and edges. Therefore, the dual to our hypergraph formulation has the more traditional form with genes as vertices, but the description of hypergraph centrality measures in this setting would be less intuitive.

To construct the hyperedges in our formulation we apply a threshold to both expression changes and p-values, so that a gene (hyperedge) will contain a condition (vertex) only if that gene is significantly expressed in that condition when compared to a control. Specifically, for each condition, we transform the $\log_2$-fold change values for all of the genes into absolute value z-scores. Then, the vertex representing condition X is contained in the hyperedge representing gene G if the absolute value z-score for G in X is greater than or equal to 2 and the adjusted p-value for that $\log_2$-fold change measurement is less than 0.05.[2] In this way, hyperedges are groups of conditions in which a given gene (the hyperedge itself) is both highly deviating from the mock infected control condition and for which that deviation is statistically significant. In the remainder of this paper we will say that the gene is "significantly deviating" in the condition. This is in contrast to the context likelihood of realtedness (CLR) approach to create a graph in which genes that show similar expression patterns across *all* conditions are linked together [27]. Thus our approach to building hypergraphs from the data can be seen as having greater sensitivity and exibility than previous approaches, since it allows similarity between genes to be assessed across two or many conditions, rather than requiring assessment across all conditions. We employ CLR in our experiments described below to serve as a baseline to compare our hypergraph results to.

As in graphs, the way in which hyperedges connect vertices in complex patterns is central to the study of hypergraphs. Our focus in this paper is applying generalizations of graph centrality measures to hypergraphs built from transcriptomics data to identify important genes. In order to define these hypergraph centrality measures we must first introduce the notions of a hypergraph walk and distance [12]. Given two hyperedges $e, f \in E$, an **s-walk of length k** between e and f is a sequence of hyperedges $e_0, e_1, \ldots, e_k$ such that $e_0 = e$, $e_k = f$, and $s \leq |e_i \cap e_{i+1}|$ for all $0 \leq i \leq k$ 1. In other words, an s-walk is a sequence of edges such that pairwise intersections between neighboring edges have size at least s.

This edge-based view may be different from the way walks are encountered in graph applications, as graph walks are generally considered "vertex-wise". In particular, a walk of length k between vertices v_0 and v_k in a graph is commonly defined as a sequence of vertices, $v_0, v_1, \ldots, v_k$, such that $\{v_i, v_{i+1}\}$ is an edge in the graph for all i. In a graph, this vertex-based concept is equivalent to an "edge-wise walk" as a sequence of graph edges $e_1, e_2, \ldots, e_k$ such that e_1 is incident to v_0, e_k is incident to v_k, and e_i and e_{i+1} are incident. This equivalence is a consequence of the fact that in a simple graph (i.e., lacking multi-edges) two vertices have at most one edge in common, and similarly two edges have at most one vertex in common. In

[2]These thresholds were chosen as commonly used in the field, and in exploring other values we have verified limited sensitivity to them.

general, hypergraphs do not have this property. Indeed, two hyperedges may have a large intersection $s > 1$, and two vertices may have many distinct hyperedges in common. So in both graphs and hypergraphs, walks and distances can be defined as either connecting vertices through common edges, or as connecting edges through common vertices. In the case of a graph these are equivalent, but in a hypergraph they typically are not, and we are free to take either approach as long as we maintain it consistently. Our approach is to define walks edgewise as above, for a variety of pragmatic reasons.

Continuing to follow Aksoy *et al.* [12], for a fixed $s > 0$, we define the **s-distance** $d_s(e, f)$ between two edges $e, f \in E$ as the length of the shortest s-walk between them. If there is no s-walk between two edges then the s-distance is infinite. Note that a graph walk is a 1-walk. Aksoy *et al.* also define a number of network science methods generalized from graphs to hypergraphs, including vertex degree, diameter, and clustering coefficients. This work will use their generalization of betweenness centrality and harmonic closeness centrality to hypergraphs using a stratification parameter s.

- The **s-betweenness centrality** of an edge e is

$$BC_s(e) := \sum_{f=e=g \quad E} \frac{\sigma^s_{fg}(e)}{\sigma^s_{fg}}$$

  where σ^s_{fg} is the total number of shortest s-walks from edge f to edge g and $\sigma^s_{fg}(e)$ is the number of those shortest s-walks that contain edge e.
- The **harmonic s-closeness centrality** of an edge e is the reciprocal of the harmonic mean of all distances from e:

$$HCC_s(e) := \frac{1}{|E_s| \quad 1} \sum_{\substack{f \quad E_s \\ f=e}} \frac{1}{d_s(e, f)}$$

  where $E_s = \{e \in E : |e| \geq s\}$. We may refer to this as s-closeness in this paper, although elsewhere in the literature this term refers to a slightly different concept where the harmonic mean is replaced with the arithmetic mean.

Intuitively, harmonic s-closeness centrality captures the extent to which a given hyperedge is close in s-distance to other hyperedges. In order to have high harmonic s-closeness a hyperedge must have small s-distance to all (or most) other hyperedges. s-Betweenness, on the other hand, identifies bottlenecks in a hypergraph. A hyperedge with high s-betweenness has many shortest s-walks pass through it. In comparison, the original formulation of betweenness and harmonic closeness centrality in the setting of graphs has the s-distance and number of s-paths replaced simply by graph distance and shortest path.

Conventional graph approaches use correlated gene expression patterns to build connections. In this context, a gene with high degree (i.e. a hub) has similar expression behavior to many other genes, implicating it as a potential master regulator of gene expression. A gene with high betweenness (i.e. a bottleneck) on the other hand, bridges two regions of the graph indicating that it spans two different behavioral profiles. Genes in this position are potentially involved in causing a transition from

one response pattern to another. Thus hubs and bottlenecks may represent master gene expression regulators of two different varieties. Previous work by our group and others has shown that graph vertices in hub and bottleneck positions are significantly enriched for genes critical to the process under study [2, 28, 29, 30]. Given these prior results and biological relevance of centrality in the setting of graphs, we hypothesized that hypergraph s-betweenness (and potentially s-harmonic closeness) will have similar biological relevance.

In order to take into account multiple s values simultaneously in our analysis we average the centrality values across a range of s values and define the **average s-betweenness centrality** and **average harmonic s-closeness centrality** as

$$\overline{BC}_s(e) = \frac{1}{s}\sum_{i=1}^{s} BC_i(e), \qquad \overline{HCC}_s(e) = \frac{1}{s}\sum_{i=1}^{s} HCC_i(e).$$

Computing (average) s-centralities for each hyperedge provides a ranked list of hyperedges from most central (high value) to least central.

Results

By analyzing the curated omnibus transcriptomic data set described above using both graph and hypergraph approaches, we illustrate the advantages of applying a hypergraph approach to uncover the underlying molecular signatures and mechanisms common across host response to viral infection broadly.

Hypergraph structure

We create hypergraphs from transcriptomics $\log_2$-fold change data calculated from gene expression levels of infected experiments relative to time-matched uninfected mock experiments[3]. As discussed above, in our hypergraphs hyperedges represent *genes* and vertices represent *conditions*. The vertex representing condition X is contained in the hyperedge representing gene G if gene G is significantly deviating, either up- or down-regulated, in condition X. A small subset of highly connected hyperedges (that is, genes with a large core of common conditions), is shown in Figure 2. The entire hypergraph represents $n = 179$ conditions (vertices) and m =7,782 genes (edges).

Distributions of even fundamental hypergraph statistics can illuminate some of the complex interaction structure present in the data. Figure 3a shows that the distribution of the sizes of the hyperedges (that is, the number of conditions a gene is significantly deviating in) is roughly power-law, sometimes referred to as "heavy tailed". This means that there are many genes (1,247 of them) significantly deviating in only one condition and relatively few genes significantly deviating in many conditions, with a maximum number of conditions for a single gene on the order of 100. The six largest hyperedges, with sizes greater than 100 in increasing order, correspond to the genes ISG15, IL6, ATF3, RSAD2, USP18, and IFIT1. All of these genes are part of the interferon response, a critical pathway in response to viral infections [31, 32].

[3]All hypergraph calculations and visualizations were performed using the Python hypergraph library HyperNetX (`https://github.com/pnnl/HyperNetX`).

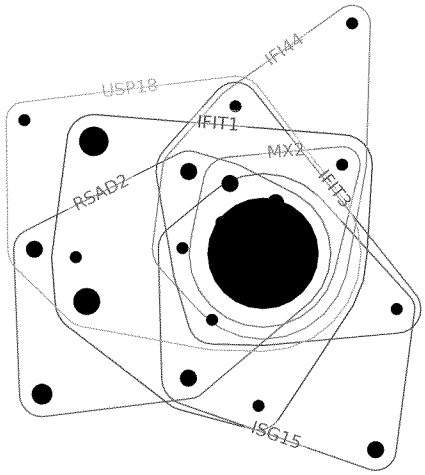
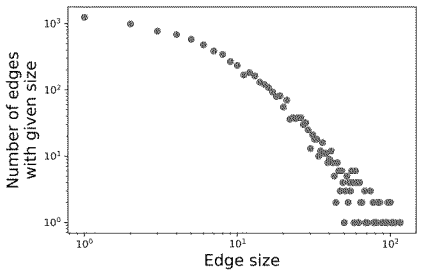


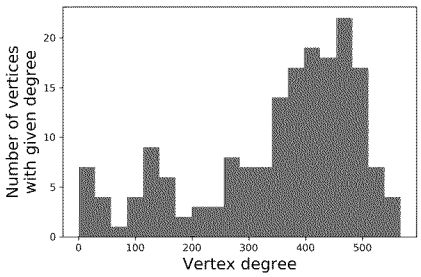
Figure 2: Small connected subset of the condition/gene hypergraph. Hyperedges are genes, and black circles indicate groups of vertices (conditions), with larger circles indicating larger groups.

On the other hand the vertex degree distribution is the number of edges a particular vertex is contained in (that is, the number of genes significantly deviating for each condition (vertex)). This is shown as a histogram in Figure 3b, and it has a very different shape than the edge size distribution. There are relatively few conditions with small numbers (less than 200) or large numbers (more than 500) of significantly deviating genes. The most common number of significantly deviating genes for a condition is between 400 and 500. This peak is likely an artifact of how we choose when a vertex is contained within an edge. The degree of a condition vertex is the number of genes that are significantly deviating for that condition. By our procedure these are genes with z-score higher than 2 and p-value less than 0.05. If we simply went by z-score, and our fold change data are normally distributed for each condition, then we would expect that 5% of the genes would have z-score greater than 2. There are 9,760 genes in our data and 5% of that would be 488 genes, which is roughly where the peak is. The skewness and additional modes of the distribution of degrees is likely due to the addition of the p-value condition.

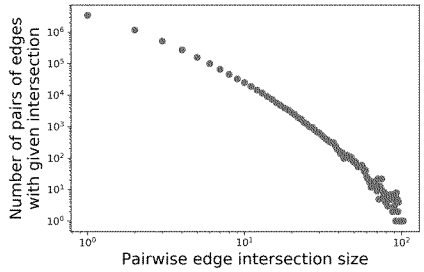
Finally, Figure 3c shows another power-law distribution, this time of the size of pairwise edge intersections, or in other words the number of conditions that pairs of genes are both significantly deviating within. We see that there are many pairs of genes that have few conditions in common and only a few pairs of genes that have many conditions in common, again with a maximum on the order of 100. The pair of genes with largest intersection is not surprisingly the two largest edges, IFIT1 and USP18, with 103 conditions in common. Interestingly, IFIT1 and USP18 are both well-established interferon response genes, with IFIT1 strongly promoting interferon activity, and USP18 serving to dampen the response [33].



(a) Edge size distribution. Each edge represents a gene, the size of the edge is the number of conditions in which the gene is significantly deviating.



(b) Vertex degree histogram. Each vertex represents a condition, the degree of a vertex is the number of genes significantly deviating in that condition.



(c) Pairwise edge intersection size distribution. Each edge represents a gene. The intersection between two edges indicates the set of conditions that both genes are significantly deviating in.

Figure 3: Distributions of simple hypergraph statistics of our hypergraph

Gene importance rankings

As noted above, previous studies using graph approaches with similar viral data have demonstrated that network measures like betweenness centrality could be used to identify critical genes [1]. In the present work we hypothesize that extensions of these common graph metrics to a hypergraph, as defined in the Methods section above, can be leveraged to improve upon this prior work. In particular, we hypothesize that, as has been shown in the graph setting, high s-centrality is correlated with the gene being more important in host response to pathogenic viruses.

We calculate average s-betweenness centrality, $\overline{BC}_s(g)$, and average harmonic s-closeness centrality, $\overline{HCC}_s(g)$, for all genes (hyperedges) in the hypergraph for $1 \leq s \leq 50$. Both of these s-centrality computations provide a numerical value for each gene which can be used to rank the genes from most important (high centrality) to least (low centrality).

To serve as a simpler, but still hypergraph-based, comparison we created another ranked list using hyperedge size for each gene, i.e., the number of conditions the gene was significantly deviating in. Larger edge sizes indicate more conditions in which the gene was significantly deviating and therefore the gene is potentially more important to host response.

In order to compare the centrality rankings from the hypergraph to more common graph methods we employed a strategy based in mutual information that we have used previously to enrich for important genes in a network [1, 2, 28]. The CLR algorithm was run on the matrix of transcriptomics $\log_2$-fold change values using parameters spline = 3 and bins = 10 and the resulting matrix was filtered for all values ≥ 2. With this approach, any two genes with shared information above the threshold have similar expression profiles and form a graph edge. This results in an association graph from which we used the NetworkX graph analytics Python package [34] to calculate vertex degree, betweenness centrality, and harmonic closeness centrality.

To provide a simple baseline for comparison a final ranked list was computed directly from the $\log_2$-fold change table without using any graph structure. For each gene we computed its average absolute value of $\log_2$-fold change and ranked the genes from highest to lowest average. Higher values mean the gene is more likely to be highly deviated from the mock-infected samples in many conditions.

Comparison of rankings

To ascertain whether our hypergraph rankings are more highly enriched for genes known to be important in host response to viral infection, we gathered three distinct sets of genes: 1) all genes associated with the Gene Ontology (GO) term "immune response" (GO:0006955), downloaded from amigo.geneontology.org, referred to as 'IR' hereafter, 2) interferon-stimulated genes gathered from interferome.org[4], referred to as 'ISG', and 3) a set of human proteins known to be targets of pathogens acquired from Dyer, et al. [35], referred to as 'PT'. Although this is a limited set in terms of number of targets, it represents a set collected from a wide number of pathogens, both viral and bacterial, and is a conservative set for assessing the performance of our method and making comparisons between different approaches and parameters. In Table 1 we show the size of each gene set (along the diagonal) and the sizes of each pairwise intersection of gene sets (off the diagonal). Since our data encompasses a wide variety of virus types and infection systems, general immune-related sets were deemed suitable for our purpose.

	IR	ISG	PT
IR	**1,202**	250	297
ISG	250	**1,071**	152
PT	297	152	**906**

Table 1: (Diagonal) Size of each gene set; (Off-diagonal) Size of the pairwise intersections of the gene sets.

In order to measure the performance of our rankings, we applied weighted gene set enrichment analysis (GSEA) [36] to each of our gene rankings (average hypergraph s-centralities, hyperedge size, CLR centralities, CLR vertex degree, and mean fold-change) using the three immune-related sets as target gene sets. The GSEA score of a ranked list, computed for a specific gene set, quantifies how concentrated the gene set is at the extremal values of the list. A high GSEA score means the gene set is concentrated at the top of the list while a low (highly negative) score indicates

[4] http://www.interferome.org/interferome/search/searchGene.jspx

that the gene set is concentrated towards the bottom of the list. A score closer to zero means that the gene set is more uniformly distributed throughout the ranked list. The significance, or p-value, of an observed enrichment score, ES, is assessed by comparing it with a set of ES_0 scores using the following steps:

1 Randomly reorder the ranked list keeping the centrality values tied to the rank (rather than tied to the gene) and recompute ES;
2 Repeat for 100,000 permutations, and create a histogram of the corresponding enrichment scores ES_0;
3 Estimate empirical p value for ES from distribution of ES_0 values by using the positive or negative portion of the distribution corresponding to the sign of ES.

Figure 4 shows GSEA scores for all rankings and for all three target gene sets. The p-values for the GSEA scores are shown in Figure 5. We note the following conclusions:

- Both hypergraph s-centrality metrics for most s values, as well as hyperedge size, showed much higher enrichment than lists derived from CLR graphs and average fold change.
- But s-betweenness enrichment was universally higher than s-closeness enrichment, suggesting that these two measurements are capturing fundamentally different behavior within hypergraphs, and that s-betweenness appears to be more effective at capturing genes that are important in host responses to viral infection.
- Both centrality's enrichment improves significantly when larger s values are taken into account, indicating that when higher order interactions are considered, they become more powerful in identifying important genes.

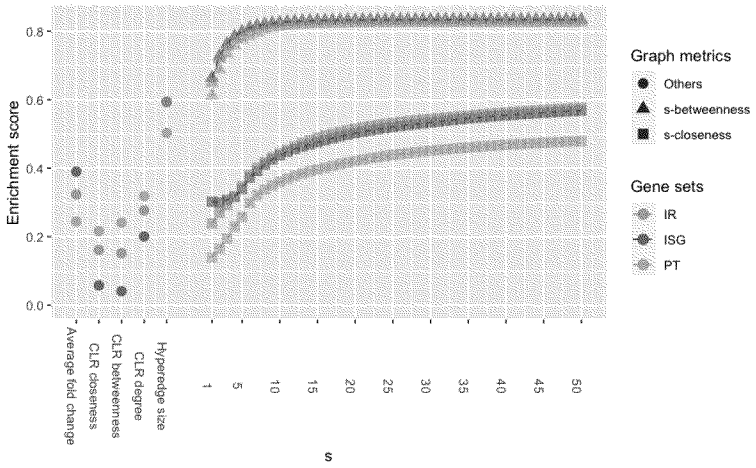


Figure 4: Enrichment scores of gene sets using s-betweenness and s-harmonic closeness metrics.

A summary visualization of our results is shown in Figure 6 taking the rankings for both s-betweenness and harmonic s-closeness for the highest level of $s = 50$ as the representative hypergraph centrality rankings. We compare those with the five

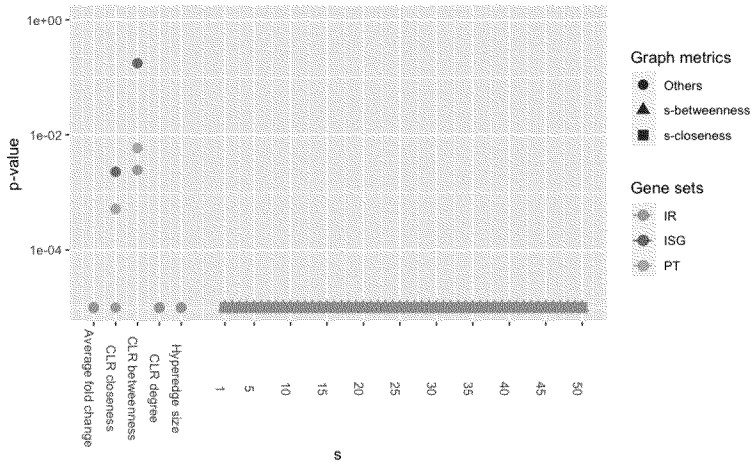


Figure 5: Significance (p-values) of enrichment analysis using s-betweenness and s-harmonic closeness metrics

other rankings and again see that s-betweenness centrality outperforms all other measures. While harmonic s-closeness centrality outperforms all graph measures it is outperformed by the simple hyperedge size ranking. The p-values, nearly all significantly less than 0.05, are shown in the same plot at the end of the bars. These results demonstrate that hypergraph s-betweenness, but not necessarily harmonic s-closeness, considers the complexity of the hypergraph and provides superior performance over graph metrics with regards to identifying biologically important genes. This aligns with prior work in which betweenness centrality computed for vertices in a graph identifies important genes in a network [1, 2, 28, 37].

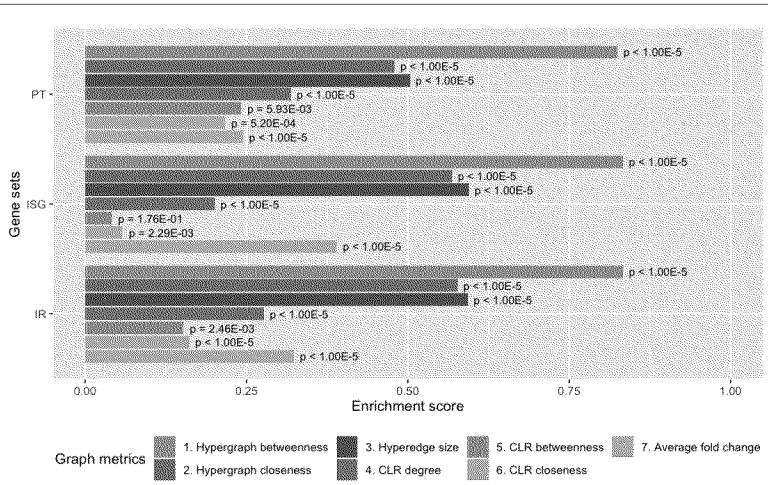


Figure 6: Comparison between different hypergraph and graph metrics

Discussion

We draw attention to two primary observations of interest in our results. First is the observation that s-betweenness centrality consistently outperforms s-closeness centrality. At first glance this seems surprising since betweenness and closeness calculated on the CLR graph have comparable performance. While the explanation for this result is the subject of ongoing investigation, we observe that these two types of centrality are measuring significantly different properties. For both graphs and hypergraphs high harmonic closeness centrality indicates that on average a gene is close to many other genes, while high betweenness centrality means that a gene is on many short paths between other genes. Sometimes these two notions coincide, as seems to be the case in the CLR graph, but there are cases in which they do not.

For example, a gene that may be more periphery, i.e., not on many (short) paths, could still be very close to a central core. Being on few short paths this gene would have very low betweenness. However, since it is close to a central core it could have high closeness score.

This seems to be the case in the hypergraphs we are studying. Since there are many conditions that have a lot of significantly expressed genes (see Figure 3b) there is likely a large central core in the hypergraph which increases the closeness scores for peripheral genes, and perhaps all genes. Indeed we have observed that for small values of s the s-closeness values do not correlate with edge size, however for large s values the s-closeness scores do tend to correlate with edge size. This likely means that for low s values the closeness is somehow washed out by this central core and any variability we see is not significant. In contrast, for s-betweenness we see a correlation between edge size and betweenness at all s values. However, even though s-betweenness is correlated to edge size for all s values its enrichment score is still much larger than that for edge size and so seems to be capturing something more significant about hypergraph structure.

This difference between closeness and betweenness may also be related to the nature of the large gene expression data set used in our study. Since both mouse and human-based gene expression data were included in the hypergraph some genes may serve as bridges between different regions of the hypergraph (e.g. predominantly human regions vs predominantly mouse regions). Genes that are truly important in host response to viral infection would be important across species and more effectively brought to light by the betweenness measure that tends to highlight elements occupying bridge-like positions in the hypergraph. Thus, betweenness centrality may be most useful for identifying critical elements when heterogeneous data sets are analyzed.

Our second observation is that our hypergraph s-betweenness centrality significantly outperforms established graph centrality techniques. This is entirely in keeping with our expectation, as the purpose of hypergraphs is to capture the complex, multi-way interactions present in a system that are beyond the ability of graphs to model. Thus where betweenness centrality has been used in prior studies to identify important biological features the application of hypergraph s-betweenness may promote discovery of additional features of interest. While the finding that hypergraph betweenness represents a new tool for identifying critical hypergraph elements is an exciting contribution of this study, it also presents an additional immediate benefit: genes highly ranked by hypergraph betweenness that do *not* appear in any of

our target gene sets represent potentially novel discoveries of genes central to viral infection. One good example of this is the ZZZ3 gene, which appears in position 4 out of 7,782 in the average hypergraph betweenness ranking, but does not appear in any of the IR, ISG or PT gene sets. ZZZ3 is part of the histone reader ATAC complex, which scans the state of histone modification and contributes to gene activation/repression mechanisms [38]. No known connection between virus infection and ZZZ3 exists, but it may serve a critical role in regulating gene expression in response to general infection.

Similarly, EPHX1, GDF15, and DUSP1 were not included in the three gene sets and ranked 29, 30 and 33, respectively. These genes are identified as an epoxide detoxification component, a stress responsive cytokine and a stress-responsive phosphatase, respectively. These roles may be related to virus-induced stress in host cells, but the specific mechanisms involved are yet to be elucidated. More exploration of these and other highly ranked genes is the subject of future work for us.

Conclusion

The work we present in this paper is similar to much of the work surveyed in our literature review in that we show the value of hypergraphs over traditional graph analysis of biological data. However, our work differs from these prior studies in a number of ways. First, our hypergraphs are built natively from transcriptomics data rather than based on existing graph models of systems. Although still capturing some multi-way complexities, hypergraphs inferred from graphs may include some induced interactions not actually present in the system that is being modeled. Creating hypergraphs natively from the data avoids this imputation. Other papers we surveyed do create hypergraphs natively from other types of data, but rather than applying centrality measures instead study more structural features like highly connected vertices.

Previous work [1, 2, 28, 37] had demonstrated that graph metrics can be used to identify important genes in association graphs, and so we set out to determine if hypergraphs provided an improvement over graphs. To assess performance of (hyper)graphs derived from our large viral infection gene expression data set, we identified three gene sets related to virus/pathogen infection and performed an enrichment analysis of our ranked lists compared to these gene sets. While the sets were partially overlapping they represented relatively distinct aspects of viral infection in general. Our results show that s-betweenness, but not necessarily harmonic s-closeness, was a useful metric that is able to identify key genes in a comprehensive gene expression data set. While s-closeness does outperform both CLR centrality measures, CLR degree, and average fold change, it does not exceed the performance of a simple ranking according to hyperedge size, which does not require the full hypergraph structure to calculate. On the other hand, ranking based on hypergraph s-betweenness outperformed all other metrics.

The hypergraphs we created used samples from a wide range of viruses, strains, cell types, and time since infection. In future work we plan to apply this measure to compare critical genes in viral response across differing sample features. For example, we will split our hypergraph based on pathogenicity (high vs. low), cell type or host, and time since infection (early vs. late). Comparing the critical genes across

these different hypergraphs may allow us to discover previously unknown indicators of viral infection for early detection or severity determination. Other future work we plan to pursue includes considering other hypergraph constructions, other data types, and hypergraph algorithms to identify highly connected vertices. We plan to combine transcriptomics with proteomics and other 'omics measurements to understand whether hybrid hypergraphs yield better results or if the inclusion of more data washes out the complexities.

Competing interests
The authors declare that they have no competing interests.

Author's contributions
SF (Feng) performed the enrichment analysis, provided biological subject matter expertise, and co-wrote the manuscript. BP and EH performed the centrality calculations. BJ, CJ, and HK developed hypergraph methodology and co-wrote the manuscript. JM, and HM provided biological subject matter expertise and co-wrote the manuscript. AE, AS, LT, SF (Fan), KW (Walters), PH, DW, QT, VM, TS, AC, JK, KS, NH, LB contributed to generation, curation, and analysis of data. MD, RB, KW (Waters), YK supervised generation and analysis of data. EP developed hypergraph methodology, supervised the hypergraph analysis team, and wrote the manuscript.

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Additional Files

GraphMetricsRankedLists.xlsx

This Microsoft Excel file contains the seven ranked lists of genes that were compared in Figure 6. Each ranked list is in its own sheet in the Excel file: hypergraph betweenness, hypergraph closeness, hyperedge size, CLR degree, CLR betweenness, CLR closeness, and average fold change. The ranked lists are of different length because some genes were not included in the hypergraph or graph based on the (hyper)graph construction criteria.

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 8/25/2020 2:57:35 PM (UTC-07:00)
To: Baric, Ralph S[rbaric@email.unc.edu]
Subject: Re: Adding NL63?

Thank you, Ralph. Ben might be out as I didn't hear back from him yet. I will email him again tomorrow if I haven't heard anything by then.

Yes, I actually made myself get the reviewer comments out and Hugh and I are meeting tomorrow to discuss this. Thank you for the reminder. So many things to do at once which is one of the many wonderful themes of 2020.

I hope you are doing well. Congratulations on finding land out by the coast. Lisa mentioned that you were finally successful. I know it's been a long time coming so I hope it is amazing! You deserve a glorious place to spend time with the family!

I will check in with Toni to see when you might have some time in the next week or so to discuss the resubmission. Thank you again, Amy

---

From: "Baric, Ralph S" <rbaric@email.unc.edu>
Date: Thursday, August 20, 2020 at 10:16 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "McGlaughon, Ben" <benmcg@email.unc.edu>
Subject: RE: Adding NL63?

Hi Amy, no problem. Ben send Amy the viruses asap. Hope your doing well. We should chat sometime, likely need to revisit your paper and make sure we get it back out for review. I hope all are well and healthy in your family. Ralph

---

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, August 20, 2020 12:35 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Cc: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Adding NL63?

Ben,

I hope you are doing well and transitioning to working in the Baric laboratory in the weirdness of the pandemic.

Can you please talk to Ralph about adding human coronavirus NL63 to our existing MTA?

I would like both the current wild type strain (should contain a point mutation in spike following tissue culture adaptation) and the virus expressing green fluorescent protein GFP. Sarah Leist should have stocks of these at BSL2.

I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: Baric, Ralph S[rbaric@email.unc.edu]
Sent: Wed 8/26/2020 6:00:24 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Adding NL63?

Hi Amy, sounds goo. Talk with you soon. The place is very nice, pretty high up 20+ feet above high tide mark, so hopefully a fewf decades before its structure for fish. Ralph

---

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, August 25, 2020 5:58 PM
To: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Re: Adding NL63?

Thank you, Ralph. Ben might be out as I didn't hear back from him yet. I will email him again tomorrow if I haven't heard anything by then.

Yes, I actually made myself get the reviewer comments out and Hugh and I are meeting tomorrow to discuss this. Thank you for the reminder. So many things to do at once which is one of the many wonderful themes of 2020.

I hope you are doing well. Congratulations on finding land out by the coast. Lisa mentioned that you were finally successful. I know it's been a long time coming so I hope it is amazing! You deserve a glorious place to spend time with the family!

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Date: Thursday, August 20, 2020 at 10:16 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "McGlaughon, Ben" <benmcg@email.unc.edu>
Subject: RE: Adding NL63?

Hi Amy, no problem. Ben send Amy the viruses asap. Hope your doing well. We should chat sometime, likely need to revisit your paper and make sure we get it back out for review. I hope all are well and healthy in your family. Ralph

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From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, August 20, 2020 12:35 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Cc: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Adding NL63?

Ben,

I hope you are doing well and transitioning to working in the Baric laboratory in the weirdness of the pandemic.

Can you please talk to Ralph about adding human coronavirus NL63 to our existing MTA?

I would like both the current wild type strain (should contain a point mutation in spike following tissue culture adaptation) and the virus expressing green fluorescent protein GFP. Sarah Leist should have stocks of these at BSL2.

I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: Leist, Sarah Rebecca[leist@email.unc.edu]
Sent: Wed 8/26/2020 6:30:11 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Hello and a little help please

Hi Amy,
I can have a look later this week.
I'm moving right now.

Sorry for the delay!

Hope you're doing fine!

Sarah

Sent from my iPhone

On Aug 20, 2020, at 12:41 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:

Hi Sarah!

I hope you and your kitty clan are doing well! I hope the boys transitioned to the US well and that everyone is getting along nicely! And that there is still somewhere for you to sleep in your apartment.

I know you are crazy busy but I am hoping you can help me with something that maybe won't take too long.

Could you help Ben with finding a few vials of the NL63 stocks from the experiment you and I worked on previously? I am asking to get the wild type (with the S point mutation) and the one with GFP. If you can't find these please let me know.
I really appreciate it as I know you are totally slammed. Congratulations on the publications! That is really great!

Thank you very much! I miss getting to catch up with you and I really hope you are getting a little down time to enjoy life! Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 8/26/2020 8:24:56 AM (UTC-07:00)
To: Leist, Sarah Rebecca[leist@email.unc.edu]
Subject: Re: Hello and a little help please

Hi Sarah,

Moving is super exciting! I hope you like your new place and that they love cats! That would be awesome and hopefully not too long of a freezer dive in Little Switzerland. Thank you very much!! I appreciate you making time to respond! Thank you again, Amy

---

From: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Date: Wednesday, August 26, 2020 at 6:30 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Hello and a little help please

Hi Amy,
I can have a look later this week.
I'm moving right now.

Sorry for the delay!

Hope you're doing fine!

Sarah

Sent from my iPhone

> On Aug 20, 2020, at 12:41 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:
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> Hi Sarah!
>
> I hope you and your kitty clan are doing well! I hope the boys transitioned to the US well and that everyone is getting along nicely! And that there is still somewhere for you to sleep in your apartment.
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> I know you are crazy busy but I am hoping you can help me with something that maybe won't take too long.
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> Could you help Ben with finding a few vials of the NL63 stocks from the experiment you and I worked on previously? I am asking to get the wild type (with the S point mutation) and the one with GFP. If you can't find these please let me know.
> I really appreciate it as I know you are totally slammed. Congratulations on the publications! That is really great!
>
> Thank you very much! I miss getting to catch up with you and I really hope you are getting a little down time to enjoy life! Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 8/26/2020 1:17:51 PM (UTC-07:00)
To: Baric, Ralph S[rbaric@email.unc.edu]; Baric, Toni C[antoinette_baric@med.unc.edu]
Subject: Meeting with Amy Week of August 31?

Toni,
Does Ralph have an hour to discuss resubmission of a manuscript the week of August 31st?

I am available the following times next week. Thank you very much! Amy

Monday: 2:30pm to 6pm eastern/11:30am PT to 3pm PT
Tuesday: 11am to 3pm eastern/8am to noon PT
Wednesday: 11am to 2pm eastern/8am to 11am PT
Thursday: 11am to 1:30pm eastern/8am to 10:30am PT
Friday: not good for Amy

From: Baric, Toni C[antoinette_baric@med.unc.edu]
Sent: Wed 8/26/2020 1:19:10 PM (UTC-07:00)
To: Baric, Ralph S[rbaric@email.unc.edu]; Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Meeting with Amy Week of August 31?

I think so. I am not home but will let you know later today.

Get Outlook for Android

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, August 26, 2020 4:17:50 PM
To: Baric, Ralph S <rbaric@email.unc.edu>; Baric, Toni C <antoinette_baric@med.unc.edu>
Subject: Meeting with Amy Week of August 31?

Toni,
Does Ralph have an hour to discuss resubmission of a manuscript the week of August 31st?

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Wednesday: 11am to 2pm eastern/8am to 11am PT
Thursday: 11am to 1:30pm eastern/8am to 10:30am PT
Friday: not good for Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 8/26/2020 1:22:14 PM (UTC-07:00)
To: Baric, Toni C[antoinette_baric@med.unc.edu]; Baric, Ralph S[rbaric@email.unc.edu]
Subject: Re: Meeting with Amy Week of August 31?

Sounds good. I appreciate it. Thank you, Amy

From: "Baric, Toni C" <antoinette_baric@med.unc.edu>
Date: Wednesday, August 26, 2020 at 1:20 PM
To: "Baric, Ralph S" <rbaric@email.unc.edu>, "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Meeting with Amy Week of August 31?

I think so. I am not home but will let you know later today.

Get Outlook for Android

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, August 26, 2020 4:17:50 PM
To: Baric, Ralph S <rbaric@email.unc.edu>; Baric, Toni C <antoinette_baric@med.unc.edu>
Subject: Meeting with Amy Week of August 31?

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Thursday: 11am to 1:30pm eastern/8am to 10:30am PT
Friday: not good for Amy

From: Baric, Toni C[antoinette_baric@med.unc.edu]
Sent: Wed 8/26/2020 3:17:36 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]; Baric, Ralph S[rbaric@email.unc.edu]
Subject: RE: Meeting with Amy Week of August 31?

Hi Amy
How about Monday 3pm ET/12 PT?
Toni

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, August 26, 2020 4:18 PM
To: Baric, Ralph S <rbaric@email.unc.edu>; Baric, Toni C <antoinette_baric@med.unc.edu>
Subject: Meeting with Amy Week of August 31?

Toni,
Does Ralph have an hour to discuss resubmission of a manuscript the week of August 31st?

I am available the following times next week. Thank you very much! Amy

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Wednesday: 11am to 2pm eastern/8am to 11am PT
Thursday: 11am to 1:30pm eastern/8am to 10:30am PT
Friday: not good for Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 8/26/2020 3:25:01 PM (UTC-07:00)
To: Baric, Toni C[antoinette_baric@med.unc.edu]; Baric, Ralph S[rbaric@email.unc.edu]
Subject: Re: Meeting with Amy Week of August 31?

That will work. I will send out an invitation with my phone number. Thank you very much, Amy

---

From: "Baric, Toni C" <antoinette_baric@med.unc.edu>
Date: Wednesday, August 26, 2020 at 3:17 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: RE: Meeting with Amy Week of August 31?

Hi Amy
How about Monday 3pm ET/12 PT?
Toni

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, August 26, 2020 4:18 PM
To: Baric, Ralph S <rbaric@email.unc.edu>; Baric, Toni C <antoinette_baric@med.unc.edu>
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Thursday: 11am to 1:30pm eastern/8am to 10:30am PT
Friday: not good for Amy

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 8/26/2020 3:27:13 PM
To: Baric, Ralph S [rbaric@email.unc.edu]; Baric, Toni C [antoinette_baric@med.unc.edu]

Subject: Meeting with Amy
Location: 5 U.S.C. § 552(b)(6) r Amy can call Ralph

Start: 8/31/2020 12:00:00 PM
End: 8/31/2020 1:00:00 PM
Show Time As: Tentative

Recurrence: (none)

Required Attendees: Baric, Ralph S; Baric, Toni C

From: Baric, Toni C[antoinette_baric@med.unc.edu]
Sent: Wed 8/26/2020 3:27:29 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]; Baric, Ralph S[rbaric@email.unc.edu]
Subject: RE: Meeting with Amy Week of August 31?

Thanks Amy. Yes on 8/31.

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, August 26, 2020 6:25 PM
To: Baric, Toni C <antoinette_baric@med.unc.edu>; Baric, Ralph S <rbaric@email.unc.edu>
Subject: Re: Meeting with Amy Week of August 31?

That will work. I will send out an invitation with my phone number. Thank you very much, Amy

---

From: "Baric, Toni C" <antoinette_baric@med.unc.edu>
Date: Wednesday, August 26, 2020 at 3:17 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: RE: Meeting with Amy Week of August 31?

Hi Amy
How about Monday 3pm ET/12 PT?
Toni

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, August 26, 2020 4:18 PM
To: Baric, Ralph S <rbaric@email.unc.edu>; Baric, Toni C <antoinette_baric@med.unc.edu>
Subject: Meeting with Amy Week of August 31?

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Wednesday: 11am to 2pm eastern/8am to 11am PT
Thursday: 11am to 1:30pm eastern/8am to 10:30am PT
Friday: not good for Amy

From: Ames, Amber A[Amber.Ames@pnnl.gov]

Sent: Thur 8/27/2020 3:44:05 PM (UTC-07:00)

To: ResAdminOSR@unc.edu[ResAdminOSR@unc.edu]; amina93@live.unc.edu[amina93@live.unc.edu]

Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]; sheahan@email.unc.edu[sheahan@email.unc.edu]

Subject: Contract No. 528372, IPF 20-5613

Attachment: PO 528372 Precontract Cost Authorization Letter.pdf

Attachment: PO 528372.pdf

Attachment: PO 528372 SOW.pdf

Attachment: REPRESENTATIONS AND CERTIFICATIONS Signed.pdf

Attachment: GP-A-409.25-EDNP_October 2019.pdf

Dear Alexie,

Attached please find the award for University of North Carolina at Chapel Hill and Principal Investigator Timothy Sheahan to support the "How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells" project. Please note I used the alterations to the General Provisions previously negotiated to help facilitate review/approval.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

Pacific Northwest NATIONAL LABORATORY

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Acting Under Contract DE-AC05-76RL01830
With the U.S. Department of Energy
Operating the Pacific Northwest National Laboratory (PNNL) (www.pnnl.gov)

Schedule - Contract No. 528372

Issued by:	**Name and Address of Contractor:**
Battelle Battelle Boulevard, K9-15 P.O. Box 999 Richland, WA 99352-0999 USA Contracts Specialist: Amber A. Ames Telephone Number: (509) 371-7050 Email: amber.ames@pnnl.gov	University of North Carolina at Chapel Hill Office of Sponsored Research 104 Airport Drive, Suite 2200 Campus Box 1350 Chapel Hill, NC 27599-1350 USA Contractor Contact: David Paul Telephone Number: (919) 966-3411 Email: resadminosr@unc.edu
Payment Terms: Net 30	**Contract Type:** Cost Reimbursement
Submit Invoices and Invoice/Payment Inquiries to ap.invoices@pnnl.gov. **Note:** Invoices must list location(s) of service (US: City, State; Foreign: Country).	**Total Contract Amount:** 5 U.S.C. § 552(b)(4)
Contract Period of Performance: July 27, 2020 through May 31, 2021	
Award Battelle hereby agrees to award this Contract to the Contractor subject to acceptance. The rights and obligations of the parties to this Contract are subject to and governed by this document and any documents attached or incorporated by reference.	**Contractor Agreement** Contractor accepts and agrees to furnish and deliver the items or perform services to the extent stated in this document for the consideration stated in this contract. The rights and obligations of the parties to this contract are subject to and governed by this document and any documents attached or incorporated by reference.

Battelle Memorial Institute Pacific Northwest Division	**Contractor shall sign and return a copy of this document**
Signature of person authorized to sign. Digitally signed by Amber A. Ames Date: 2020.08.27 15:38:32 -07'00'	**Signature of person authorized to sign**
Name Amber A. Ames	**Name**
Title Contracts Specialist	Title
Date	Date

IMPORTANT NOTE: Any domestic and foreign travel associated with this contract (including contractor travel within a country of presence) shall be approved in writing by the Battelle Contracts Representative in advance of travel arrangements being finalized. Without the advance approval of the Battelle Contracts Representative for any such travel, any invoiced costs related to such travel will not be paid.

Statement of Work

Contractor agrees to perform the scope outlined in the attached Statement of Work dated July 16, 2020.

Indirect Rates

The following indirect cost rates are hereby established until and unless changed by mutual agreement:

Category	Rate	Base	Type	Effective			
Indirect Costs	55.5%	On Campus Organized Research MTDC*	Provisional	From	07/01/2020	Through	Until amended

*Modified Total Direct Costs

Fringe Benefits: *The fringe benefits are specifically identified to each employee and are charged individually as direct costs.*

The provisional rate(s) specific above may be prospectively or retroactively revised by mutual agreement, at either Battelle or the Contractor's request, to prevent substantial overpayment.

Upon establishment/approval of finalized, or final rates, for any period consistent with the period of performance, the Contractor agrees to supply such approval to Battelle, within 30 days or receipt of approval from the cognizant agency.

Technical Oversight Representative

All technical questions should be directed to the Technical Oversight Representative, Pamela M. Kinsey at (509) 375-6848 or pamela.kinsey@pnnl.gov. The Technical Oversight Representative cannot modify this agreement.

Battelle Contracts Representative

All contractual questions should be directed to the Battelle Contracts Representative, Amber A. Ames at (509) 371-7050 or amber.ames@pnnl.gov.

Approval of Subcontracts

Subcontracts require the prior written approval of the Battelle Contracts Representative.

Contract Contents

In addition to this Schedule, the Contract consists of:

- Representations and Certifications dated July 27, 2020
- The General Provisions Applicable for Educational Institutions and Nonprofit Organizations, Form A-409.25-Ed/NP dated October 2019, apply and may be viewed at http://www.pnnl.gov/contracts/contractdocuments.aspx
- Precontract Cost Authorization Letter dated July 24, 2020
- Statement of Work dated July 16, 2020

Alterations to General Provisions

- **Insurance – Liability to Third Persons (cl. 378b – Mar 1996)** This clause is hereby deleted and replaced with:

  "Contractor is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."
- **Disputes (cl. 331-Nov 2014)** This clause is hereby deleted and replaced with the following: "Except as otherwise provided or agreed, any dispute relating to this contract which is not disposed of by agreement shall be decided by litigation in a court of competent jurisdiction upon filing of a legal action by the aggrieved party. During the pendency of any dispute, the Contractor shall proceed diligently with the performance of the contract and in accordance with the direction of Battelle."

- **Insurance Requirements (cl. 378 - April 2017)** This clause is hereby deleted and replaced with:

  "Contractor is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."
- **Laws and Regulations, DOE Directives, and Indemnification (cl. 3121 -Mar 2014)** Delete the word "indemnification" in the title and all of Section C."
- **FAR 52.227-3 Patent Indemnity (Apr 1984)** This clause is self-deleting because work being performed under this contract does not include the delivery of commercial items.
- **FAR 52.227-10 Filing of Patent Applications-Classified Subject Matter (DEC 2007)** This clause is self-deleting because this contract is not expected to result in a patent application containing classified subject matter.
- **FAR 52.246-5 Inspection Service - Cost Reimbursement (Apr 1984)** and **FAR 52.246-8 Inspection of Research and Development—Cost Reimbursement (May 2001)** are hereby deleted and replaced with **52.246-9 Inspection of Research and Development (Short Form) (Apr 1984)**.
- **DEAR 970.5229-1 State and Local Taxes (Dec 2000)** This clause is deleted.

Integration

This Contract contains the entire understanding between the parties, and there are no understandings or representations not set forth or incorporated by reference herein. No subsequent modifications of this Contract shall be of any force or effect unless in writing signed by the party claimed to be bound thereby. No communications, written or oral, by other than a Battelle Contracts Representative shall be effective to modify or otherwise affect the provisions of this Contract.

Statement of Work
How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
University of North Carolina at Chapel Hill, Principal Investigator Timothy Sheahan
July 16, 2020

I. Background

The molecular mechanisms regulating emerging highly pathogenic human respiratory coronavirus pathogenesis are complex and include dampening of the host innate immune response allowing higher viral titers immediately following entry. Previous studies tracking the expression of interferon stimulated gene (ISG) expression in Middle East respiratory syndrome coronavirus (MERS-CoV) infected continuous human lung epithelial cells demonstrated that specific ISG expression patterns could be detected and these patterns could be used to determine how CoV were modulating the innate immune response. Epigenetic/chromatin remodeling mechanisms were found to be important regulators of host chromatin remodeling that altered host expression ISG patterns. This proposal will build on these foundational studies performed in continuous human lung cell lines and define ways that MERS-CoV regulates innate immunity in primary human lung fibroblasts and microvascular endothelial cells.

II. Scope

University of North Carolina at Chapel Hill will analyze the fibroblast ChIP PCR samples collected in 2019 and discuss data with PNNL to determine next steps. University of North Carolina at Chapel Hill will perform ChIP Seq analysis of MERS-CoV infected microvascular endothelial cells at a single time point for three donors. University of North Carolina at Chapel Hill will perform BioRad Primer PCR Pathway Arrays on MERS-CoV infected microvascular endothelial cells and fibroblasts. Drs Sheahan and Schaefer will work in close collaboration with PNNL to analyze datasets to determine how MERS-CoV regulates ISG expression in human lung microvascular endothelial cells and fibroblasts.

III. Deliverables

- Evaluate project results and direction, in collaboration with PNNL
- Collaborate on experiment direction and identify alternatives for experiments
- Participate in meetings to discuss project status/progress, findings, and trouble shoot as needed
- Write and submit progress report and manuscript draft in collaboration with PNNL

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 8/27/2020 3:49:53 PM (UTC-07:00)
To: Parrish, Kalyn[klparrish@unc.edu]; Moore, Victoria L[victoria_moore@unc.edu]; Burkhart, Carol J.[carol_burkhart@unc.edu]; Caldwell, Chandra[ccaldwel@email.unc.edu]
Subject: FW: Contract No. 528372, IPF 20-5613
Attachment: PO 528372 Precontract Cost Authorization Letter.pdf
Attachment: PO 528372.pdf
Attachment: PO 528372 SOW.pdf
Attachment: REPRESENTATIONS AND CERTIFICATIONS Signed.pdf
Attachment: GP-A-409.25-EDNP_October 2019.pdf

All,

Just keeping you in the loop. I hope everyone is doing well and staying safe. Please let me know if you have any questions. Thank you, Amy

---

From: "Ames, Amber A" <Amber.Ames@pnnl.gov>
Date: Thursday, August 27, 2020 at 3:44 PM
To: "ResAdminOSR@unc.edu" <ResAdminOSR@unc.edu>, "amina93@live.unc.edu" <amina93@live.unc.edu>
Cc: "Sandoval, Norma I" <Norma.Sandoval@pnnl.gov>, "Sims, Amy C" <amy.sims@pnnl.gov>, "Kinsey, Pamela M" <Pamela.Kinsey@pnnl.gov>, "sheahan@email.unc.edu" <sheahan@email.unc.edu>
Subject: Contract No. 528372, IPF 20-5613

Dear Alexie,

Attached please find the award for University of North Carolina at Chapel Hill and Principal Investigator Timothy Sheahan to support the "How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells" project. Please note I used the alterations to the General Provisions previously negotiated to help facilitate review/approval.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov



902 Battelle Boulevard
P.O. Box 999, MSIN K9-15
Richland, WA 99352
(509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

Transmitted via e-mail to: sheahan@email.unc.edu

July 24, 2020

Timothy Sheahan, PhD
University of North Carolina at Chapel Hill
Department of Epidemiology
3302 Michael Hooker Research Building
CB #7435
Chapel Hill, NC 27599

Dear Dr. Sheahan:

SUBJECT: PROPOSED CONTRACT NO. 528372

Battelle is in the process of preparing the subject contract to be finalized with you in accordance with the negotiations to be concluded no later than August 31, 2020.

To facilitate commencement of work under Contract No. 528372 as recognized during contract negotiations, Battelle proposes to include a clause in the contract to the effect that precontract costs in the amount of 5 U.S.C. § 552(b)(4) incurred from July 27, 2020, but prior to the award date of Contract No. 528372, will be allowable to the extent that they would have been allowable if incurred after the date of Contract No. 528372. Precontract costs will not include costs of preparing bid/proposals or of participating in contract negotiations.

It is understood that the commencement of work by University of North Carolina at Chapel Hill, prior to the date of Contract No. 528372, is entirely at its own risk. Invoices for reimbursement for precontract costs will not be paid until after execution of Contract No. 528372 by both parties. Work efforts charged as precontract costs shall be limited to the following activities: "How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells" Statement of Work dated July 16, 2020. All work shall be conducted with strict adherence to the Statement of Work and any specified Quality Assurance requirements.

Please acknowledge your acceptance of these conditions by signing below and returning to my attention.

Sincerely,

Digitally signed by Amber A. Ames
Date: 2020.07.24 10:59:15 -07'00'

Amber A. Ames
Senior Contracts Specialist

Acknowledge: University of North Carolina at Chapel Hill

Alexie Mina Digitally signed by Alexie Mina
Date: 2020.07.27 14:26:04 -04'00'

Alexie Mina

By: (signature and printed name) Date:

U.S. DEPARTMENT OF ENERGY

Pacific Northwest
NATIONAL LABORATORY
Proudly Operated by Battelle Since 1965

Battelle Memorial Institute, Pacific Northwest Division
Acting Under Contract DE-AC05-76RL01830
With the U.S. Department of Energy
Operating the Pacific Northwest National Laboratory (PNNL) (www.pnnl.gov)

Schedule - Contract No. 528372

Issued by:	**Name and Address of Contractor:**
Battelle Battelle Boulevard, K9-15 P.O. Box 999 Richland, WA 99352-0999 USA Contracts Specialist: Amber A. Ames Telephone Number: (509) 371-7050 Email: amber.ames@pnnl.gov	University of North Carolina at Chapel Hill Office of Sponsored Research 104 Airport Drive, Suite 2200 Campus Box 1350 Chapel Hill, NC 27599-1350 USA Contractor Contact: David Paul Telephone Number: (919) 966-3411 Email: resadminosr@unc.edu
Payment Terms: Net 30	**Contract Type:** Cost Reimbursement
Submit Invoices and Invoice/Payment Inquiries to ap.invoices@pnnl.gov. **Note:** Invoices must list location(s) of service (US: City, State; Foreign: Country).	**Total Contract Amount:** 5 U.S.C. § 552(b)(4)
Contract Period of Performance: July 27, 2020 through May 31, 2021	
Award Battelle hereby agrees to award this Contract to the Contractor subject to acceptance. The rights and obligations of the parties to this Contract are subject to and governed by this document and any documents attached or incorporated by reference.	**Contractor Agreement** Contractor accepts and agrees to furnish and deliver the items or perform services to the extent stated in this document for the consideration stated in this contract. The rights and obligations of the parties to this contract are subject to and governed by this document and any documents attached or incorporated by reference.

Battelle Memorial Institute Pacific Northwest Division	**Contractor shall sign and return a copy of this document**
Signature of person authorized to sign. Digitally signed by Amber A. Ames Date: 2020.08.27 15:38:32 -07'00'	**Signature of person authorized to sign**
Name Amber A. Ames	**Name**
Title Contracts Specialist	Title
Date	Date

IMPORTANT NOTE: Any domestic and foreign travel associated with this contract (including contractor travel within a country of presence) shall be approved in writing by the Battelle Contracts Representative in advance of travel arrangements being finalized. Without the advance approval of the Battelle Contracts Representative for any such travel, any invoiced costs related to such travel will not be paid.

Statement of Work

Contractor agrees to perform the scope outlined in the attached Statement of Work dated July 16, 2020.

Indirect Rates

The following indirect cost rates are hereby established until and unless changed by mutual agreement:

Category	Rate	Base	Type	Effective			
Indirect Costs	55.5%	On Campus Organized Research MTDC*	Provisional	From	07/01/2020	Through	Until amended

*Modified Total Direct Costs

Fringe Benefits: *The fringe benefits are specifically identified to each employee and are charged individually as direct costs.*

The provisional rate(s) specific above may be prospectively or retroactively revised by mutual agreement, at either Battelle or the Contractor's request, to prevent substantial overpayment.

Upon establishment/approval of finalized, or final rates, for any period consistent with the period of performance, the Contractor agrees to supply such approval to Battelle, within 30 days or receipt of approval from the cognizant agency.

Technical Oversight Representative

All technical questions should be directed to the Technical Oversight Representative, Pamela M. Kinsey at (509) 375-6848 or pamela.kinsey@pnnl.gov. The Technical Oversight Representative cannot modify this agreement.

Battelle Contracts Representative

All contractual questions should be directed to the Battelle Contracts Representative, Amber A. Ames at (509) 371-7050 or amber.ames@pnnl.gov.

Approval of Subcontracts

Subcontracts require the prior written approval of the Battelle Contracts Representative.

Contract Contents

In addition to this Schedule, the Contract consists of:

- Representations and Certifications dated July 27, 2020
- The General Provisions Applicable for Educational Institutions and Nonprofit Organizations, Form A-409.25-Ed/NP dated October 2019, apply and may be viewed at http://www.pnnl.gov/contracts/contractdocuments.aspx
- Precontract Cost Authorization Letter dated July 24, 2020
- Statement of Work dated July 16, 2020

Alterations to General Provisions

- **Insurance – Liability to Third Persons (cl. 378b – Mar 1996)** This clause is hereby deleted and replaced with:

  "Contractor is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."
- **Disputes (cl. 331-Nov 2014)** This clause is hereby deleted and replaced with the following: "Except as otherwise provided or agreed, any dispute relating to this contract which is not disposed of by agreement shall be decided by litigation in a court of competent jurisdiction upon filing of a legal action by the aggrieved party. During the pendency of any dispute, the Contractor shall proceed diligently with the performance of the contract and in accordance with the direction of Battelle."

- **Insurance Requirements (cl. 378 - April 2017)** This clause is hereby deleted and replaced with:

  "Contractor is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."
- **Laws and Regulations, DOE Directives, and Indemnification (cl. 3121 -Mar 2014)** Delete the word "indemnification" in the title and all of Section C."
- **FAR 52.227-3 Patent Indemnity (Apr 1984)** This clause is self-deleting because work being performed under this contract does not include the delivery of commercial items.
- **FAR 52.227-10 Filing of Patent Applications-Classified Subject Matter (DEC 2007)** This clause is self-deleting because this contract is not expected to result in a patent application containing classified subject matter.
- **FAR 52.246-5 Inspection Service - Cost Reimbursement (Apr 1984)** and **FAR 52.246-8 Inspection of Research and Development—Cost Reimbursement (May 2001)** are hereby deleted and replaced with **52.246-9 Inspection of Research and Development (Short Form) (Apr 1984)**.
- **DEAR 970.5229-1 State and Local Taxes (Dec 2000)** This clause is deleted.

Integration

This Contract contains the entire understanding between the parties, and there are no understandings or representations not set forth or incorporated by reference herein. No subsequent modifications of this Contract shall be of any force or effect unless in writing signed by the party claimed to be bound thereby. No communications, written or oral, by other than a Battelle Contracts Representative shall be effective to modify or otherwise affect the provisions of this Contract.

Statement of Work
How MERS-CoV Regulates Innate Immunity in Primary Human Lung Cells
University of North Carolina at Chapel Hill, Principal Investigator Timothy Sheahan
July 16, 2020

I. Background

The molecular mechanisms regulating emerging highly pathogenic human respiratory coronavirus pathogenesis are complex and include dampening of the host innate immune response allowing higher viral titers immediately following entry. Previous studies tracking the expression of interferon stimulated gene (ISG) expression in Middle East respiratory syndrome coronavirus (MERS-CoV) infected continuous human lung epithelial cells demonstrated that specific ISG expression patterns could be detected and these patterns could be used to determine how CoV were modulating the innate immune response. Epigenetic/chromatin remodeling mechanisms were found to be important regulators of host chromatin remodeling that altered host expression ISG patterns. This proposal will build on these foundational studies performed in continuous human lung cell lines and define ways that MERS-CoV regulates innate immunity in primary human lung fibroblasts and microvascular endothelial cells.

II. Scope

University of North Carolina at Chapel Hill will analyze the fibroblast ChIP PCR samples collected in 2019 and discuss data with PNNL to determine next steps. University of North Carolina at Chapel Hill will perform ChIP Seq analysis of MERS-CoV infected microvascular endothelial cells at a single time point for three donors. University of North Carolina at Chapel Hill will perform BioRad Primer PCR Pathway Arrays on MERS-CoV infected microvascular endothelial cells and fibroblasts. Drs Sheahan and Schaefer will work in close collaboration with PNNL to analyze datasets to determine how MERS-CoV regulates ISG expression in human lung microvascular endothelial cells and fibroblasts.

III. Deliverables

- Evaluate project results and direction, in collaboration with PNNL
- Collaborate on experiment direction and identify alternatives for experiments
- Participate in meetings to discuss project status/progress, findings, and trouble shoot as needed
- Write and submit progress report and manuscript draft in collaboration with PNNL

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 8/31/2020 1:44:46 PM (UTC-07:00)
To: Dinnon, Kenneth Harold[kdinnon@email.unc.edu]
Subject: CONGRATULATIONS!!

Dude,

A Nature paper is totally amazing! I've been wondering how you are doing and I am terribly sorry I haven't checked in with you before now. I suspect you were too busy to care.

What are your plans for the future? I would love to hear how things are going and I hope you and your family are doing well!

Miss talking to you! Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 8/31/2020 1:46:29 PM (UTC-07:00)
To: Fritch, Ethan James[ejfritch@email.unc.edu]
Subject: How goes life?

Hi Ethan,

How the heck are you? I can't imagine how busy life has been for you guys and I really hope you and your family are doing well.

Is there anything I can do from afar to help you? I would love to read any paper drafts you may have in the works!

I would love to hear how it's going you have a few minutes! Thanks, Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 9/1/2020 11:02:07 AM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]
Subject: FW: Adding NL63?

Hi Ben,

Just wanted to make sure you saw this! Thank you, Amy

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Thursday, August 20, 2020 at 9:34 AM
To: "McGlaughon, Ben" <benmcg@email.unc.edu>
Cc: "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: Adding NL63?

Ben,

I hope you are doing well and transitioning to working in the Baric laboratory in the weirdness of the pandemic.

Can you please talk to Ralph about adding human coronavirus NL63 to our existing MTA?

I would like both the current wild type strain (should contain a point mutation in spike following tissue culture adaptation) and the virus expressing green fluorescent protein GFP. Sarah Leist should have stocks of these at BSL2.

I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Tue 9/1/2020 11:06:26 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Adding NL63?

I swore yesterday that I had an email from you last week that I hadn't responded to, but then I searched your name but nothing came up. I will bring this up with him when I meet with him Thursday, I can't imagine he'll have any issue with adding the NL63 viruses.

I can probably start shipping stuff next week if that works for you. I need to look back at all the virus you're requesting and start tracking it down.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, September 1, 2020 2:02 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: FW: Adding NL63?

Hi Ben,

Just wanted to make sure you saw this! Thank you, Amy

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Thank you very much, Amy

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Tue 9/1/2020 11:07:22 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Adding NL63?

Oh, he already confirmed. Sorry, hard to keep track of everything these days. I'll submit a request to amend the MTA.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, September 1, 2020 2:02 PM
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I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Tue 9/1/2020 11:10:38 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Adding NL63?

- wild type infectious clone derived Middle East Respiratory syndrome coronavirus (MERS-CoV)
- MERS-CoV expressing the red fluorescent protein gene
- MERS-CoV expressing the nanoluciferase protein gene
- MERS-CoV delta open reading frame 3 to 5 (MERS-CoV delta 3-5)
- Wild type infectious clone derived severe acute respiratory syndrome coronavirus 2002-2003 outbreak** select agent (SARS-CoV)
- Wild type infectious clone derived SARS-CoV 2
- SARS-CoV 2 expressing the green fluorescent protein gene
- SARS-CoV 2 expressing the nanoluciferase protein gene

Is this still the full list? Plus the NL63?

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, September 1, 2020 2:02 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: FW: Adding NL63?

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Thank you very much, Amy

From: Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]
Sent: Tue 9/1/2020 11:48:29 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: CONGRATULATIONS!!

Hey Amy!

It has been far too long. But that's the result of 2020 being a totally crazy year. I still feel like it could've been fall of 2019 last week with you still here. I am struggling every time I realize that it is already September…

Thanks for the congrats! It has been a crazy year (in every way as I am sure you know). But lab has been insane. Both in all the best ways and some of the worst. We have been crazy busy and productive, which has been a mix of feeling super motivated and exhausted. But a Nature paper (and pathogenic 'MA10' paper in Cell to follow! Just got to finish final edits and get back to the editor this week) has definitely made things worth it. And while I was over working myself in lab, it is not like I was missing out on socializing as everyone else was stuck home and bored out of their minds. Didn't have that problem here in the Baric lab…

Future plans are still unclear. Still aiming to graduate next spring/summer, only holding on by my stubbornness to finish up each project and not leave them abandoned. But I also feel like it is silly to leave the Baric lab right now when every other virology lab in the world is doing coronavirus work. So hopefully things calm down by next fall and I can find a good postdoc with a slight change of research focus. I am not opposed to staying with CoVs, but I am thinking I want to bring my expertise to a truly molecular lab and try to do some more detailed mechanistic stuff.

How are things with you and the Sims lab?!?

My next week is looking generally light if you have an hour or two for a call to catch up?

KD3

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Monday, August 31, 2020 at 4:44 PM
To: "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu>
Subject: CONGRATULATIONS!!

Dude,

A Nature paper is totally amazing! I've been wondering how you are doing and I am terribly sorry I haven't checked in with you before now. I suspect you were too busy to care.

What are your plans for the future? I would love to hear how things are going and I hope you and your family are doing well!

Miss talking to you! Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 9/2/2020 8:28:13 AM (UTC-07:00)
To: Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]
Subject: Re: CONGRATULATIONS!!

Hi Kenny!

It is so very good to hear from you! I miss getting to see you every other week to catch up and hear how it's going!

I can make next week work for sure. How about Wednesday, September 9th from 1 to 3pm eastern?? That should be 10am to noon on my end and will work nicely.

I am going to send you a calendar invitation (as that's how we roll here at the national laboratory) so its on my calendar but if that time is bad please let me know and it is easy enough to reschedule.

I hadn't thought about this being a crappy time to be a postdoc if you want to branch out from the 'rona virus!

So good to hear from you and congratulations again on the awesome publications.

Thank you! Amy

From: "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu>
Date: Tuesday, September 1, 2020 at 11:50 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: CONGRATULATIONS!!

Hey Amy!

It has been far too long. But that's the result of 2020 being a totally crazy year. I still feel like it could've been fall of 2019 last week with you still here. I am struggling every time I realize that it is already September…

Thanks for the congrats! It has been a crazy year (in every way as I am sure you know). But lab has been insane. Both in all the best ways and some of the worst. We have been crazy busy and productive, which has been a mix of feeling super motivated and exhausted. But a Nature paper (and pathogenic 'MA10' paper in Cell to follow! Just got to finish final edits and get back to the editor this week) has definitely made things worth it. And while I was over working myself in lab, it is not like I was missing out on socializing as everyone else was stuck home and bored out of their minds. Didn't have that problem here in the Baric lab…

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From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 9/2/2020 8:29:50 AM (UTC-07:00)
To: Dinnon, Kenneth Harold[kdinnon@email.unc.edu]
Subject: SECOND EMAIL FW: CONGRATULATIONS!!

Amy is losing her mind. Same time of day but on Friday the 11th instead!! That would be 1pm to 3pm eastern.

Thanks, Amy

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Wednesday, September 2, 2020 at 8:28 AM
To: "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu>
Subject: Re: CONGRATULATIONS!!

Hi Kenny!

It is so very good to hear from you! I miss getting to see you every other week to catch up and hear how it's going!

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I hadn't thought about this being a crappy time to be a postdoc if you want to branch out from the 'rona virus!

So good to hear from you and congratulations again on the awesome publications.

Thank you! Amy

From: "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu>
Date: Tuesday, September 1, 2020 at 11:50 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: CONGRATULATIONS!!

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Miss talking to you! Amy

From:	Sims, Amy C[amy.sims@pnnl.gov]
Attendees:	Dinnon, Kenneth Harold
Location:	Microsoft Teams Meeting
Subject:	Catch up with Kenny
Importance:	Normal
Start Time:	Fri 9/11/2020 10:00:00 AM (UTC-07:00)
End Time:	Fri 9/11/2020 12:00:00 PM (UTC-07:00)
Required Attendees:	Dinnon, Kenneth Harold

From: Sims, Amy C[amy.sims@pnnl.gov]
Attendees: Dinnon, Kenneth Harold
Location: Microsoft Teams Meeting
Subject: Catch up with Kenny
Importance: Normal
Start Time: Fri 9/11/2020 10:00:00 AM (UTC-07:00)
End Time: Fri 9/11/2020 12:00:00 PM (UTC-07:00)
Required Attendees: Dinnon, Kenneth Harold

Hi Kenny,

Let me know if this will work. Thank you! Looking forward to it! Amy

---

Join Microsoft Teams Meeting

+1 509-408-1681 United States, Spokane (Toll)

Conference ID: 866 278 423#

Local numbers | Reset PIN | Learn more about Teams | Meeting options

---

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 9/2/2020 8:37:05 AM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]
Cc: Baric, Ralph S[rbaric@email.unc.edu]
Subject: Re: Adding NL63?

Hi Ben,

Yes this is still the list. Please add both the wild type NL63 plus spike point mutation and NL63 expressing GFP to the MTA. I appreciate it.

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The BL3 strains will have to be shipped in a couple of different shipments and will need to go to the lab in Seattle which will require more coordination especially for the select agent transfer of the 2003 strain of SARS-CoV.

We can discuss this further once we can agree on shipping dates. Thank you very much. Amy

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From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, September 1, 2020 at 11:12 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Adding NL63?

- wild type infectious clone derived Middle East Respiratory syndrome coronavirus (MERS-CoV)
- MERS-CoV expressing the red fluorescent protein gene
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- MERS-CoV delta open reading frame 3 to 5 (MERS-CoV delta 3-5)
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- Wild type infectious clone derived SARS-CoV 2
- SARS-CoV 2 expressing the green fluorescent protein gene
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Is this still the full list? Plus the NL63?

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, September 1, 2020 2:02 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: FW: Adding NL63?

Hi Ben,

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From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Thursday, August 20, 2020 at 9:34 AM
To: "McGlaughon, Ben" <benmcg@email.unc.edu>

Cc: "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: Adding NL63?

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Thank you very much, Amy

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Wed 9/2/2020 9:25:18 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Adding NL63?

Amy,

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I will also submit a request to amend the MTA right now, to add the NL63 viruses.

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Thank you very much, Amy

From: Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]
Sent: Wed 9/2/2020 9:27:14 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: SECOND EMAIL FW: CONGRATULATIONS!!

That works for me!

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Wednesday, September 2, 2020 at 11:29 AM
To: "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu>
Subject: SECOND EMAIL FW: CONGRATULATIONS!!

Amy is losing her mind. Same time of day but on Friday the 11th instead!! That would be 1pm to 3pm eastern.

Thanks, Amy

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Wednesday, September 2, 2020 at 8:28 AM
To: "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu>
Subject: Re: CONGRATULATIONS!!

Hi Kenny!

It is so very good to hear from you! I miss getting to see you every other week to catch up and hear how it's going!

I can make next week work for sure. How about Wednesday, September 9th from 1 to 3pm eastern?? That should be 10am to noon on my end and will work nicely.

I am going to send you a calendar invitation (as that's how we roll here at the national laboratory) so its on my calendar but if that time is bad please let me know and it is easy enough to reschedule.

I hadn't thought about this being a crappy time to be a postdoc if you want to branch out from the 'rona virus!

So good to hear from you and congratulations again on the awesome publications.

Thank you! Amy

From: "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu>
Date: Tuesday, September 1, 2020 at 11:50 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: CONGRATULATIONS!!

Hey Amy!

It has been far too long. But that's the result of 2020 being a totally crazy year. I still feel like it could've been fall of 2019 last week with you still here. I am struggling every time I realize that it is already September…

Thanks for the congrats! It has been a crazy year (in every way as I am sure you know). But lab has been insane. Both in all the best ways and some of the worst. We have been crazy busy and productive, which has been a mix of feeling super motivated and exhausted. But a Nature paper (and pathogenic 'MA10' paper in Cell to follow! Just got to finish

final edits and get back to the editor this week) has definitely made things worth it. And while I was over working myself in lab, it is not like I was missing out on socializing as everyone else was stuck home and bored out of their minds. Didn't have that problem here in the Baric lab…

Future plans are still unclear. Still aiming to graduate next spring/summer, only holding on by my stubbornness to finish up each project and not leave them abandoned. But I also feel like it is silly to leave the Baric lab right now when every other virology lab in the world is doing coronavirus work. So hopefully things calm down by next fall and I can find a good postdoc with a slight change of research focus. I am not opposed to staying with CoVs, but I am thinking I want to bring my expertise to a truly molecular lab and try to do some more detailed mechanistic stuff.

How are things with you and the Sims lab?!?

My next week is looking generally light if you have an hour or two for a call to catch up?

KD3

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Monday, August 31, 2020 at 4:44 PM
To: "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu>
Subject: CONGRATULATIONS!!

Dude,

A Nature paper is totally amazing! I've been wondering how you are doing and I am terribly sorry I haven't checked in with you before now. I suspect you were too busy to care.

What are your plans for the future? I would love to hear how things are going and I hope you and your family are doing well!

Miss talking to you! Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Wed 9/2/2020 9:31:21 AM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]
Subject: Re: Adding NL63?

Sounds great. Sarah Leist should have stocks of both of the NL63 viruses and she already knows you will be asking for them.

Thank you, Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Wednesday, September 2, 2020 at 9:26 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Adding NL63?

Amy,

I just sent an email to Boyd, Tim, and Lisa to start getting an idea of the availability of these viruses and when we could realistically expect to have them ready to ship. I will keep you updated.

I've been sending out the SARS2 viruses non-stop so those will be easy. And I just sent some NL63-GFP today, so I can definitely get that one sent easily and soon. Assuming I can track down the spike point mutation version, I'll aim to send the two NL63 viruses the week of Sept 14th.

I will also submit a request to amend the MTA right now, to add the NL63 viruses.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, September 2, 2020 11:37 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Cc: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Re: Adding NL63?

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We can discuss this further once we can agree on shipping dates. Thank you very much. Amy

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Is this still the full list? Plus the NL63?

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, September 1, 2020 2:02 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: FW: Adding NL63?

Hi Ben,

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From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Thursday, August 20, 2020 at 9:34 AM
To: "McGlaughon, Ben" <benmcg@email.unc.edu>
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Subject: Adding NL63?

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I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Wed 9/2/2020 9:37:21 AM (UTC-07:00)
To: UNC Office of Tech Dev MTA[mta@unc.edu]
Cc: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Amendment to MO-16244

Nate,

I'd like to amend MO-16244 to add a couple more viruses, if possible. I have copied Amy Sims who should be able to coordinate on behalf of the recipients.

We would like to add:

- wild type human coronavirus NL63 plus spike point mutation
- human coronavirus NL63 expressing GFP

Let me know if you need any further information from me. Thanks!

Ben

Ben McGlaughon, MS
Baric Lab Manager | UNC-Chapel Hill
(919) 966-7991
benmcg@unc.edu

From: Fritch, Ethan James[ejfritch@email.unc.edu]
Sent: Wed 9/2/2020 1:53:47 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: How goes life?

Amy,

Thanks for reaching out! Things have been super busy as you can imagine, I've been working on some SARS2 stuff, but I'm hoping to finish up one or two more experiments and then will have enough data to put together a paper together and pivot back towards my one MERS project that is almost finished. Once I do have a draft going I'll be sure to send it along to you since it's mostly kinome related things which you were involved in in the beginning and will definitely appreciate your input.

If you want to chat over the phone and catch up I should have some time next week, no pressure though as I'm sure you're equally as busy!

Best,

Ethan J. Fritch
(570) 294-4249
PhD Candidate | Baric Laboratory
Department of Microbiology and Immunology
University of North Carolina at Chapel Hill

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, August 31, 2020 4:46 PM
To: Fritch, Ethan James <ejfritch@email.unc.edu>
Subject: How goes life?

Hi Ethan,

How the heck are you? I can't imagine how busy life has been for you guys and I really hope you and your family are doing well.

Is there anything I can do from afar to help you? I would love to read any paper drafts you may have in the works!

I would love to hear how it's going you have a few minutes! Thanks, Amy

From: UNC Office of Tech Dev MTA[mta@unc.edu]
Sent: Thur 9/3/2020 9:01:17 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Cc: McGlaughon, Ben[benmcg@email.unc.edu]; UNC Office of Tech Dev MTA[mta@unc.edu]
Subject: RE: Amendment to MO-16244
Attachment: AMDMO-16244 BARIC UNC-PNNL AMD 1 Draft.docx
Attachment: MO-16244 BARIC UNC-PNL MTA FE.pdf

Thanks, Ben.

Amy, please find attached a draft amendment that adds the below mentioned material to the original MTA. Let me know there are any questions or if PNNL requests any revisions.

Thanks,
Nate

Nathan Whitman, PhD
Licensing Fellow

THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
INNOVATION, ENTREPRENEURSHIP AND ECONOMIC DEVELOPMENT – INNOVATE CAROLINA
Office of Technology Commercialization
Campus Box 4105
109 Church Street | Chapel Hill, NC 27516
T: 919.962.6369 | F: 919.962.0646
Email: nathan.whitman@unc.edu | Twitter: @innovateunc | Facebook: @InnovateUNC
Web: otc.unc.edu | innovate.unc.edu

From: McGlaughon, Ben <benmcg@email.unc.edu>
Sent: Wednesday, September 2, 2020 12:37 PM
To: UNC Office of Tech Dev MTA <mta@unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>
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Baric Lab Manager | UNC-Chapel Hill
(919) 966-7991
benmcg@unc.edu

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 9/3/2020 8:01:52 PM (UTC-07:00)
To: Fritch, Ethan James[ejfritch@email.unc.edu]
Subject: Re: How goes life?

Hi,

Sorry. This has been one of those weeks. This whole month will be pretty nutty.

I can chat at 11:30am eastern on Friday the 11th for an hour and a half if that works for you.

Otherwise I might need to push back until the week of the 14th. Let me know what is better for you.

Looking forward to catching up!! Amy

Get Outlook for iOS

From: Fritch, Ethan James <ejfritch@email.unc.edu>
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To: Sims, Amy C
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From: Fritch, Ethan James[ejfritch@email.unc.edu]
Sent: Sat 9/5/2020 12:48:06 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: How goes life?

You're totally fine, it was one of those weeks for me as well. I can do Friday at 11:30 if you're still free, if not, the week after works for me as well.

Ethan J. Fritch
(570) 294-4249
PhD Candidate | Baric Laboratory
Department of Microbiology and Immunology
University of North Carolina at Chapel Hill

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, September 3, 2020 11:01 PM
To: Fritch, Ethan James <ejfritch@email.unc.edu>
Subject: Re: How goes life?

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Sent: Wednesday, September 2, 2020 1:54 PM
To: Sims, Amy C
Subject: Re: How goes life?

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PhD Candidate | Baric Laboratory
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To: Fritch, Ethan James <ejfritch@email.unc.edu>
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From: Lu, Lu[llu@uthsc.edu]

Sent: Sun 9/6/2020 5:35:23 PM (UTC-07:00)

To: Silke Bergmann[silke.bergmann@gmx.net]; Sims, Amy C[amy.sims@pnnl.gov]; Ashbrook, David[dashbroo@uthsc.edu]; Baric, Ralph S[rbaric@email.unc.edu]; Cui, Yan[ycui2@uthsc.edu]; Jonsson, Colleen Beth[cjonsson@uthsc.edu]

Cc: Williams, Robert W[rwilli10@uthsc.edu]; Klaus Schughart[klaus.schughart@helmholtz-hzi.de]; Xu, Fuyi[fxu10@uthsc.edu]; Li, Kui[kli1@uthsc.edu]; JUN GAO[(b) (6) gmail.com]

Subject: Ace2

Attachment: Ace2_V19_082820.docx

Dear all authors:
Here is the revised version of Ace2 paper based on new analysis and some of new data. We plan to submit it at coming week. Please review it and feel free to edit, and send it back to me before end of September 10 if you has modification. Thanks.

Lu Lu
Professor
Department of Genetics, Genomics and Informatics
University of Tennessee Health Science Center
71 S. Manassas St., Room 410K
Memphis, TN 38163
Tel: (901) 448-7557 (O)
Fax: (901) 448-3500 (Dept)

Genetic Dissection of the Regulatory Mechanisms of *Ace2* in the Infected Mouse Lung

Fuyi Xu[1#], Jun Gao[1, 5#], Silke Bergman[4], Amy C. Sims[7, 9], David G. Ashbrook[1], Ralph S. Baric[6,7, 8], Yan Cui[1], Colleen B Jonsson[4], Kui Li[4], Robert W. Williams[1*], Klaus Schughart[2, 3, 4*], and Lu Lu[1*]

[1]Department of Genetics, Genomics, and Informatics, University of Tennessee Health Science Center, Memphis, TN, USA;

[2]Department of Infection Genetics, Helmholtz Centre for Infection Research, Braunschweig, Germany

[3]University of Veterinary Medicine Hannover, Hannover, Germany;

[4]Department of Microbiology, Immunology, and Biochemistry, University of Tennessee Health Science Center, Memphis, TN, USA;

[5]Institute of Animal Husbandry and Veterinary Science, Shanghai Academy of Agricultural Sciences, Shanghai, China.

[6]Department of Microbiology and Immunology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA;

[7]Department of Genetics, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA;

[8]Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA;

[9]present address: Pacific Northwest National Laboratory in Richland, WA, USA

[#] These authors contributed equally to this work.

* Correspondence:
Lu Lu: llu@uthsc.edu
Department of Genetics, Genomics and Informatics
University of Tennessee Health Science Center
Memphis, TN 38163, United States

Klaus Schughart: klaus.schughart@helmholtz-hzi.de
Department of Infection Genetics
Helmholtz Centre for Infection Research
Braunschweig, Germany

Robert W. Williams: rwilliams@uthsc.edu
Department of Genetics, Genomics and Informatics
University of Tennessee Health Science Center
Memphis, TN 38163, United States

Abstract

Acute lung injury (ALI) is an important cause of morbidity and mortality after viral infections, including influenza A virus H1N1, SARS-CoV, MERS-CoV, and SARS-CoV-2. The angiotensin 1 converting enzyme 2 (ACE2) is a key host membrane-bound protein that modulates ALI induced by viral infection, pulmonary acid aspiration, and sepsis. However, the contributions of *ACE2* sequence variants to individual differences in disease risk and severity after viral infection are not understood. In this study, we quantified H1N1 influenza-infected lung transcriptomes across a family of 41 BXD recombinant inbred strains of mice and both parents—C57BL/6J and DBA/2J. In response to infection *Ace2* mRNA levels decreased significantly across all family members and the extent of decline was associated with disease severity including body weight loss and survival times. Pulmonry RNA-seq for 43 lines were analyzed using weighted gene co-expression network analysis (WGCNA) and Bayesian network approaches. *Ace2* not only participated in virus-induced ALI by interacting with TNF, MAPK, and NOTCH signaling pathways, but was also linked with high confidence to gene products that have important functions in the pulmonary epithelium, including *Rnf128*, *Muc5b*, and *Tmprss2* and others. Comparable sets of transcripts were also highlighted in parallel studies of human SARS-CoV-infected primary human airway epithelial cells. Using conventional mapping methods, we determined that weight loss at two and three days after viral infection maps to chromosome X—the location of *Ace2*. This finding motivated the hierarchical Bayesian network analysis, which defined molecular endophenotypes of lung infection linked to *Ace2* expression and to a key disease outcome. Core members of this Bayesian network include *Ace2, Atf4*, *Csf2*, *Cxcl2*, *Lif, Maml3*, *Muc5b*, *Reg3g*, *Ripk3*, and *Traf3*. Collectively, these findings define a causally-rooted *Ace2* modulatory network relevant to host response to viral infection and identify potential therapeutic targets for virus-induced respiratory diseases, including those caused by influenza and coronaviruses.

Key words: H1N1, acute lung injury, BXD family, *Ace2,* host response, viremia network

Introduction

Five major influenza A virus (IAV) pandemics have swept through human populations in the last 130 years—the 1890 H3N8 pandemic, the devastating 1918 H1N1 pandemic [1], and serious global outbreaks in 1957 (H2N2), 1968 (H3N2), and the 2009 H1N1 swine influenza. The current COVID-19 pandemic is caused by a novel coronavirus, termed severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2). This pathogen has spread with unprecedent speed and efficiency from an initial outbreak in November or December 2019.

The primary pathological features of the influenza A outbreaks and both the 2002 SARS and current COVID-19 outbreaks are viral pneumonia and acute lung injury (ALI) [2]. The well documented symptoms of influenza A (H1N1) and COVID-19 have substantial overlap. For both viral pathogens, infected humans can have symptoms ranging from mild coughing, congestion, and fever, to severe and lethal pulmonary edema and disseminating diseases of other organs. Individual host genetic differences almost certainly play an important role in the development and severity of the illness and its time course [3-7].

The human angiotensin 1 converting enzyme 2 (ACE2) is a cell membrane carboxypeptidase and negative modulator of the renin angiotensin system (RAS). This protein also has a key role in ciliary function in epithelial cells and is the principal receptor bound by spike proteins of SARS-CoV [8, 9] and SARS-CoV-2 [10]. *ACE2* is highly expressed in nasal cavity epithelial cells, especially on apical cilia of small airway cells and in alveolar epithelial type II cells (AT2) [11, 12].

Paradoxically, while serving as a key node in cellular entry of SARS-CoV and SARS-CoV-2 virions, ACE2 also protects against lung disease in animal models [13]. For example, treatment with recombinant human ACE2 protects against acute lung failure induced by acid aspiration or sepsis in *Ace2* knockout mice as well as in wild-type controls [14]. Of note, *Ace2* expression in mouse lungs is downregulated following SARS-CoV infection. The spike protein alone induces ACE2 downregulation in cell culture and enhances the severity of ALI induced by acid aspiration in wildtype mice [8]. In contrast, viral spike protein is unable to affect the severity of lung failure in *Ace2* knockout animals, indicating the effect of spike protein on acid-induced ALI is ACE2 specific [8]. Interestingly, expression of ACE2 is also significantly downregulated by IAVs in infected cell cultures, although in this case ACE2 is dispensable for viral entry and replication [15]. In mice, *Ace2* deficiency is associated with aggravated ALI induced by IAV H7N9 or

respiratory syncytial virus [16, 17]. The precise mechanism underlying these findings is unclear, as is how alterations in ACE2 expression modulate the severity of pulmonary disease inflicted by coronaviruses and other IAV subtypes.

Expression of *ACE2* in human lung has an impressive level of variation among healthy humans. In the GTEx RNA-seq transcriptome survey [18], the maximum range of expression in the lung is about 22-fold, the interquartile range is 1.8-fold, and the coefficient of variation (standard deviation/mean) is high—nearly 0.6 (genenetwork.org/show_trait?trait_id=ENSG00000130234 &dataset=GTEXv8_Lung_tpm_0220). Given this finding, it is possible, even likely, that there are marked genetic differences in host susceptibility that are a function of numbers or ratios of ACE2-positive AT2 cells and epithelial cells in lung [11] or the level expression by these cells of *ACE2*. However, we emphasize that causal linkage between genetic variation in *ACE2* and to susceptibility or progress of infection is still poorly defined in humans, or even in mouse models.

Susceptibility to IAV, such as H1N1 and H7N7 influenza infections, varies greatly among strains of mice [19], and especially between the two key inbred strains we use here—C57BL/6J (B6), the reference strain for most genetic and molecular studies—and DBA/2J (D2), the oldest inbred strain of mice [20]. B6 is relatively resistant to IAV and often survives infection. In contrast, D2 loses body weight rapidly, and at the same inoculum dose as given to B6 dies within 5–7 days. Our laboratory has generated and maintains approximately 120 BXD recombinant inbred (RI) strains derived from crosses between B6 and D2 parents. Collectively, this family of RI strains segregates for ~6 million variants with minor allele frequencies above 0.3 [21], making it an ideal reference population to model genetic variation in susceptibility to IAV infections [22]. Indeed, in previous genetic mapping using the BXD family we have defined loci and even cloned gene variants that control the host response to IAV (H1N1) infection [23] and to other infectious diseases [24-27]. Here we have analyzed the lung transcriptome of 41 members of the family and both parental strains after infection with IAV (H1N1). We define patterns of covariation of RNA-seq data with induced variation in *Ace2* expression, as well as with outcome measures and with key molecular networks and endophenotypes likely to contribute to host defense and pathologies of H1N1 and possibly to SARS-CoV-induced ALI.

Materials and methods

Mice

We used females from 41 BXD RI strains and both parental strains—B6 and D2. Mice were between 8 and 12 weeks of age when infected. They were housed and maintained on a 12:12 light/ dark cycle, with *ad libitum* access to food and water.

Ethics

Protocols for the mouse experiments were approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Tennessee Health Science Center (UTHSC).

Virus

Original stocks of mouse-adapted A/Puerto Rico/8/34 (H1N1, PR8M) virus were obtained from Stefan Ludwig, University of Münster [28]. Virus stocks were propagated in the chorioallantoic cavity of 10-day-old pathogen-free embryonated chicken eggs for 48 h at 37 °C as described previously [29]. Viral titer was determined using a focus-forming unit (FFU) assay as described previously [29].

Infection of mice

Animals were anesthetized by intraperitoneal injection of ketamine/xylazine (10 % (v/v) of 100 mg/ml ketamine and 5 % (v/v) of 20 mg/ml xylazine in 0.9 % (w/v) NaCl with a dose adjusted to body weight (200 µl/20 g body weight). Infection was performed by intranasal application of virus solution in 20 µl sterile phosphate-buffered saline (PBS), with a PR8M dosage of 2×10^3 FFU. Mice were bred and infected at the animal facilities at UTHSC.

RNA isolation and sequencing

Mice were sacrificed three days post-infection (dpi) and both lungs were extracted and transferred immediately to RNAlater (Qiagen), stored at 4 °C for one day, and then stored at –20 °C. RNA was isolated using Qiagen Midi kit [30]. RNA quality was evaluated on a 2100 Bioanalyzer (Agilent). Five-hundred nanograms of total RNA was used to prepare libraries for sequencing using the Lexogen SENSE RNA-seq library kit for Ion Torrent. Libraries were amplified for 11 cycles as the final step of library preparation. Before sequencing, 1 µl aliquots were pooled and sequenced on an Ion Torrent PGM 314 chip. Barcoded data from the PGM was used to balance the final pool before sequencing. Library pools were sized to ~260 bp on a Pippin Prep instrument using 2% Pippin agarose gel. The sized libraries were evaluated on an Agilent High Sensitivity chip, quantified using real-time PCR, and used to prepare beads using a One-Touch 2 device. Beads were sequenced on an Ion Torrent Proton P1 chip. On average, 67 million reads were obtained per strain.

Read mapping and gene expression quantification

RNA-seq reads were quality-trimmed using Trim Galore [31] and mapped to the mm10 reference genome or to the influenza A virus PR8M genome using STAR [32]. Counts were summarized at the gene level using the R-package *Rsubread* [33], normalized and log transformed using the R-package *DESeq2* [34], and batch-corrected using the *ComBat* function of the R-package *sva* [35,

36]. For annotations of genes, ENTREZID from *Rsubread* were matched to RefSeq annotations using R-package *biomart* [37].

Heritability estimates for *Ace2*

Heritability of *Ace2* gene expression was estimated with GEMMA [38] using the following formula. This approach estimates the proportion of variance that can be explained (PVE) by genotypes converging nearly the whole genome:

$$\mathrm{PVE}(\boldsymbol{\beta}, \mathbf{u}, \tau) := \frac{\mathrm{V}(\mathbf{X}\boldsymbol{\beta} + \mathbf{u})}{\mathrm{V}(\mathbf{X}\boldsymbol{\beta} + \mathbf{u}) + \tau^{-1}}$$

Where "Xβ" is the sparse effects, "u" is the random effects, and "τ^{-1}" is the variance of the residual errors. GEMMA uses a Markov chain Monte Carlo method to estimate β, and u. We used the BXD genotype file generated at on January 2017 (www.genenetwork.org/webqtl/main.py?FormID=sharinginfo&GN_AccessionId=600) and *Ace2* gene expression values across the 41 BXD family as input.

Correlation analysis

The correlation analysis in this study, including gene-gene and gene-phenotype rely on Pearson correlation coefficients [38]. We reviewed data to ensure that outliers and distributional anomalies did not compromise downstream analyses.

Weighted gene co-expression network analysis (WGCNA)

WGCNA is a method that defines modules of co-expression, and that is often used to explore the associations between variation in mRNA levels and phenotypes of interest. It can be used to define hub genes and clusters in molecular and genetic networks. In this study, gene co-expression networks were constructed using the *WGCNA package* [39] following standard methods (https://horvath.genetics.ucla.edu/html/CoexpressionNetwork/Rpackages/WGCNA/Tutorials/). Modules were generated using the subset of 5500 H1N1-infected lung mRNAs that covaried well with *Ace2* expression (Pearson *r*) at a nominal $p < 0.05$. We used the standard WGCNA beta weighting parameter of 8 to achieve close to a scale-free distribution.

Gene set enrichment analysis

To understand the biological function and clusters detected as *Ace2* covariates and WGCNA modules, we compared set membership to Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways and to the mammalian phenotype ontology (MPO) using WebGestalt (http://www.webgestalt.org) [40]. This analysis uses a hypergeometric statistic test to generate adjusted *p* values and enrichment ratios. In this analysis, we used only protein coding genes as the reference background and a threshold minimum of five genes/transcripts per category.

Quantitative trait loci (QTLs) mapping

QTLs define chromosomal regions that contribute to genetic variation in levels of gene expresssion, endophenotypes and higher order outcome variables such as body weight loss and survival after infection. QTL mapping exploited methods in our GeneNetwork (www.genenetwork.org) [41, 42]. Linkage statistics were computed initially using Haley-Knott equations [43], and genome-wide significance levels were estimated from 2000 permutations of trait values. We used the new BXD genotype file of January 2017 (Ashbrook et al, bioRxiv, 2019). Those traits associated with significant and suggestive QTLs or expression QTLs (eQTLs) using the Haley and Knott regression were validated using GEMMA [44]. GEMMA uses a linear mixed model mapping algorithm that accounts for complex kinship among strain genometypes.

Genetic variations between B6 and D2

Sequence differences segregating among BXDs are taken from our previous work [45]. Here, we focus exclusively on protein-coding variants—nonsense, missense, and frameshift mutations.

Bayesian network construction

The Bayesian Network Webserver (BNW, compbio.uthsc.edu/BNW) [46-48] was used to create and evaluate plausible causal models among genes, transcripts, and outcome measures. The 100 highest scoring networks were used for model averaging, and those directed edges—unidirectional connections between nodes—with posterior probabilities greater than 0.8 were retained in the final model. We constrained each node to have at most four direct parents. We assigned nodes into one of three tiers of the Bayesian network: 1) SNP variant within selected QTL, 2) mRNA expression traits in a molecular endophenotype tier, and 3) the disease outcome measures—*Body Weight Loss* in the third tier. We allowed causal connections going from the first to second, and from second to the third tiers.

RNA-seq time-course data for H1N1 infection of the parental strains

Lung RNA-seq data was generated previously in our laboratory [20]. In brief, the two parental strains, B6 and D2, were infected with the H1N1 virus at 10–12 weeks of age as described above. RNA was isolated from lungs of B6 at 1, 3, 5, 8, and 14 dpi and from lungs of D2 at 1, 3, and 5 dpi. Three RNA samples per strain and per time point were used for library preparation and sequencing. Raw counts were extracted, normalized, and log2 transformed with *DEseq2* [34] after adding 1 to all raw counts. In this study, we extracted the *Ace2* expression levels from this dataset. We also performed differential expression analysis of mice at 3 dpi and their mock treated controls using *DESeq2* [34] using strain as a covariate. The resulting p values were adjusted using the Benjamini and Hochberg's approach [49] and are referred throughout this paper as adj. p. values. We reported transcripts with adj.$p < 0.05$, and fold change (FC) > 1.3 as differentially

expressed genes (DEGs). This data set was also used for evaluating the gene expression patterns post-infection.

Transcriptome data for SARS-CoV infected primary human airway epithelial (HAE) cells

The experimental details for this study are described in Ref. [50]. In brief, human tracheobronchial epithelial cells were resected from airway specimens of patients undergoing surgery. Primary cells were expanded to generate passage-1 cells, and passage-2 cells were plated at a density of 2.5×10^5 cells per well. Human airway epithelium (HAE) cultures were generated by provision of an air-liquid interface for 6 to 8 weeks to form well-differentiated, polarized cultures. Wild-type infectious clone-derived SARS-CoV (icSARS-CoV) and ic-SARS-CoV ORF6 were derived from infectious clone constructs as described [50]. Bat-SARS-CoV is comprised of the HKU3 backbone and SARS-CoV receptor binding domain and was derived from an infectious clone as described in [51]. Triplicate cultures were infected with a multiplicity of infection 3 (MOI 3) icSARS-CoV, and icSARS-CoV ORF6 on the apical surface. Total RNA was isolated from infected cells, and equivalent amounts of RNA from three biological replicates from each condition were pooled. Transcriptome profiling was performed using Agilent 4x44K whole human gene expression arrays. Raw data were downloaded from GEO (GSE47963_series_matrix.txt.gz). Expression values were normalized and sample descriptions quality controlled. A strong batch effect with respect to the donor from which HAE were derived was corrected using the R package *sva* [35, 36]. Rows with no gene description were deleted. Differentially expressed genes were determined using the R package *Limma* [52].

Data availability

The RNA-seq data from infected BXD strains has been deposited at GeneNetwork.org under the accession ID GN807. The summarized RNA-seq data as entered in GN can be accessed and downloaded at www.genenetwork.org/webqtl/main.py?FormID=sharinginfo&GN_AccessionId=807&InfoPageName=HZI_LungBXD_RNA-Seq_1116.

RNA-seq data for infected B6 and D2 parents are available at NCBI GEO under the accession number GSE66040. Array data from infected primary HAE cells are available at GEO under accession number GSE47963.

3 Results

3.1 *Ace2* expression level decreased in both B6 and D2 after H1N1 infection

We have previously generated H1N1-inflected lung RNA-seq for B6 and D2 parental strains at 1, 3, 5, 8, and 14 dpi. The B6 maternal parent of the BXDs is resistant to H1N1 infection, whereas the D2 paternal parent is highly susceptible to low virulent PR8 (H1N1) virus. Here we have

exploited these parental time-series data to define the *Ace2* mRNA post-infection dynamic response. Overall, expression of *Ace2* in lungs dropped progressively in both strains after infection (**Figure 1**). In B6, *Ace2* transcript reached its nadir at 8 dpi (7.20 ± 0.15 SD log2 units) and stayed low at 14 dpi (7.23 ± 0.12). Expression relative to 1 dpi was significantly lower at the following timepoints: 3 dpi (p = 0.026, log2FC = –0.25), 5 dpi (p = 0.008, log2FC = –0.49), 8 dpi (p = 0.003, log2FC = –0.73), and 14 dpi (p = 0.002, log2FC = –0.70). In comparison, the same infection titer was lethal for D2 which died at 5 dpi, and this was matched with lower expression of *Ace2* (7.10 ± 0.25) at 1 dpi. Statistically, *Ace2* expression 3 dpi (p = 0.003, log2FC = –0.37) and 5 dpi (p = 0.006, log2FC = –0.80) were significant reduced compared to 1 dpi. Although the differences in *Ace2* expression between B6 and D2 at 3 dpi and 5 dpi were not statistically significant different, D2 mice had a consistently more rapid decline in expression compared to B6.

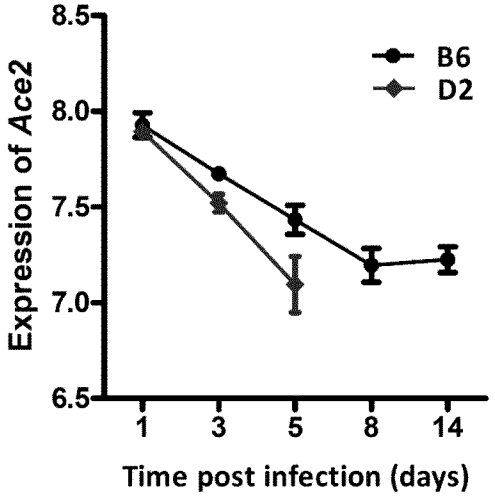

Figure 1. Line charts of the *Ace2* expression level in strains C57BL/6J (B6) and DBA/2J (D2) after H1N1 infection. Lung transcriptomes were quantified with RNA-seq for B6 and D2 strains at 1, 3, 5, 8, and 14 dpi of H1N1 infection. Three female mice (8–12 weeks of age) per strain were used per time point. The x-axis shows the time point (days) post the infection. The y-axis shows the expression level of *Ace2* on a log2 transformed scale.

3.2 *Ace2* expression exhibited variability across BXD strains at 3 dpi

All infected D2 mice died at 5 dpi. We therefore generated RNA-seq data at 3 dpi for infected BXD strains. Changes in *Ace2* transcript level after infection varies considerably across the BXD family with a 1.5-fold range (**Figure 2**). Mean expression of *Ace2* across all 43 strains is 8.02 ± 0.15 SD. BXD22 has the lowest expression of 7.78 and BXD77 has the highest expression of 8.36. The estimated heritability of *Ace2* expression variation is ~0.18, suggesting that expression of *Ace2* is partly impacted by genetic factor.

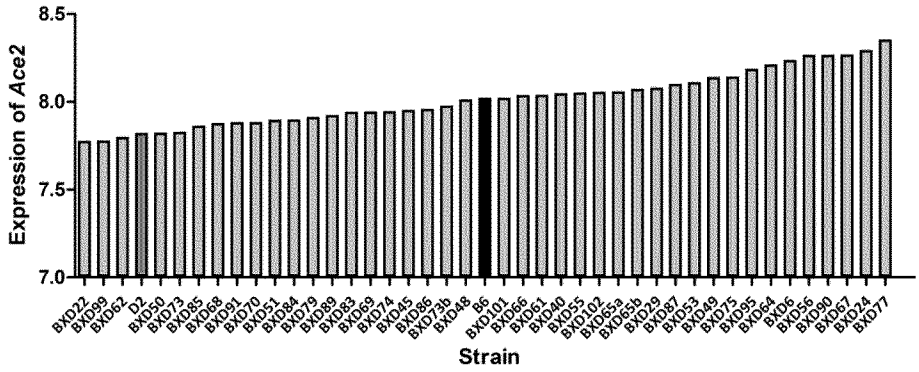

Figure 2. Expression of *Ace2* in BXD family. Bar plots of the pulmonary *Ace2* expression levels across the BXD family at 3 dpi. The x-axis shows BXDs strains and the two parental strains. The y-axis shows the normalized log2 expression levels of *Ace2*.

3.3 *Ace2* is associated with disease severity after infection

In order to investigate whether there is an association of *Ace2* expression with severity of disease and/or viral replication as infection progresses, we computed correlations of *Ace2* expression against body weight loss, mean time to death, and viral gene expression levels (as a surrogate for viral load). *Ace2* expression was significantly correlated with both body weight loss ($r = 0.575$, $p = 0.008$, **Figure 3A**) and median body weight loss ($r = 0.468$, $p = 0.028$, **Figure 3B**) at 3 dpi. Further, *Ace2* was positively and significantly correlated with the mean time to death ($r = 0.458$, $p = 0.032$, **Figure 3C**). In contrast, *Ace2* had a negative significant correlation with virus NA gene expression levels ($r = 0.381$, $p = 0.029$, **Figure 3D**).

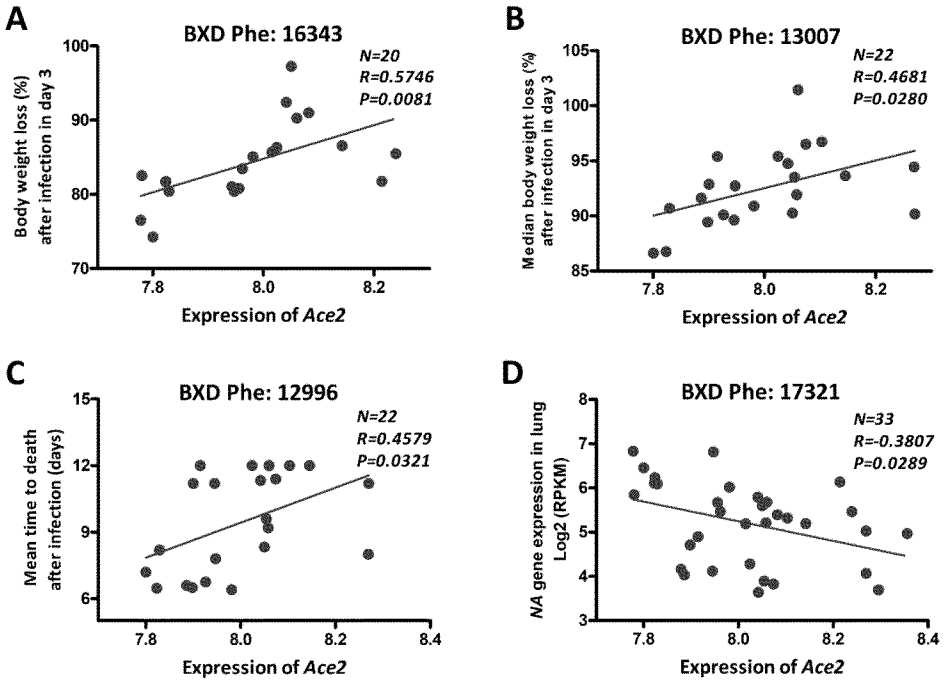

Figure 3. *Ace2* is associated with disease severity after infection. Scatter plots of the correlations of *Ace2* expression with body weight loss (**A**), median body weight loss (**B**) at 3 dpi, mean time to death (**C**), and viral neuraminidase (*NA)* gene expression levels (**D**). Pearson correlation coefficient was used to determine the relationship. Gene expression levels represent normalized log2 values. GeneNetwork BXD phenotype identifiers (e.g. ID "BXD_16343") are at the top of each plot.

3.4 *Ace2*-correlated transcripts are significantly involved in immune system-related networks

To gain insight into the pulmonary networks and biological functions that *Ace2* is involved in after viral infection, we computed Pearson correlation coefficient against the entire lung transcriptome. This analysis returned 5,500 transcripts nominally correlated with *Ace2* ($p < 0.05$, **Supplemental Data 1**). A total of 5,118 transcripts with Entrez gene IDs were submitted to WebGestalt (http://www.webgestalt.org/) for gene ontology analyses. The analysis highlighted strong enrichment in TNF signaling, MAPK signaling, Notch signaling pathways, HTLV-I infection, and VEGF signaling pathway (**Figure 4A**). Furthermore, we also found that these genes were enriched for categories related to chemokine secretion, lung morphology, and respiratory system morphology (**Figure 4B**).

Forty-eight genes are within the TNF signaling pathway (**Supplemental Data 1**), of which most have transcripts that covary negatively ($n = 35$) with *Ace2* ($p < 0.05$), including tumor necrosis factor (*Tnf,* $r = –0.414$, $p = 0.005$). Ninty-two genes are part of the extended MAPK signaling

network (**Supplemental Data 1**). Of these *Tgfb1* ($r = -0.459$, $p = 0.002$) and 59 other transcripts covary negatively with *Ace2*. Finally, 25 genes are part of Notch signaling pathways (**Supplemental Data 1**), and again the majority of transcripts ($n = 21$) covary negatively with *Ace2*.

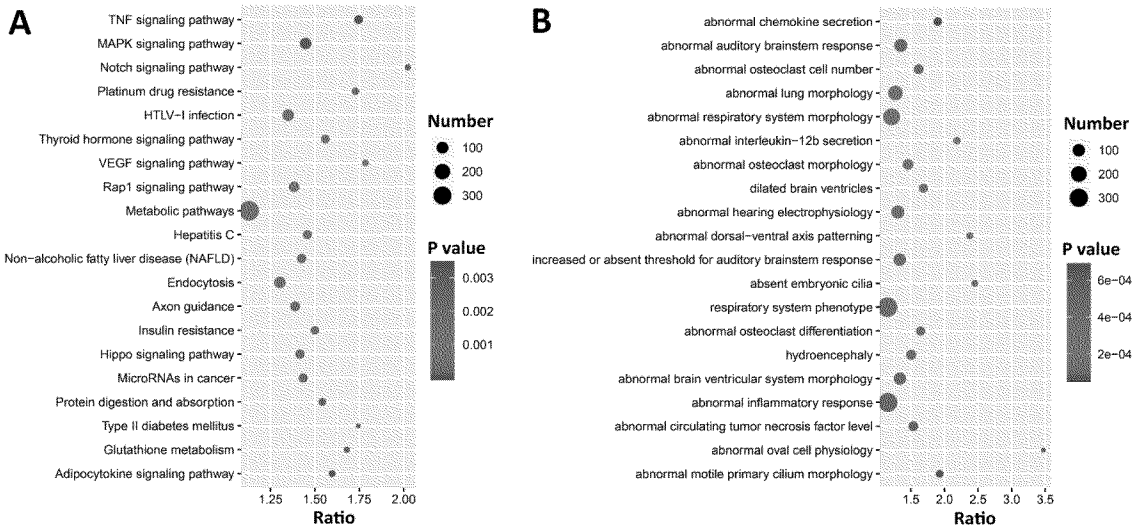

Figure 4. Bubble charts of the top 20 KEGG pathways (A) and 20 Mammalian Phenotype Ontologies (B) enriched for *Ace2* significantly correlated genes. Gene over-representation analysis for KEGG pathway and Mammalian Phenotype Ontology of the *Ace2* correlated transcripts ($p < 0.05$) were performed with WebGestalt (www.webgestalt.org). The *x*-axis represents the enrich ratio and *y*-axis represents enriched pathways/terms. The size of the dots denotes the number of genes and the color the *p* value.

3.5 Co-expression network analysis narrowed down *Ace2*-correlated transcripts

To identify genes that interact more directly with *Ace2*, we constructed co-expression modules using WGCNA with *Ace2* correlated transcripts. The top most varaint 5,500 transcripts were parsed into 10 co-expression modules using a soft-thresholding power of 8 (**Figure 5A-C**). Modules have a wide range of sizes, with a *brown* module containing 1,673 transcripts and *lightcyan* containing only 68 transcripts. *Ace2* was located in the *purple* module with 461 other genes/transcripts (**Figure 5C**). Genes in this module are significantly involved in cilium function (**Figure 5D**)

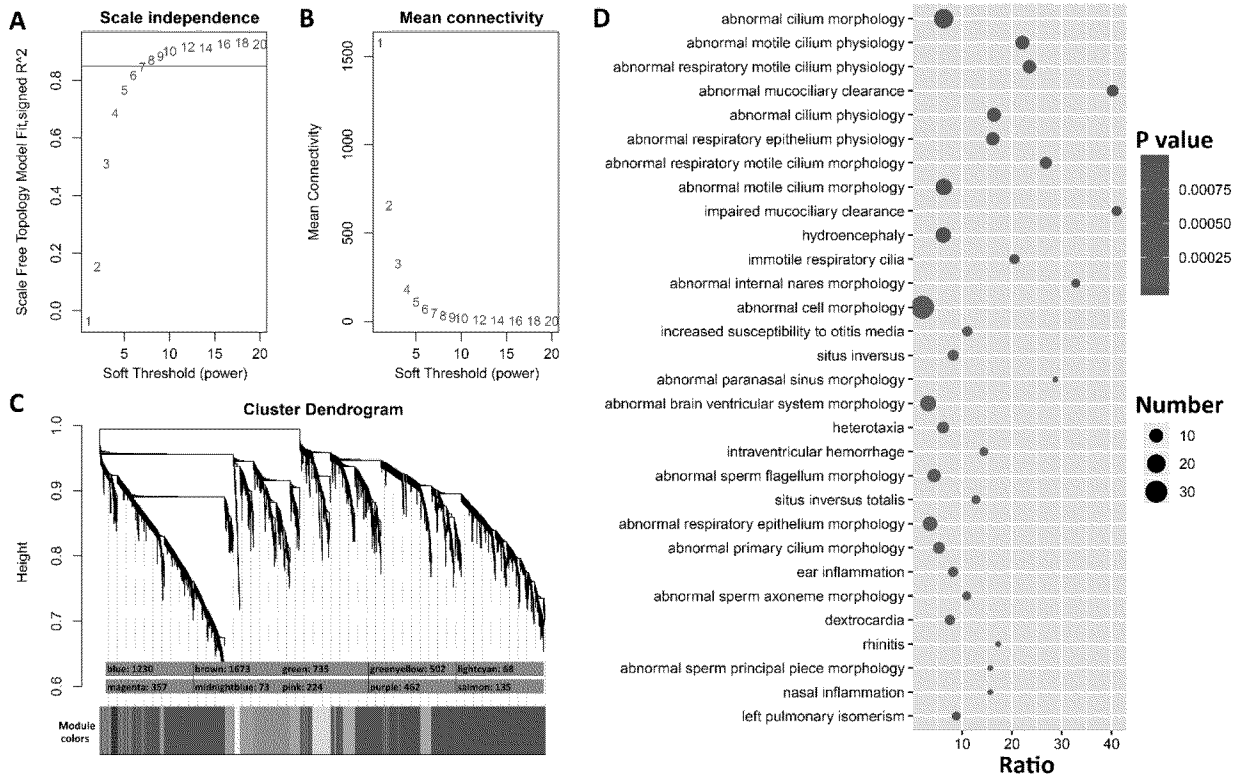

Figure 5. WGCNA modules associated with *Ace2* expression in H1N1 infected lung. (A) The soft thresholding index R^2 (*y*-axis) as a function of different powers β (x-axis) indicating the threshold of 8 chosen. **(B)** Mean connectivity (degree, y -axis) as a function of the soft-thresholding power (*x*-axis). **(C)** 10 co-expression modules identified from *Ace2* correlated genes. Modules are color coded as shown. The number of genes in each module is also indicated. **(D)** Bubble charts of top 30 enriched Mammalian Phenotype Ontologies of the purple module. Analysis by WebGestalt.

In subsequent analyses we focused on transcriptps within the *purple* module (**Supplemental Data 2**). We carried out differential expression analysis between cases and mock-infected controls and defined 281 transcripts (61% of the module) with differential expression (adj.$p < 0.05$ and FC > 1.3). eQTL mapping of the H1N1-infected whole lung transcriptom defined 23 cis-modulate transcripts and 106 *trans*-modulated transcripts, of which 69 are likely to harbor coding sequence variants. A subset of 42 of these genes have been implicated in cilium function. By comparing the above four categories (**Figure 6**), 31 cilium genes were differentially expressed (**Table 1**). Of these, *Sox11*, *Tff2*, *Rnf128*, and *Muc5b* are either *cis*- or *trans*-controlled, whereas *Sox11*, *Tmprss2*, *Ulk4*, *Cckar*, *Wdpcp*, *Ift140*, and *Ccdc40* contain functional variants (**Table 1**).

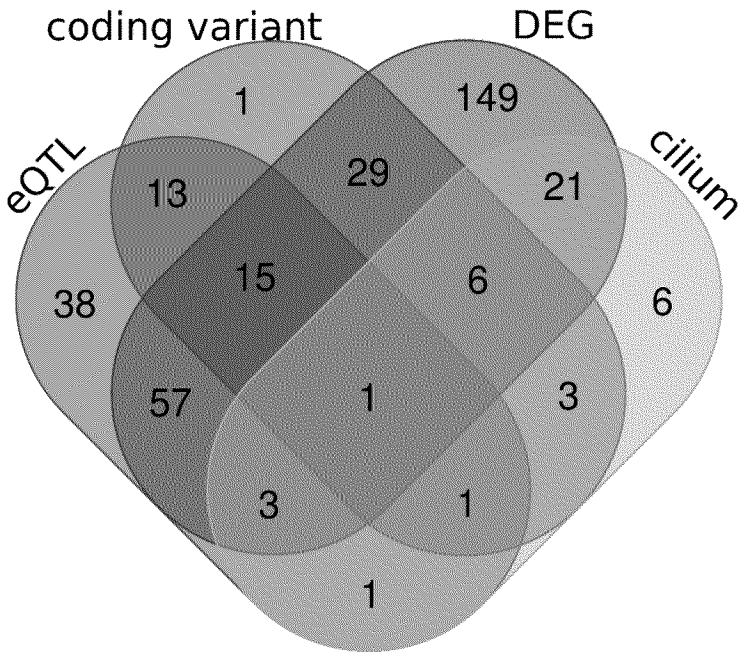

Figure 6. Venn diagrams of the purple module genes. A total of 462 genes were included in the purple module. Four criteria were applied to explore the module genes, including coding sequence variants between parental strain B6 and D2 (**coding variant**), eQTL (LRS > 15) regulation in H1N1 affected lung tissue (**eQTL**), cilium functional relevance (**cilium**), and differential expression (adj.p < 0.05 and FC > 1.3) between infected and normal controls in parental strains (**DEG**). The Venn diagram shows the number of overlapping genes among the four categories.

Table 1 Lists of prioritized genes in the purple module that were differentially expressed (adj.p < 0.05 and FC > 1.3) and implicated in cilium biological functions.

Gene ID	Symbol	Description	Log2 FC	Adj.p	eQTL	Functional Variant
20666	***Sox11***	SRY-box 11	-1.19	1.95E-12	cis	Nonsynonymous
21785	***Tff2***	trefoil factor 2 (spasmolytic protein 1)	-1.01	5.38E-04	trans	-
66889	***Rnf128***	ring finger protein 128	-0.77	2.81E-05	trans	-
74180	***Muc5b***	mucin 5, subtype B, tracheobronchial	0.54	1.13E-02	trans	-
50528	***Tmprss2***	transmembrane protease, serine 2	-1.06	8.58E-10	-	Nonsynonymous
209012	***Ulk4***	unc-51-like kinase 4 (C. elegans)	-0.87	3.43E-07	-	Nonsynonymous
12425	***Cckar***	cholecystokinin A receptor	-0.73	1.91E-05	-	Nonsynonymous
216560	***Wdpcp***	WD repeat containing planar cell polarity effector	-0.69	2.36E-06	-	Nonsynonymous
106633	***Ift140***	intraflagellar transport 140 homolog (Chlamydomonas)	-0.68	3.50E-07	-	Nonsynonymous
207607	***Ccdc40***	coiled-coil domain containing 40	-0.66	1.06E-03	-	Nonsynonymous
320752	*Dpy19l2*	dpy-19-like 2 (C. elegans)	-1.81	2.13E-03	-	-
51938	*Ccdc39*	coiled-coil domain containing 39	-1.30	1.15E-13	-	-
244653	*Hydin*	hydrocephalus inducing	-1.30	8.51E-16	-	-

74362	*Spag17*	sperm associated antigen 17	-1.29	9.27E-13	-	-
73873	*Fam161a*	family with sequence similarity 161, member A	-1.28	1.70E-09	-	-
320662	*Casc1*	cancer susceptibility candidate 1	-1.27	2.44E-08	-	-
66722	*Spag16*	sperm associated antigen 16	-1.27	1.61E-10	-	-
74934	*Armc4*	armadillo repeat containing 4	-1.21	8.50E-09	-	-
18703	*Pigr*	polymeric immunoglobulin receptor	1.18	1.10E-09	-	-
69707	*Iqcg*	IQ motif containing G	-1.18	2.97E-20	-	-
78801	*Ak7*	adenylate kinase 7	-1.17	4.75E-09	-	-
27078	*B9d1*	B9 protein domain 1	1.09	1.00E-02	-	-
68922	*Dnaic1*	dynein, axonemal, intermediate chain 1	-1.07	3.67E-08	-	-
226265	*Eno4*	enolase 4	-0.98	1.49E-09	-	-
71877	*Efhc1*	EF-hand domain (C-terminal) containing 1	-0.92	3.77E-11	-	-
75533	*Nme5*	expressed in non-metastatic cells 5	-0.82	5.92E-05	-	-
75050	*Kif27*	kinesin family member 27	-0.71	3.05E-03	-	-
70008	*Ace2*	angiotensin I converting enzyme (peptidyl-dipeptidase A) 2	-0.61	9.88E-05	-	-
20878	*Aurka*	serine/threonine kinase 6	0.60	2.36E-02	-	-
22062	*Trp73*	transformation related protein 73	-0.60	1.81E-03	-	-
252973	*Grhl2*	grainyhead-like 2 (Drosophila)	-0.44	5.36E-04	-	-

3.6 The differentially expressed cilium function related genes in the *purple* module were replicated in SARS-CoV-infected HAE cells

In order to evaluate whether cilium related genes (**Table 1**) are also modulated in humans, especially in the context of SARS-CoV infection, we analyzed our transcriptome data set for HAE cells infected with SARS-CoV (icSARS-CoV), ic-SARS-CoV ORF6 and BAT-SARS_CoV [50]. Very few of these transcripts were significantly affected after infection with BAT-SARS (**Figure 7A**). However, most of them were differentially expressed in icSARS-CoV and ic-SARS-CoV ORF6-infected HAE cells when compared to mock control, with 21 transcripts modulated at 96 hours after infection (**Figure 7A**). More importantly, those overlapping transcipts, except *Ace2*, exhibited the same up- or down-expression patterns in both HAE cells and our mouse model (**Table 1** and **Figure 7B**). *ACE2* was up-regulated in HAE cultures whereas in whole mouse lungs it was down-regulated. This is an important observation because HAE cultures consist almost exclusively of airway epithelial cells, with few if any interstitial cells, endothelial cells, resident and infiltrating immune cells. This indicates that *ACE2* networks detected in whole lungs are much more complex than those detected in isolated epithelial cells. It may be the case that *ACE2* is downregulated in all cells in lung after infection, but alternatively, *ACE2* may be up-regulated only in infected cells [50, 53]. In the lungs, infected cells represent a minority of all cells. Since our lung transcriptome quantifies steady-state expression changes of all cell types, it is conceivable that we do not detect up-regulation in a smaller population of infected cells. It may be important to quantify *Ace2* expression in infected mouse lungs by immunohistochemistry, by single-cell methods, or by *in situ* hybridization to resolve specificity and kinetics of responses.

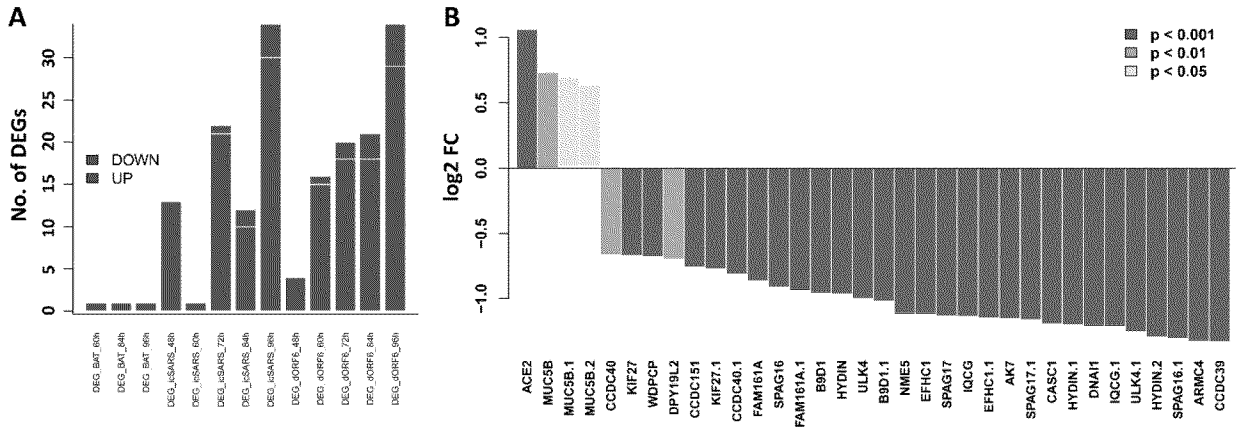

Figure 7. Bar plots of the cilium function related genes in the SARS-CoV infected HAE cells. Primary human HAE cells were infected with MOI 3 SARS-CoV (icSARS-CoV), ic-SARS-CoV ORF6 and BAT-SARS_CoV and gene expression was analyzed by arrays. (**A**) Number of up-and downregulated differentially expressed genes for cilium function related genes that had orthologous genes in humans and were represented on the array (adj.p < 0.05 and log2 FC > 0.58); y-axis: number of differentially expressed genes. (**B**) Log2 FC differences in expression values between HAE cells infected with icSARS-CoV at 96_h pi and mock-treated controls for cilium function related genes that had orthologous genes in humans and were represented on the array; y-axis: differences in log2 FC expression levels between groups. Adjusted p-values were taken from the Limma analysis of the entire transcriptome data.

3.7 Bayesian network analysis of causal pathways underlying post-infection weight loss

Body weight loss is an important indicator of post-infection severity. We performed QTL mapping for body weight changes after infection. This allowed us to identify loci on Chr X at 164 Mb that clearly modulate body weight loss at 2 and 3 dpi (**Figure 8A-B**), respectively. This locus is precisely aligned to the chromosomal position of the *Ace2* gene (Chr X at 164.2 Mb), which supports a central hypothesis of this study—that variants in or near *Ace2* influence influenza disease severity.

In order to investigate how this locus modulate influenza disease severity, hereafter refering as to body weight loss, we created a Bayesian network model (**Figure 8D**) comprising genotypes at this QTL location (Chr X: rs31223993) plus its candidate gene *Ace2* as genetic driver, and body weight loss as the key outcome response. We tested causal networks that included nine transcripts as putative disease mediators. All nine are highly expressed in the lung, have a significant correlation with *Ace2* and body weight loss at 2 and 3 dpi ($p < 0.05$), have a significant expression changes (FC > 1.3 and adj.$p < 0.05$) after infection at multiple time points between the infected and the mock controls (**Figure 8C**). Moreover, all of these transcripts and their cognate genes have been implicated in functions related to the infection related pathways (TNF signaling pathway, IL-17 signaling pathway, Th1 and Th2 cell differentiation).

The Bayesian network model (**Figure 8D**) linked Chr X QTL for body weight loss outcome at 2 and 3 dpi with multiple gene mediators, including C*sf2, Cxcl2*, *Maml3*, *Muc5b*, Ripk3, and*Traf3*. It is worth noting that any pathway leading from the major Chr X QTL to body weight loss must pass through *Atf4*, *Lif,* or *Reg3g*. For instance, one causal path for body weight loss begins at the Chr X QTL genotype (rs31223993), continues to the expression of *Ace2* and *lif,* and finally impacts phenotype outcomes.

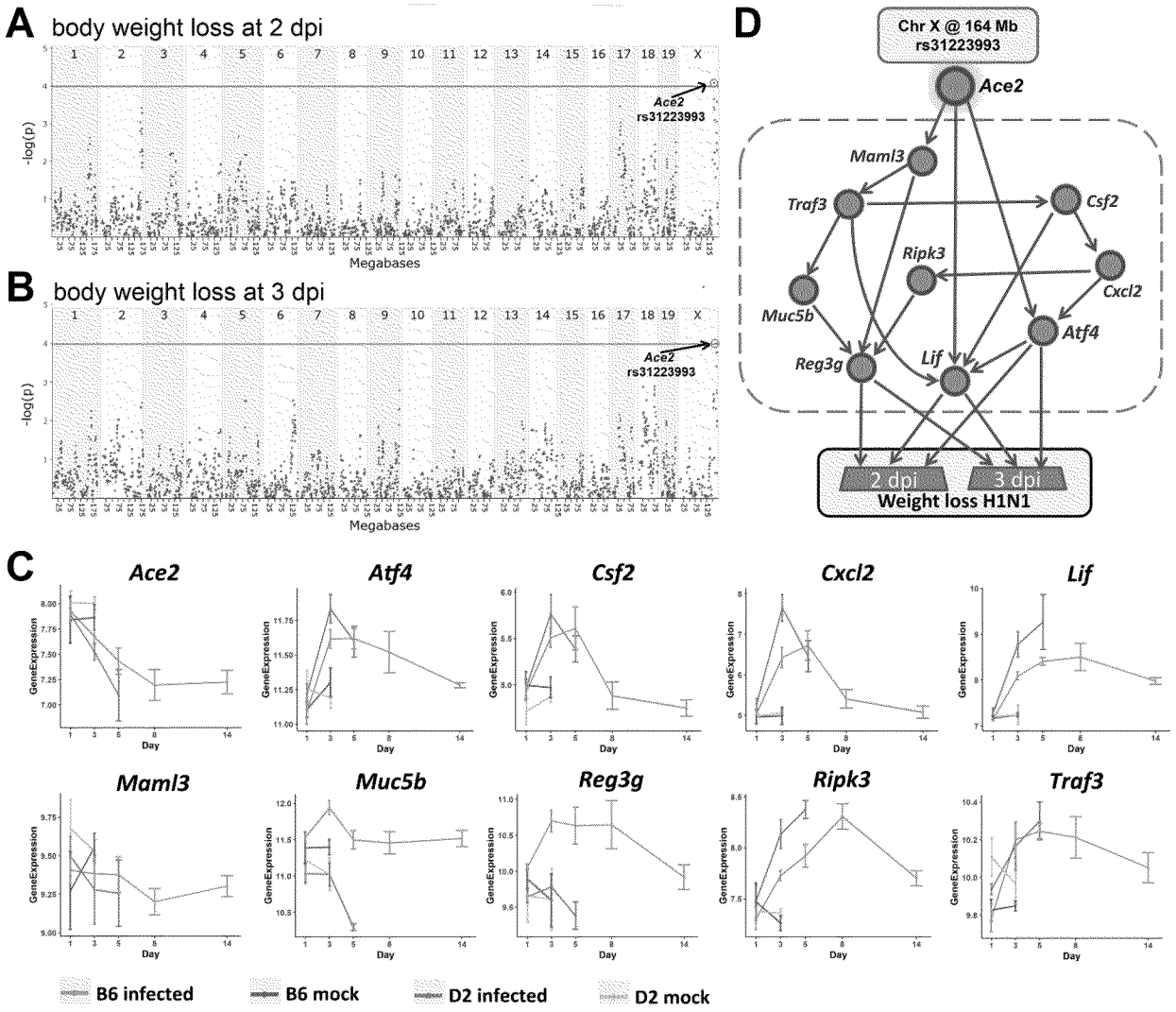

Figure 8. A **Bayesian network for the influenza disease severity in the BXD family**. QTL maps of body weight loss at 2 (**A**) and 3 dpi (**B**) with peaks on Chr X at 164 Mb, respectively. The *x*-axis is chromosome position on a megabases (Mb) scale, while the *y*-axis gives the –log(p) of linkage. Each point on this plot is a single SNP marker used to evaluate linkage. The red line indicates the genome-wide significant threshold of ~4. (**C**) Kinetics of expression changes of the ten transcripts that are part of the Bayesian network. The *x*-axis defines days after infection, and the *y*-axis defines expression on a log2 scale. (**D**) Candidate Bayesian network comprising a top tier of genotypes on Chr X that predict weight loss (rs31223993), a middle tier within the blue dashed box of gene expression endophenotypes, and a bottom tier of body weight loss.

Discussion

Gene variants significantly influence the susceptibility of humans to IAV infections [54]. This is just as true in mouse and other organisms [19]. In our case, it is especially true of the two parents

of the BXD family [20]. Here we have systemically analyzed the potential causal role of *Ace2* expression in disease sensitivity and severity. Our focus is on networks of transcripts that covary with differences in *Ace2* expression after H1N1 infection. Expression of *Ace2* in lung is marked but differentially decreased in a time-dependent manner. Expression variation is negatively correlated with body weight loss and with differences in survival time after infection. More importantly, the locus that modulates body weight loss at 2 and 3 dpi is co-located precisely with the location of *Ace2* on distal Chr X. These results strongly suggest that *Ace2* polymorphisms and responses are linked to H1N1 disease progression and that lower levels of *Ace2* may play a role in virus-induced ALI. This idea is corroborated by studies of *Ace2*$^{-/-}$ knockouts infected with influenza H7N9 [17] or with respiratory syncytial virus [16]. In both cases, lung pathology is more severe in the knockouts. These observations suggest that *Ace2* may mediate virus-induced ALI [16, 17]. However, the underlying processes remain elusive and direct causes, versus reactive changes, are still not proved.

Ace2 correlated genes are implicated in inflammatory related pathways

By using 41 isogenic RI strains, we defined *Ace2*-associated modules and molecular networks. We identified a total of ~5000 *Ace2*-correlated transcripts in infected lungs. As a set they are enriched in genes associated with respiratory and inflammatory networks and in several well understood pathways, including TNF, MAPK, and Notch signaling pathways. Extending this type of analysis to the corresponding proteomic, metabolomic, and metagenomic levels would provide a complementary and more accurate understanding of lung pathogenesis.

Key factors associated with H1N1-virus-induced lethality include virus-induced inflammatory cytokine storm and subsequent tissue destruction. Tumor necrosis factor (*TNF*) is a cytokine with multiple effects, including promoting cell growth, differentiation, apoptosis, and inducing inflammation [55, 56]. *TNF-α*, a member of the *TNF* family, can activate caspase protease, JNK, and transcription factor NF-κB, thereby amplifying its roles in cytotoxicity, antiviral action, and immuno-regulation. A previous study reported that inhibition of *Tnf-α* can protect mice from lethal H1N1 infection [57]. In the present study, we found *Ace2* was negatively correlated (r = –0.414, p = 0.005) with the expression of *Tnf* and 34 other TNF signaling pathway genes, suggesting that *Ace2* may dampen excessive inflammatory immune responses by downregulating this signaling pathway and mitigating immune-mediated tissue destruction. We also highlighted 92 genes in the MAPK signaling pathway that covary with *Ace2*, including *Tgfb1* (r = –0.459, p = 0.002). Of note, it was shown that IAV can activate this pathway to support its replication [58]. The authors proposed a model in which *Tgfb1* acts as a pro-viral host factor by suppressing early immune responses, creating an environment conducive for IAV infection [59]. Moreover, another set of 25 *Ace2*-correlated transcripts involved in the Notch signaling, most with negative

covariation. This pathway is a bridge between antigen-presenting cells (APCs) and T cell communication circuits and plays a critical role in driving the immune system to overcome infectious disease [60].

WGCNA identifies *Ace2* co-expressed genes in the respiratory epithelium system

There are essentially two parallel perturbation in this experiment—the actual infection with H1N1, and the natural genetic variation among these 43 diverse strains and their genomes. When performing WGCNA, a core of 461 transcripts covaried with *Ace2* after infection was identified (*purple* module). This set of covarying transcripts contained 31 genes that were related to ciliary function, including *Ace2* itself. *Ace2* expression may also modulate respiratory epithelial activity, although we stress that the causal polarity is still unknown.

Among the 31 prioritized cilium function related genes from the purple module (**Table 1**), *Rnf128*, *Muc5b*, *Sox11*, and *Tff2* showed *cis*- or *trans*-regulation, and *Tmprss2*, *Ccdc40, Ulk4*, *Cckar*, *Wdpcp*, and *Ift140* contained functional variants. *Rnf128* encodes a ring-finger-containing protein which has been shown to possess E3 ubiquitin ligase activity [61]. *RNF128* is implicated in the induction of T cell anergic phenotype through inhibiting activation-induced IL2 and IL4 cytokine production [62] and mediating T cell receptor-CD3 degradation [63]. In a recent study, Song *et al*. [64] reported that *RNF128* promotes lysine-63-linked ubiquitination and activation of a critical kinase TBK1, thereby augmenting the induction of type I interferon antiviral cytokines that curb viral replication. The authors' *in vivo* experiments further showed that *Rnf128* deficient mice were more susceptible to vesicular stomatitis virus (an RNA virus) and herpes simplex virus (a DNA virus). *MUC5B* (mucin 5, subtype B, tracheobronchial), encodes a member of the mucin family of proteins, and is associated with idiopathic pulmonary fibrosis in humans [65]. Overexpression of this gene in mice causes mucociliary dysfunction, and enhances lung fibrosis [66]. It was reported to be required for airway defense in another study [67]. *TMPRSS2* (transmembrane protease, serine 2) encodes a protein that belongs to the serine protease family. *Tmprss2* knockout mice show reduced lung inflammation with IAVs (H1N1, H3N2, or H7N9) infection and exhibit decreased susceptibility to virus-induced morbidity/mortality [68]. Studies also demonstrated that SARS coronavirus engages *ACE2* as the entry receptor on the cell surface [8, 9] and employs the *TMPRSS2* for Spike protein priming, which facilitates viral entry and infection [69, 70]. *CCDC40* (coiled-coil domain containing 40) encodes a protein that is essential for motile cilia function. According to the OMIM database, this gene is associated with recurrent respiratory infections (HP:0002205) and abnormal axonemal organization of respiratory motile cilia (HP:0012258). Malfunction of *Ccdc40* in mice resulted in left pulmonary isomerism and lung situs inversus [71]. In addition, *Ulk4*, *Sox11*, and *Tff2* are associated with abnormal respiratory

motile cilium [72], pulmonary hypoplasia [73], and abnormal adaptive immunity [74], respectively.

Genetic casual pathways for the host responses to infection

The innate immune system plays a crucial role in the early recognition and subsequent triggering of proinflammatory responses. Our Bayesian network model suggests that this response may be modulated in part by TNF signaling pathway related genes (*Atf4*, *Csf2*, *Cxcl2*, *lif* , and *Traf3*), particularly for genes *Atf4 and Lif*, two mediators for body weight loss at 2 and 3 dpi. *Atf4* encodes a transcription factor that was originally identified as a widely expressed mammalian DNA binding protein that could bind a tax-responsive enhancer element in the LTR of HTLV-1. Coronavirus replication is structurally and functionally associated with the endoplasmic reticulum (ER). The over-expression of the spike protein of SARS-CoV, MHV and HCoV-HKU1 has been shown to induce potent ER stress in cell culture [75-78]. In response to ER stress, phosphorylated eIF2α induces the expression of *ATF4* [79]. A previous study has demonstrated the protective effect of Ang 1–7 against Ang II induced ER stress and endothelial dysfunction [80]. It indicates that the expression level of *Ace2* and *Atf4* show a negative correlation, which is consistent with the results of our analysis. Furthermore, as an ER sensor, *ATF4* defends lungs via induction of heme oxygenase 1 and its dependent responsiveness to ER stress is significantly impaired in the elderly [81]. *Lif* (leukemia inhibitory factor) encodes a pleiotropic cytokine with roles in several different systems (http://www.informatics.jax.org/marker/MGI:96787). A study shown that LIF is expressed in the airspace of pneumonic lungs and the endogenous LIF facilitates tissue protection during pneumonia. In addition, The LIF-STAT3 axis has been identified as a key determinant of lung injury [82]. The proactive role of *Lif* on lungs during infection was also demonstrated by another study [83].Therefore, SM Metcalfe proposed to use LIF to protect the lungs and reduce disease severity caused by SARS-CoV-2 [84].

Immune responses not only act to control and eliminate infections, but often times inflict collateral damage of host lungs and other tissues. A diversity of molecules, metabolites, and cells types are invovled including some of genes implicated in host defense against pathogens (*Atf4*, *Cxcl2*, *Lif*, *Muc5b*, *Reg3g*, *Ripk3*, and *Traf3*) in the Bayesian network. The key genetic driver of this damage in the BXD family is a locus on Chr X at 164 Mb precisely at the position of *Ace2*. This root causal path to body weight loss is mediated in part by variation in *Ace2* and *Reg3g expression* (regenerating islet-derived 3 γ). The protein encoded by this gene is an antimicrobial lectin with activity against Gram-positive bacteria. *Reg3g* is a critical STAT3 target in lung epithelium, and is also highly expressed in gastrointestinal epithelium [85]. Our previous study revealed that *Reg3g* was significantly up-regulated in B6 but not in D2 after the H1N1 infection. *Reg3g* knockout mice in the B6 background showed a decrease in body weight at 4-6 dpi. [20].

STAT3-mediated induction of the antimicrobial protein REG3G is required for host defense against methicillin-resistant *Staphylococcus aureus* pneumonia [85]. A study has shown that IL22 and IL6 influence *Reg3g* expression in the gut and lungs, respectively. Gastrointestinal delivery of recombinant REG3G decreased lung inflammatory gene expression and protected *Il22*$^{-/-}$ mice from weight-loss during infection [86].

Implications for COVID-19

The ongoing outbreak of the COVID-19 caused by SARS-CoV-2 poses a global public health threat [87-89]. SARS-CoV-2 entry into host cells is partly dependent on *ACE2* [10], the receptor for SARS-CoV [8, 9]. How ACE2 interacts with other proteins involved in the progression of SARS-CoV-2-induced respiratory diseases remains to be determined. The first report based on autopsy samples demonstrated that the pathological characteristics of COVID-19 are similar to those of SARS-CoV and MERS-CoV infected patients [90]. We therefore focued most attention on 31 prioritized genes involved in cilium function (**Table 1**) that are co-expressed with *Ace2* after H1N1 infection in mouse and in SARS-CoV-infected human HAE cells. Twenty out of these 31 transcripts are consistently up- or down-regulated, suggesting these two viruses share common *Ace2* networks that participate in the development and severity of lung pathology. In addition, our Bayesian network model also suggests several genes could be targeted for lung protection during SARS-CoV-2 infection, such as *Atf4, Lif,* and *Reg3g*.

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Author Contributions

LL, KS, RWW and RSB conceived the study; SB and ACS conducted the experiments; FX, KS and RWW performed data analysis; LL, FX, KS, RWW, and JG wrote the manuscript. FX, KS, and JG prepared the figures and tables; RWW, KL, DGA, CBJ edited the manuscript; all authors read and approved the final version of the manuscript for publication.

Conflicts of Interest

The authors declare no conflicts of interests.

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90. Xu, Z., et al., *Pathological findings of COVID-19 associated with acute respiratory distress syndrome.* The Lancet Respiratory Medicine, 2020.

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To: Lu, Lu[llu@uthsc.edu]; Silke Bergmann[silke.bergmann@gmx.net]; Sims, Amy C[amy.sims@pnnl.gov]; Ashbrook, David[dashbroo@uthsc.edu]; Baric, Ralph S[rbaric@email.unc.edu]; Cui, Yan[ycui2@uthsc.edu]; Jonsson, Colleen Beth[cjonsson@uthsc.edu]
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Subject: AW: Ace2

Excellent!
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not clinical .....
klaus

Von meinem iPhone gesendet

Am 07.09.2020 um 22:01 schrieb Lu, Lu <llu@uthsc.edu>:

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Subject: Re: Ace2
Attachment: Ace2_V19_082820_DA.docx

Dear Lu,

Please find attached my edited version, just minor things.

Best,
David

David Ashbrook
Assistant Professor

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Genetic Dissection of the Regulatory Mechanisms of *Ace2* in the Infected Mouse Lung

Fuyi Xu[1#], Jun Gao[1, 5#], Silke Bergman[4], Amy C. Sims[7, 9], David G. Ashbrook[1], Ralph S. Baric[6,7, 8], Yan Cui[1], Colleen B Jonsson[4], Kui Li[4], Robert W. Williams[1*], Klaus Schughart[2, 3, 4*], and Lu Lu[1*]

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Abstract

Acute lung injury (ALI) is an important cause of morbidity and mortality after viral infections, including influenza A virus H1N1, SARS-CoV, MERS-CoV, and SARS-CoV-2. The angiotensin 1 converting enzyme 2 (ACE2) is a key host membrane-bound protein that modulates ALI induced by viral infection, pulmonary acid aspiration, and sepsis. However, the contributions of *ACE2* sequence variants to individual differences in disease risk and severity after viral infection are not understood. In this study, we quantified H1N1 influenza-infected lung transcriptomes across a family of 41 BXD recombinant inbred strains of mice and both parents—C57BL/6J and DBA/2J. In response to infection *Ace2* mRNA levels decreased significantly across all family members and the extent of decline was associated with disease severity including body weight loss and survival times. Pulmonry RNA-seq for 43 lines were analyzed using weighted gene co-expression network analysis (WGCNA) and Bayesian network approaches. *Ace2* not only participated in virus-induced ALI by interacting with TNF, MAPK, and NOTCH signaling pathways, but was also linked with high confidence to gene products that have important functions in the pulmonary epithelium, including *Rnf128*, *Muc5b*, and *Tmprss2*. Comparable sets of transcripts were also highlighted in parallel studies of human SARS-CoV-infected primary human airway epithelial cells. Using conventional mapping methods, we determined that weight loss at two and three days after viral infection maps to chromosome X—the location of *Ace2*. This finding motivated the hierarchical Bayesian network analysis, which defined molecular endophenotypes of lung infection linked to *Ace2* expression and to a key disease outcome. Core members of this Bayesian network include *Ace2, Atf4*, *Csf2*, *Cxcl2*, *Lif, Maml3*, *Muc5b*, *Reg3g*, *Ripk3*, and *Traf3*. Collectively, these findings define a causally-rooted *Ace2* modulatory network relevant to host response to viral infection and identify potential therapeutic targets for virus-induced respiratory diseases, including those caused by influenza and coronaviruses.

Key words: H1N1, acute lung injury, BXD family, *Ace2,* host response, viremia network

Introduction

Five major influenza A virus (IAV) pandemics have swept through human populations in the last 130 years—the 1890 H3N8 pandemic, the devastating 1918 H1N1 pandemic [1], and serious global outbreaks in 1957 (H2N2), 1968 (H3N2), and the 2009 H1N1 swine influenza. The current COVID-19 pandemic is caused by a novel coronavirus, termed severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2). This pathogen has spread with unprecedented speed and efficiency from an initial outbreak in November or December 2019.

The primary pathological features of the influenza A outbreaks and both the 2002 SARS and current COVID-19 outbreaks are viral pneumonia and acute lung injury (ALI) [2]. The well documented symptoms of influenza A (H1N1) and COVID-19 have substantial overlap. For both viral pathogens, infected humans can have symptoms ranging from mild coughing, congestion, and fever, to severe and lethal pulmonary edema and disseminating diseases of other organs. Individual host genetic differences almost certainly play an important role in the development and severity of the illness and its time course [3-7].

The human angiotensin 1 converting enzyme 2 (ACE2) is a cell membrane carboxypeptidase and negative modulator of the renin angiotensin system (RAS). This protein also has a key role in ciliary function in epithelial cells and is the principal receptor bound by spike proteins of SARS-CoV [8, 9] and SARS-CoV-2 [10]. *ACE2* is highly expressed in nasal cavity epithelial cells, especially on apical cilia of small airway cells and in alveolar epithelial type II cells (AT2) [11, 12].

Paradoxically, while serving as a key node in cellular entry of SARS-CoV and SARS-CoV-2 virions, ACE2 also protects against lung disease in animal models [13]. For example, treatment with recombinant human ACE2 protects against acute lung failure induced by acid aspiration or sepsis in *Ace2* knockout mice as well as in wild-type controls [14]. Of note, *Ace2* expression in mouse lungs is downregulated following SARS-CoV infection. The spike protein alone induces ACE2 downregulation in cell culture and enhances the severity of ALI induced by acid aspiration in wildtype mice [8]. In contrast, viral spike protein is unable to affect the severity of lung failure in *Ace2* knockout animals, indicating the effect of spike protein on acid-induced ALI is ACE2 specific [8]. Interestingly, expression of ACE2 is also significantly downregulated by IAVs in infected cell cultures, although in this case, ACE2 is dispensable for viral entry and replication [15]. In mice, *Ace2* deficiency is associated with aggravated ALI induced by IAV H7N9 or respiratory syncytial virus [16, 17]. The precise mechanism underlying these findings is unclear, as

is how alterations in ACE2 expression modulate the severity of pulmonary disease inflicted by coronaviruses and other IAV subtypes.

Expression of *ACE2* in human lung has an impressive level of variation among healthy humans. In the GTEx RNA-seq transcriptome survey [18], the maximum range of expression in the lung is about 22-fold, the interquartile range is 1.8-fold, and the coefficient of variation (standard deviation/mean) is high—nearly 0.6 (genenetwork.org/show_trait?trait_id=ENSG00000130234 &dataset=GTEXv8_Lung_tpm_0220). Given this finding, it is possible, even likely, that there are marked genetic differences in host susceptibility that are a function of numbers or ratios of ACE2-positive AT2 cells and epithelial cells in lung [11] or the level expression by these cells of *ACE2*. However, we emphasize that causal linkage between genetic variation in *ACE2* and to susceptibility or progress of infection is still poorly defined in humans, or even in mouse models.

Susceptibility to IAV, such as H1N1 and H7N7 influenza infections, varies greatly among strains of mice [19], and especially between the two key inbred strains we use here—C57BL/6J (B6), the reference strain for most genetic and molecular studies—and DBA/2J (D2), the oldest inbred strain of mice [20]. B6 is relatively resistant to IAV and often survives infection. In contrast, D2 loses body weight rapidly, and at the same inoculum dose as given to B6 dies within 5–7 days. Our laboratory has generated and maintains approximately 120 BXD recombinant inbred (RI) strains derived from crosses between B6 and D2 parents. Collectively, this family of RI strains segregates for ~6 million variants with minor allele frequencies above 0.3 [21], making it an ideal reference population to model genetic variation in susceptibility to IAV infections [22]. Indeed, in previous genetic mapping using the BXD family we have defined loci and even cloned gene variants that control the host response to IAV (H1N1) infection [23] and to other infectious diseases [24-27]. Here we have analyzed the lung transcriptome of 41 members of the family and both parental strains after infection with IAV (H1N1). We define patterns of covariation of RNA-seq data with induced variation in *Ace2* expression, as well as with outcome measures and with key molecular networks and endophenotypes likely to contribute to host defense and pathologies of H1N1 and possibly to SARS-CoV-induced ALI.

Materials and methods

Mice

We used females from 41 BXD RI strains and both parental strains—B6 and D2. Mice were between 8 and 12 weeks of age when infected. They were housed and maintained on a 12:12 light/ dark cycle, with *ad libitum* access to food and water.

Ethics

Protocols for the mouse experiments were approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Tennessee Health Science Center (UTHSC).

Virus

Original stocks of mouse-adapted A/Puerto Rico/8/34 (H1N1, PR8M) virus were obtained from Stefan Ludwig, University of Münster [28]. Virus stocks were propagated in the chorioallantoic cavity of 10-day-old pathogen-free embryonated chicken eggs for 48 h at 37 °C as described previously [29]. Viral titer was determined using a focus-forming unit (FFU) assay as described previously [29].

Infection of mice

Animals were anesthetized by intraperitoneal injection of ketamine/xylazine (10 % (v/v) of 100 mg/ml ketamine and 5 % (v/v) of 20 mg/ml xylazine in 0.9 % (w/v) NaCl with a dose adjusted to body weight (200 µl/20 g body weight). Infection was performed by intranasal application of virus solution in 20 µl sterile phosphate-buffered saline (PBS), with a PR8M dosage of 2×10^3 FFU. Mice were bred and infected at the animal facilities at UTHSC.

RNA isolation and sequencing

Mice were sacrificed three days post-infection (dpi) and both lungs were extracted and transferred immediately to RNAlater (Qiagen), stored at 4 °C for one day, and then stored at –20 °C. RNA was isolated using Qiagen Midi kit [30]. RNA quality was evaluated on a 2100 Bioanalyzer (Agilent). Five-hundred nanograms of total RNA was used to prepare libraries for sequencing using the Lexogen SENSE RNA-seq library kit for Ion Torrent. Libraries were amplified for 11 cycles as the final step of library preparation. Before sequencing, 1 µl aliquots were pooled and sequenced on an Ion Torrent PGM 314 chip. Barcoded data from the PGM was used to balance the final pool before sequencing. Library pools were sized to ~260 bp on a Pippin Prep instrument using 2% Pippin agarose gel. The sized libraries were evaluated on an Agilent High Sensitivity chip, quantified using real-time PCR, and used to prepare beads using a One-Touch 2 device. Beads were sequenced on an Ion Torrent Proton P1 chip. On average, 67 million reads were obtained per strain.

Read mapping and gene expression quantification

RNA-seq reads were quality-trimmed using Trim Galore [31] and mapped to the mm10 reference genome or to the influenza A virus PR8M genome using STAR [32]. Counts were summarized at the gene level using the R-package *Rsubread* [33], normalized and log transformed using the R-package *DESeq2* [34], and batch-corrected using the *ComBat* function of the R-package *sva* [35,

36]. For annotations of genes, ENTREZID from *Rsubread* were matched to RefSeq annotations using R-package *biomart* [37].

Heritability estimates for *Ace2*

Heritability of *Ace2* gene expression was estimated with GEMMA [38] using the following formula. This approach estimates the proportion of variance that can be explained (PVE) by genotypes converging nearly the whole genome:

$$\mathrm{PVE}(\boldsymbol{\beta}, \mathbf{u}, \tau) := \frac{\mathrm{V}(\mathbf{X}\boldsymbol{\beta} + \mathbf{u})}{\mathrm{V}(\mathbf{X}\boldsymbol{\beta} + \mathbf{u}) + \tau^{-1}}$$

Where "Xβ" is the sparse effects, "u" is the random effects, and "τ^{-1}" is the variance of the residual errors. GEMMA uses a Markov chain Monte Carlo method to estimate β, and u. We used the BXD genotype file generated on January 2017 (www.genenetwork.org/webqtl/main.py?FormID=sharinginfo&GN_AccessionId=600) and *Ace2* gene expression values across the 41 BXD family as input.

Correlation analysis

The correlation analysis in this study, including gene-gene and gene-phenotype rely on Pearson correlation coefficients [38]. We reviewed data to ensure that outliers and distributional anomalies did not compromise downstream analyses.

Weighted gene co-expression network analysis (WGCNA)

WGCNA is a method that defines modules of co-expression, and that is often used to explore the associations between variation in mRNA levels and phenotypes of interest. It can be used to define hub genes and clusters in molecular and genetic networks. In this study, gene co-expression networks were constructed using the *WGCNA package* [39] following standard methods (https://horvath.genetics.ucla.edu/html/CoexpressionNetwork/Rpackages/WGCNA/Tutorials/). Modules were generated using the subset of 5500 H1N1-infected lung mRNAs that covaried well with *Ace2* expression (Pearson *r*) at a nominal $p < 0.05$. We used the standard WGCNA beta weighting parameter of 8 to achieve close to a scale-free distribution.

Gene set enrichment analysis

To understand the biological function and clusters detected as *Ace2* covariates and WGCNA modules, we compared set membership to Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways and to the mammalian phenotype ontology (MPO) using WebGestalt (http://www.webgestalt.org) [40]. This analysis uses a hypergeometric statistic test to generate adjusted *p* values and enrichment ratios. In this analysis, we used only protein coding genes as the reference background and a threshold minimum of five genes/transcripts per category.

Quantitative trait loci (QTLs) mapping

QTLs define chromosomal regions that contribute to genetic variation in levels of gene expression, endophenotypes, and higher order outcome variables such as body weight loss and survival after infection. QTL mapping exploited methods in our GeneNetwork (www.genenetwork.org) [41, 42]. Linkage statistics were computed initially using Haley-Knott equations [43], and genome-wide significance levels were estimated from 2000 permutations of trait values. We used the new BXD genotype file of January 2017 (Ashbrook et al, bioRxiv, 2019). Those traits associated with significant and suggestive QTLs or expression QTLs (eQTLs) using the Haley and Knott regression were validated using GEMMA [44]. GEMMA uses a linear mixed model mapping algorithm that accounts for complex kinship among strain genometypes.

Genetic variations between B6 and D2

Sequence differences segregating among BXDs are taken from our previous work [45]. Here, we focus exclusively on protein-coding variants—nonsense, missense, and frameshift mutations.

Bayesian network construction

The Bayesian Network Webserver (BNW, compbio.uthsc.edu/BNW) [46-48] was used to create and evaluate plausible causal models among genes, transcripts, and outcome measures. The 100 highest scoring networks were used for model averaging, and those directed edges—unidirectional connections between nodes—with posterior probabilities greater than 0.8 were retained in the final model. We constrained each node to have at most four direct parents. We assigned nodes into one of three tiers of the Bayesian network: 1) SNP variant within selected QTL, 2) mRNA expression traits in a molecular endophenotype tier, and 3) the disease outcome measures—*Body Weight Loss* in the third tier. We allowed causal connections going from the first to second, and from second to the third tiers.

RNA-seq time-course data for H1N1 infection of the parental strains

Lung RNA-seq data was generated previously in our laboratory [20]. In brief, the two parental strains, B6 and D2, were infected with the H1N1 virus at 10–12 weeks of age as described above. RNA was isolated from lungs of B6 at 1, 3, 5, 8, and 14 dpi and from lungs of D2 at 1, 3, and 5 dpi. Three RNA samples per strain and per time point were used for library preparation and sequencing. Raw counts were extracted, normalized, and log2 transformed with *DEseq2* [34] after adding 1 to all raw counts. In this study, we extracted the *Ace2* expression levels from this dataset. We also performed differential expression analysis of mice at 3 dpi and their mock treated controls using *DESeq2* [34] using strain as a covariate. The resulting *p* values were adjusted using the Benjamini and Hochberg's approach [49] and are referred throughout this paper as adj. *p*. values. We reported transcripts with adj.$p < 0.05$, and fold change (FC) > 1.3 as differentially

expressed genes (DEGs). This data set was also used for evaluating the gene expression patterns post-infection.

Transcriptome data for SARS-CoV infected primary human airway epithelial (HAE) cells

The experimental details for this study are described in Ref. [50]. In brief, human tracheobronchial epithelial cells were resected from airway specimens of patients undergoing surgery. Primary cells were expanded to generate passage-1 cells, and passage-2 cells were plated at a density of 2.5×10^5 cells per well. Human airway epithelium (HAE) cultures were generated by provision of an air-liquid interface for 6 to 8 weeks to form well-differentiated, polarized cultures. Wild-type infectious clone-derived SARS-CoV (icSARS-CoV) and ic-SARS-CoV ORF6 were derived from infectious clone constructs as described [50]. Bat-SARS-CoV is comprised of the HKU3 backbone and SARS-CoV receptor binding domain and was derived from an infectious clone as described in [51]. Triplicate cultures were infected with a multiplicity of infection 3 (MOI 3) icSARS-CoV, and icSARS-CoV ORF6 on the apical surface. Total RNA was isolated from infected cells, and equivalent amounts of RNA from three biological replicates from each condition were pooled. Transcriptome profiling was performed using Agilent 4x44K whole human gene expression arrays. Raw data were downloaded from GEO (GSE47963_series_matrix.txt.gz). Expression values were normalized and sample descriptions quality controlled. A strong batch effect with respect to the donor from which HAE were derived was corrected using the R package *sva* [35, 36]. Rows with no gene description were deleted. Differentially expressed genes were determined using the R package *Limma* [52].

Data availability

The RNA-seq data from infected BXD strains has been deposited at GeneNetwork.org under the accession ID GN807. The summarized RNA-seq data as entered in GN can be accessed and downloaded at www.genenetwork.org/webqtl/main.py?FormID=sharinginfo&GN_AccessionId=807&InfoPageName=HZI_LungBXD_RNA-Seq_1116.

RNA-seq data for infected B6 and D2 parents are available at NCBI GEO under the accession number GSE66040. Array data from infected primary HAE cells are available at GEO under accession number GSE47963.

3 Results

3.1 *Ace2* expression level decreased in both B6 and D2 after H1N1 infection

We have previously generated H1N1-inflected lung RNA-seq for B6 and D2 parental strains at 1, 3, 5, 8, and 14 dpi. The B6 maternal parent of the BXDs is resistant to H1N1 infection, whereas the D2 paternal parent is highly susceptible to low virulent PR8 (H1N1) virus. Here we have

exploited these parental time-series data to define the *Ace2* mRNA post-infection dynamic response. Overall, expression of *Ace2* in lungs dropped progressively in both strains after infection (**Figure 1**). In B6, *Ace2* transcript reached its nadir at 8 dpi (7.20 ± 0.15 SD log2 units) and stayed low at 14 dpi (7.23 ± 0.12). Expression relative to 1 dpi was significantly lower at the following timepoints: 3 dpi (p = 0.026, log2FC = –0.25), 5 dpi (p = 0.008, log2FC = –0.49), 8 dpi (p = 0.003, log2FC = –0.73), and 14 dpi (p = 0.002, log2FC = –0.70). In comparison, the same infection titer was lethal for D2 which died at 5 dpi, and this was matched with lower expression of *Ace2* (7.10 ± 0.25) at 1 dpi. Statistically, *Ace2* expression 3 dpi (p = 0.003, log2FC = –0.37) and 5 dpi (p = 0.006, log2FC = –0.80) were significant reduced compared to 1 dpi. Although the differences in *Ace2* expression between B6 and D2 at 3 dpi and 5 dpi were not statistically significant, D2 mice had a consistently more rapid decline in expression compared to B6.

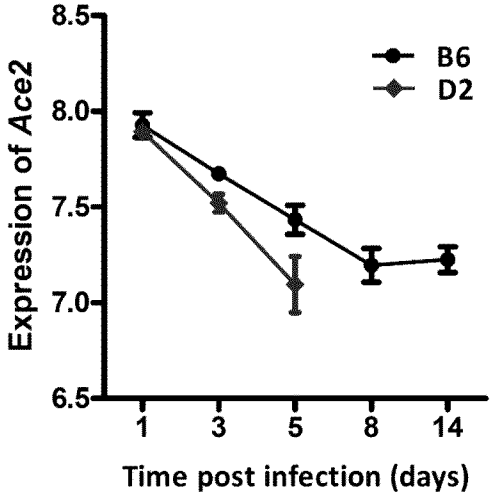

Figure 1. Line charts of the *Ace2* expression level in strains C57BL/6J (B6) and DBA/2J (D2) after H1N1 infection. Lung transcriptomes were quantified with RNA-seq for B6 and D2 strains at 1, 3, 5, 8, and 14 dpi of H1N1 infection. Three female mice (8–12 weeks of age) per strain were used per time point. The x-axis shows the time point (days) post the infection. The y-axis shows the expression level of *Ace2* on a log2 transformed scale.

3.2 *Ace2* expression exhibited variability across BXD strains at 3 dpi

All infected D2 mice died at 5 dpi. We therefore generated RNA-seq data at 3 dpi for infected BXD strains. Changes in *Ace2* transcript level after infection varies considerably across the BXD family with a 1.5-fold range (**Figure 2**). Mean expression of *Ace2* across all 43 strains is 8.02 ± 0.15 SD. BXD22 has the lowest expression of 7.78 and BXD77 has the highest expression of 8.36. The estimated heritability of *Ace2* expression variation is ~0.18, suggesting that expression of *Ace2* is partly impacted by genetic factors.

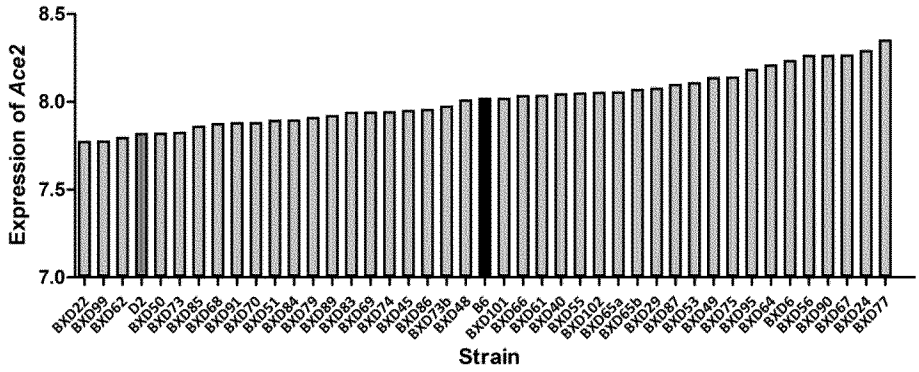

Figure 2. Expression of *Ace2* in the BXD family. Bar plots of the pulmonary *Ace2* expression levels across the BXD family at 3 dpi. The x-axis shows BXDs strains and the two parental strains. The y-axis shows the normalized log2 expression levels of *Ace2*.

3.3 *Ace2* is associated with disease severity after infection

In order to investigate whether there is an association of *Ace2* expression with severity of disease and/or viral replication as infection progresses, we computed correlations of *Ace2* expression against body weight loss, mean time to death, and viral gene expression levels (as a surrogate for viral load). *Ace2* expression was significantly correlated with both body weight loss ($r = 0.575$, $p = 0.008$, **Figure 3A**) and median body weight loss ($r = 0.468$, $p = 0.028$, **Figure 3B**) at 3 dpi. Further, *Ace2* was positively and significantly correlated with the mean time to death ($r = 0.458$, $p = 0.032$, **Figure 3C**). In contrast, *Ace2* had a negative significant correlation with virus NA gene expression levels ($r = 0.381$, $p = 0.029$, **Figure 3D**).

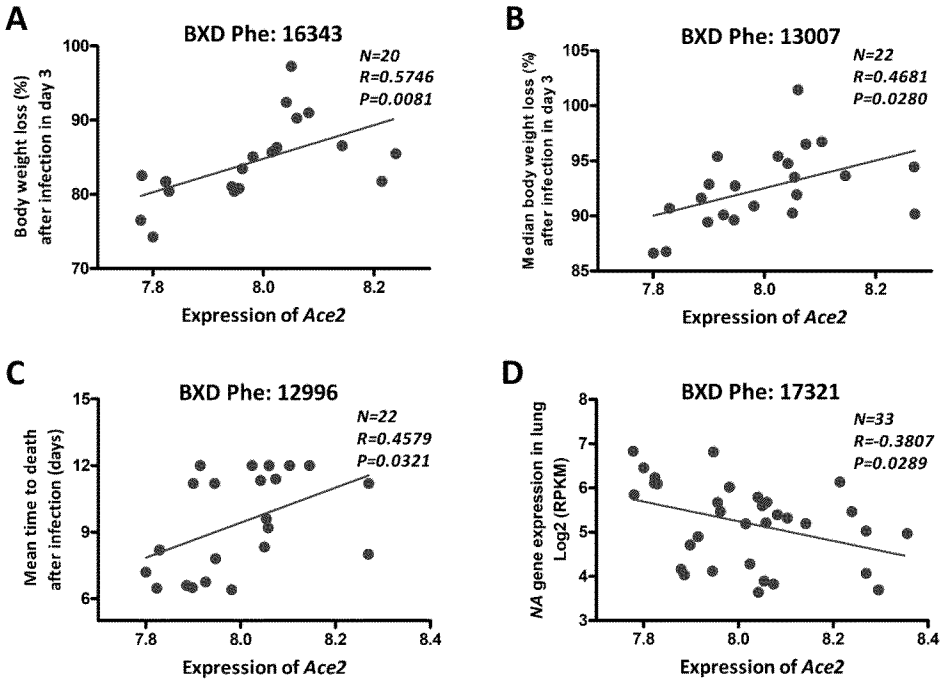

Figure 3. *Ace2* is associated with disease severity after infection. Scatter plots of the correlations of *Ace2* expression with body weight loss (**A**), median body weight loss (**B**) at 3 dpi, mean time to death (**C**), and viral neuraminidase (*NA)* gene expression levels (**D**). Pearson correlation coefficient was used to determine the relationship. Gene expression levels represent normalized log2 values. GeneNetwork BXD phenotype identifiers (e.g. ID "BXD_16343") are at the top of each plot.

3.4 *Ace2*-correlated transcripts are significantly involved in immune system-related networks

To gain insight into the pulmonary networks and biological functions that *Ace2* is involved in after viral infection, we computed Pearson correlation coefficients against the entire lung transcriptome. This analysis returned 5,500 transcripts nominally correlated with *Ace2* ($p < 0.05$, **Supplemental Data 1**). A total of 5,118 transcripts with Entrez gene IDs were submitted to WebGestalt (http://www.webgestalt.org/) for gene ontology analyses. The analysis highlighted strong enrichment in TNF signaling, MAPK signaling, Notch signaling pathways, HTLV-I infection, and VEGF signaling pathway (**Figure 4A**). Furthermore, we also found that these genes were enriched for categories related to chemokine secretion, lung morphology, and respiratory system morphology (**Figure 4B**).

Forty-eight genes are within the TNF signaling pathway (**Supplemental Data 1**), of which most have transcripts that covary negatively ($n = 35$) with *Ace2* ($p < 0.05$), including tumor necrosis factor (*Tnf,* $r = –0.414$, $p = 0.005$). Ninty-two genes are part of the extended MAPK signaling

network (**Supplemental Data 1**). Of these *Tgfb1* ($r = -0.459$, $p = 0.002$) and 59 other transcripts covary negatively with *Ace2*. Finally, 25 genes are part of Notch signaling pathways (**Supplemental Data 1**), and again the majority of transcripts ($n = 21$) covary negatively with *Ace2*.

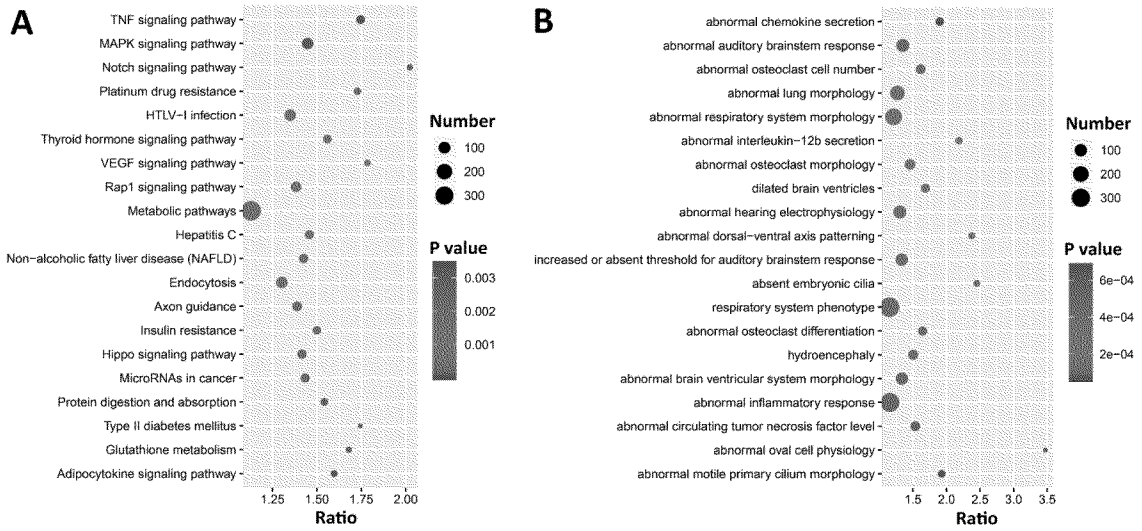

Figure 4. Bubble charts of the top 20 KEGG pathways (A) and 20 Mammalian Phenotype Ontologies (B) enriched for *Ace2* significantly correlated genes. Gene over-representation analysis for KEGG pathway and Mammalian Phenotype Ontology of the *Ace2* correlated transcripts ($p < 0.05$) were performed with WebGestalt (www.webgestalt.org). The *x*-axis represents the enrich ratio and the *y*-axis represents enriched pathways/terms. The size of the dots denotes the number of genes and the color denotes the *p*-value.

3.5 Co-expression network analysis narrowed down *Ace2*-correlated transcripts

To identify genes that interact more directly with *Ace2*, we constructed co-expression modules using WGCNA with *Ace2* correlated transcripts. The top most variant 5,500 transcripts were parsed into 10 co-expression modules using a soft-thresholding power of 8 (**Figure 5A-C**). Modules have a wide range of sizes, with a *brown* module containing 1,673 transcripts and *lightcyan* containing only 68 transcripts. *Ace2* was located in the *purple* module with 461 other genes/transcripts (**Figure 5C**). Genes in this module are significantly involved in cilium function (**Figure 5D**)

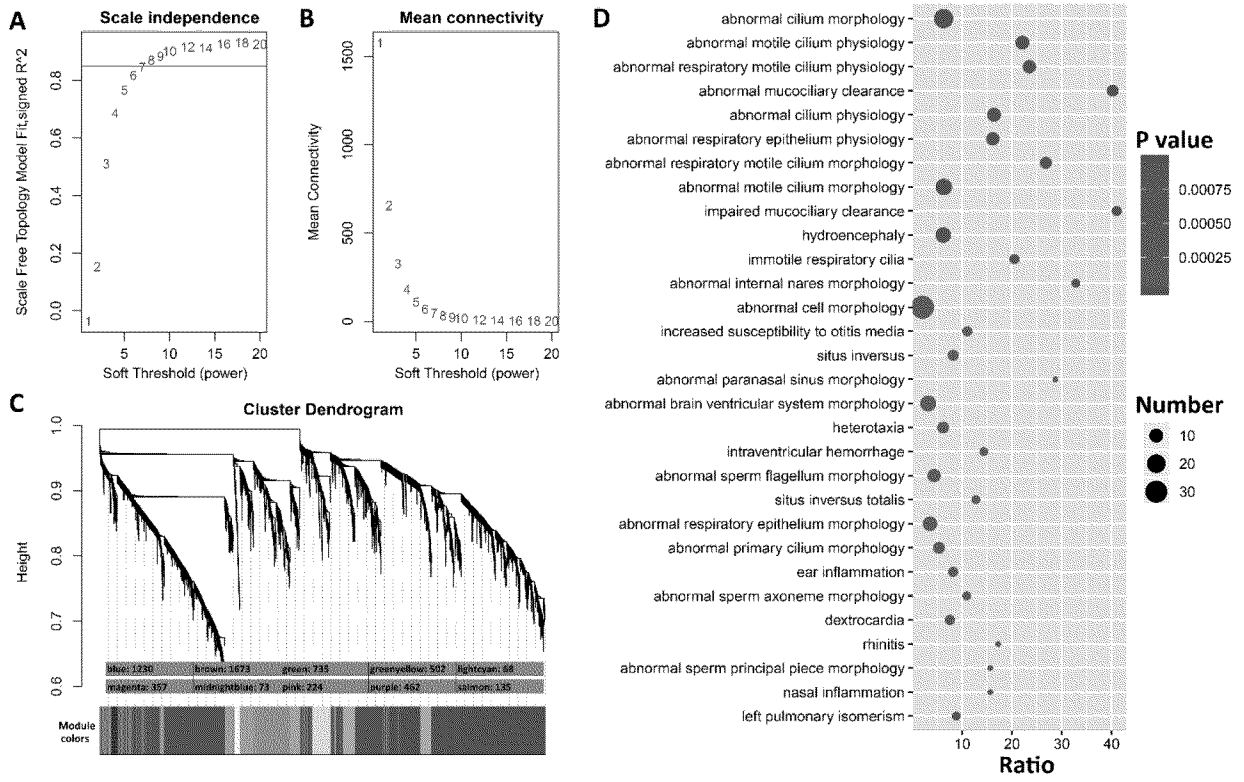

Figure 5. WGCNA modules associated with *Ace2* expression in H1N1 infected lung. (A) The soft thresholding index R^2 (*y*-axis) as a function of different powers β (x-axis) indicating the threshold of 8 chosen. **(B)** Mean connectivity (degree, y-axis) as a function of the soft-thresholding power (*x*-axis). **(C)** 10 co-expression modules identified from *Ace2* correlated genes. Modules are color coded as shown. The number of genes in each module is also indicated. **(D)** Bubble charts of top 30 enriched Mammalian Phenotype Ontologies of the purple module. Analysis by WebGestalt.

In subsequent analyses we focused on transcripts within the *purple* module (**Supplemental Data 2**). We carried out differential expression analysis between cases and mock-infected controls and defined 281 transcripts (61% of the module) with differential expression (adj.$p < 0.05$ and FC > 1.3). eQTL mapping of the H1N1-infected whole lung transcriptome defined 23 cis-modulate transcripts and 106 *trans*-modulated transcripts, of which 69 are likely to harbor coding sequence variants. A subset of 42 of these genes have been implicated in cilium function. By comparing the above four categories (**Figure 6**), 31 cilium genes were differentially expressed (**Table 1**). Of these, *Sox11*, *Tff2*, *Rnf128*, and *Muc5b* are either *cis*- or *trans*-controlled, whereas *Sox11*, *Tmprss2*, *Ulk4*, *Cckar*, *Wdpcp*, *Ift140*, and *Ccdc40* contain functional variants (**Table 1**).

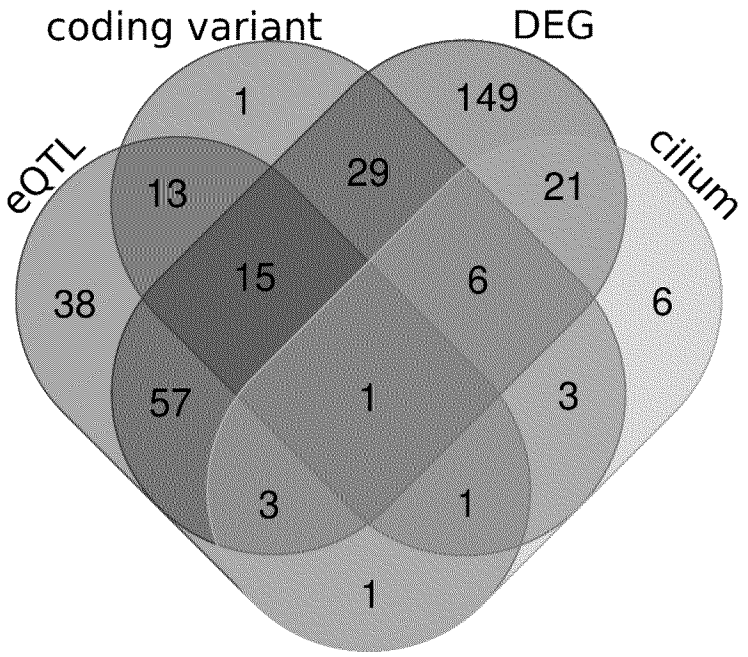

Figure 6. Venn diagrams of the purple module genes. A total of 462 genes were included in the purple module. Four criteria were applied to explore the module genes, including coding sequence variants between parental strain B6 and D2 (**coding variant**), eQTL (LRS > 15) regulation in H1N1 affected lung tissue (**eQTL**), cilium functional relevance (**cilium**), and differential expression (adj.p < 0.05 and FC > 1.3) between infected and normal controls in parental strains (**DEG**). The Venn diagram shows the number of overlapping genes among the four categories.

Table 1 Lists of prioritized genes in the purple module that were differentially expressed (adj.p < 0.05 and FC > 1.3) and implicated in cilium biological functions.

Gene ID	Symbol	Description	Log2 FC	Adj.p	eQTL	Functional Variant
20666	***Sox11***	SRY-box 11	-1.19	1.95E-12	cis	Nonsynonymous
21785	***Tff2***	trefoil factor 2 (spasmolytic protein 1)	-1.01	5.38E-04	trans	-
66889	***Rnf128***	ring finger protein 128	-0.77	2.81E-05	trans	-
74180	***Muc5b***	mucin 5, subtype B, tracheobronchial	0.54	1.13E-02	trans	-
50528	***Tmprss2***	transmembrane protease, serine 2	-1.06	8.58E-10	-	Nonsynonymous
209012	***Ulk4***	unc-51-like kinase 4 (C. elegans)	-0.87	3.43E-07	-	Nonsynonymous
12425	***Cckar***	cholecystokinin A receptor	-0.73	1.91E-05	-	Nonsynonymous
216560	***Wdpcp***	WD repeat containing planar cell polarity effector	-0.69	2.36E-06	-	Nonsynonymous
106633	***Ift140***	intraflagellar transport 140 homolog (Chlamydomonas)	-0.68	3.50E-07	-	Nonsynonymous
207607	***Ccdc40***	coiled-coil domain containing 40	-0.66	1.06E-03	-	Nonsynonymous
320752	*Dpy19l2*	dpy-19-like 2 (C. elegans)	-1.81	2.13E-03	-	-
51938	*Ccdc39*	coiled-coil domain containing 39	-1.30	1.15E-13	-	-
244653	*Hydin*	hydrocephalus inducing	-1.30	8.51E-16	-	-

74362	*Spag17*	sperm associated antigen 17	-1.29	9.27E-13	-	-
73873	*Fam161a*	family with sequence similarity 161, member A	-1.28	1.70E-09	-	-
320662	*Casc1*	cancer susceptibility candidate 1	-1.27	2.44E-08	-	-
66722	*Spag16*	sperm associated antigen 16	-1.27	1.61E-10	-	-
74934	*Armc4*	armadillo repeat containing 4	-1.21	8.50E-09	-	-
18703	*Pigr*	polymeric immunoglobulin receptor	1.18	1.10E-09	-	-
69707	*Iqcg*	IQ motif containing G	-1.18	2.97E-20	-	-
78801	*Ak7*	adenylate kinase 7	-1.17	4.75E-09	-	-
27078	*B9d1*	B9 protein domain 1	1.09	1.00E-02	-	-
68922	*Dnaic1*	dynein, axonemal, intermediate chain 1	-1.07	3.67E-08	-	-
226265	*Eno4*	enolase 4	-0.98	1.49E-09	-	-
71877	*Efhc1*	EF-hand domain (C-terminal) containing 1	-0.92	3.77E-11	-	-
75533	*Nme5*	expressed in non-metastatic cells 5	-0.82	5.92E-05	-	-
75050	*Kif27*	kinesin family member 27	-0.71	3.05E-03	-	-
70008	*Ace2*	angiotensin I converting enzyme (peptidyl-dipeptidase A) 2	-0.61	9.88E-05	-	-
20878	*Aurka*	serine/threonine kinase 6	0.60	2.36E-02	-	-
22062	*Trp73*	transformation related protein 73	-0.60	1.81E-03	-	-
252973	*Grhl2*	grainyhead-like 2 (Drosophila)	-0.44	5.36E-04	-	-

3.6 The differentially expressed cilium function related genes in the *purple* module were replicated in SARS-CoV-infected HAE cells

In order to evaluate whether cilium related genes (**Table 1**) are also modulated in humans, especially in the context of SARS-CoV infection, we analyzed our transcriptome data set for HAE cells infected with SARS-CoV (icSARS-CoV), ic-SARS-CoV ORF6 and BAT-SARS_CoV [50]. Very few of these transcripts were significantly affected after infection with BAT-SARS (**Figure 7A**). However, most of them were differentially expressed in icSARS-CoV and ic-SARS-CoV ORF6-infected HAE cells when compared to mock control, with 21 transcripts modulated at 96 hours after infection (**Figure 7A**). More importantly, those overlapping transcripts, except *Ace2*, exhibited the same up- or down-expression patterns in both HAE cells and our mouse model (**Table 1** and **Figure 7B**). *ACE2* was up-regulated in HAE cultures whereas in whole mouse lungs it was down-regulated. This is an important observation because HAE cultures consist almost exclusively of airway epithelial cells, with few if any interstitial cells, endothelial cells, resident and infiltrating immune cells. This indicates that *ACE2* networks detected in whole lungs are much more complex than those detected in isolated epithelial cells. It may be the case that *ACE2* is downregulated in all cells in lung after infection, but alternatively, *ACE2* may be up-regulated only in infected cells [50, 53]. In the lungs, infected cells represent a minority of all cells. Since our lung transcriptome quantifies steady-state expression changes of all cell types, it is conceivable that we do not detect up-regulation in a smaller population of infected cells. It may be important to quantify *Ace2* expression in infected mouse lungs by immunohistochemistry, by single-cell methods, or by *in situ* hybridization to resolve specificity and kinetics of responses.

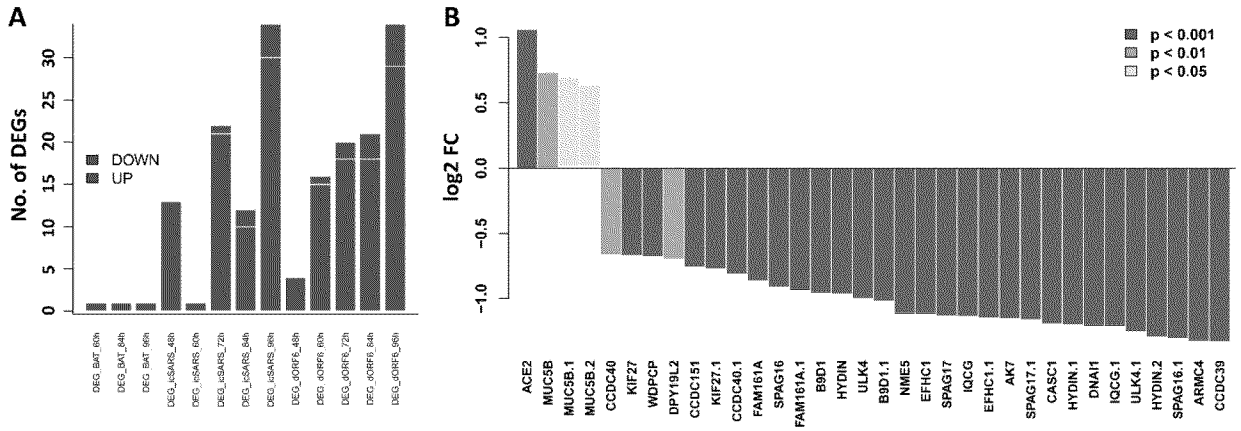

Figure 7. Bar plots of the cilium function related genes in the SARS-CoV infected HAE cells. Primary human HAE cells were infected with MOI 3 SARS-CoV (icSARS-CoV), ic-SARS-CoV ORF6 and BAT-SARS_CoV and gene expression was analyzed by arrays. (**A**) Number of up-and downregulated differentially expressed genes for cilium function related genes that had orthologous genes in humans and were represented on the array (adj.p < 0.05 and log2 FC > 0.58); y-axis: number of differentially expressed genes. (**B**) Log2 FC differences in expression values between HAE cells infected with icSARS-CoV at 96_h pi and mock-treated controls for cilium function related genes that had orthologous genes in humans and were represented on the array; y-axis: differences in log2 FC expression levels between groups. Adjusted p-values were taken from the Limma analysis of the entire transcriptome data.

3.7 Bayesian network analysis of causal pathways underlying post-infection weight loss

Body weight loss is an important indicator of post-infection severity. We performed QTL mapping for body weight changes after infection. This allowed us to identify loci on Chr X at 164 Mb that clearly modulate body weight loss at 2 and 3 dpi (**Figure 8A-B**), respectively. This locus is precisely aligned to the chromosomal position of the *Ace2* gene (Chr X at 164.2 Mb), which supports a central hypothesis of this study—that variants in or near *Ace2* influence influenza disease severity.

In order to investigate how this locus modulates influenza disease severity, hereafter referred to as body weight loss, we created a Bayesian network model (**Figure 8D**) comprising genotypes at this QTL location (Chr X: rs31223993) plus its candidate gene *Ace2* as a genetic driver, and body weight loss as the key outcome response. We tested causal networks that included nine transcripts as putative disease mediators. All nine are highly expressed in the lung, have a significant correlation with *Ace2* and body weight loss at 2 and 3 dpi ($p < 0.05$), and have a significant expression change (FC > 1.3 and adj.$p < 0.05$) after infection at multiple time points between the infected and the mock controls (**Figure 8C**). Moreover, all of these transcripts and their cognate genes have been implicated in functions related to the infection related pathways (TNF signaling pathway, IL-17 signaling pathway, Th1 and Th2 cell differentiation).

The Bayesian network model (**Figure 8D**) linked the Chr X QTL for body weight loss outcome at 2 and 3 dpi with multiple gene mediators, including C*sf2, Cxcl2*, *Maml3*, *Muc5b*, Ripk3, and*Traf3*. It is worth noting that any pathway leading from the major Chr X QTL to body weight loss must pass through *Atf4*, *Lif,* or *Reg3g*. For instance, one causal path for body weight loss begins at the Chr X QTL genotype (rs31223993), continues to the expression of *Ace2* and *Lif,* and finally impacts phenotype outcomes.

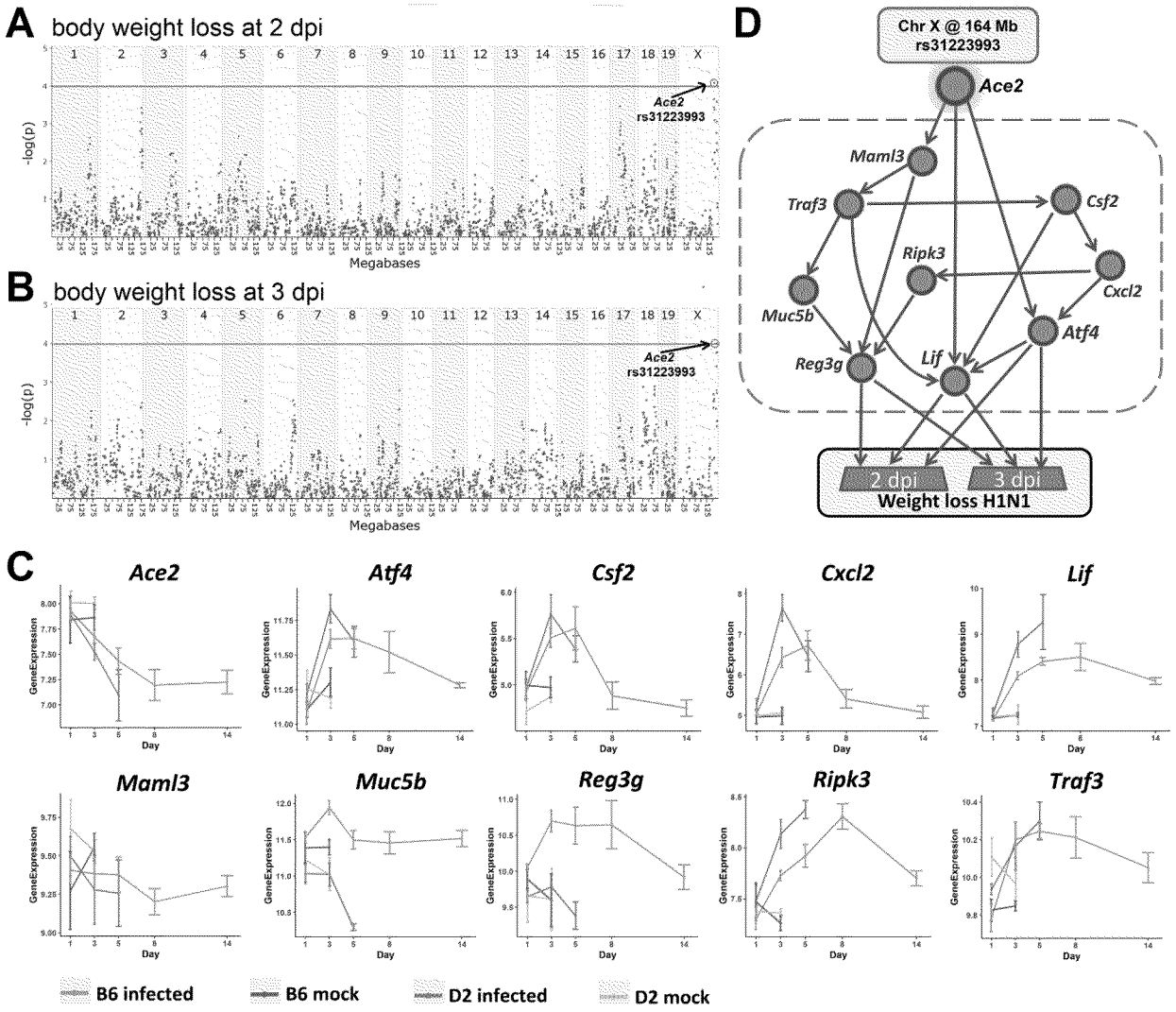

Figure 8. A **Bayesian network for the influenza disease severity in the BXD family**. QTL maps of body weight loss at 2 (**A**) and 3 dpi (**B**) with peaks on Chr X at 164 Mb, respectively. The *x*-axis is chromosome position on a megabases (Mb) scale, while the *y*-axis gives the –log(p) of linkage. Each point on this plot is a single SNP marker used to evaluate linkage. The red line indicates the genome-wide significance threshold of ~4. (**C**) Kinetics of expression changes of the ten transcripts that are part of the Bayesian network. The *x*-axis defines days after infection, and the *y*-axis defines expression on a log2 scale. (**D**) Candidate Bayesian network comprising a top tier of genotypes on Chr X that predict weight loss (rs31223993), a middle tier within the blue dashed box of gene expression endophenotypes, and a bottom tier of body weight loss.

Discussion

Gene variants significantly influence the susceptibility of humans to IAV infections [54]. This is just as true in mouse and other organisms [19]. In our case, it is especially true of the two parents

of the BXD family [20]. Here we have systemically analyzed the potential causal role of *Ace2* expression in disease sensitivity and severity. Our focus is on networks of transcripts that covary with differences in *Ace2* expression after H1N1 infection. Expression of *Ace2* in lung is marked but differentially decreased in a time-dependent manner. Expression variation is negatively correlated with body weight loss and with differences in survival time after infection. More importantly, the locus that modulates body weight loss at 2 and 3 dpi is co-located precisely with the location of *Ace2* on distal Chr X. These results strongly suggest that *Ace2* polymorphisms and responses are linked to H1N1 disease progression and that lower levels of *Ace2* may play a role in virus-induced ALI. This idea is corroborated by studies of *Ace2*$^{-/-}$ knockouts infected with influenza H7N9 [17] or with respiratory syncytial virus [16]. In both cases, lung pathology is more severe in the knockouts. These observations suggest that *Ace2* may mediate virus-induced ALI [16, 17]. However, the underlying processes remain elusive and direct causes, versus reactive changes, are still not proved.

Ace2 correlated genes are implicated in inflammatory related pathways

By using 41 isogenic RI strains, we defined *Ace2*-associated modules and molecular networks. We identified a total of ~5000 *Ace2*-correlated transcripts in infected lungs. As a set they are enriched in genes associated with respiratory and inflammatory networks and in several well understood pathways, including TNF, MAPK, and Notch signaling pathways. Extending this type of analysis to the corresponding proteomic, metabolomic, and metagenomic levels would provide a complementary and more accurate understanding of lung pathogenesis.

Key factors associated with H1N1-virus-induced lethality include virus-induced inflammatory cytokine storm and subsequent tissue destruction. Tumor necrosis factor (*TNF*) is a cytokine with multiple effects, including promoting cell growth, differentiation, apoptosis, and inducing inflammation [55, 56]. *TNF-α*, a member of the *TNF* family, can activate caspase protease, JNK, and transcription factor NF-κB, thereby amplifying its roles in cytotoxicity, antiviral action, and immuno-regulation. A previous study reported that inhibition of *Tnf-α* can protect mice from lethal H1N1 infection [57]. In the present study, we found *Ace2* was negatively correlated (r = –0.414, p = 0.005) with the expression of *Tnf* and 34 other TNF signaling pathway genes, suggesting that *Ace2* may dampen excessive inflammatory immune responses by downregulating this signaling pathway and mitigating immune-mediated tissue destruction. We also highlighted 92 genes in the MAPK signaling pathway that covary with *Ace2*, including *Tgfb1* (r = –0.459, p = 0.002). Of note, it was shown that IAV can activate this pathway to support its replication [58]. The authors proposed a model in which *Tgfb1* acts as a pro-viral host factor by suppressing early immune responses, creating an environment conducive for IAV infection [59]. Moreover, another set of 25 *Ace2*-correlated transcripts involved in the Notch signaling, most with negative

covariation. This pathway is a bridge between antigen-presenting cells (APCs) and T cell communication circuits and plays a critical role in driving the immune system to overcome infectious disease [60].

WGCNA identifies *Ace2* co-expressed genes in the respiratory epithelium system

There are essentially two parallel perturbation in this experiment—the actual infection with H1N1, and the natural genetic variation among these 43 diverse strains and their genomes. When performing WGCNA, a core of 461 transcripts covaried with *Ace2* after infection was identified (*purple* module). This set of covarying transcripts contained 31 genes that were related to ciliary function, including *Ace2* itself. *Ace2* expression may also modulate respiratory epithelial activity, although we stress that the causal polarity is still unknown.

Among the 31 prioritized cilium function related genes from the purple module (**Table 1**), *Rnf128*, *Muc5b*, *Sox11*, and *Tff2* showed *cis*- or *trans*-regulation, and *Tmprss2*, *Ccdc40, Ulk4*, *Cckar*, *Wdpcp*, and *Ift140* contained functional variants. *Rnf128* encodes a ring-finger-containing protein which has been shown to possess E3 ubiquitin ligase activity [61]. *RNF128* is implicated in the induction of T cell anergic phenotype through inhibiting activation-induced IL2 and IL4 cytokine production [62] and mediating T cell receptor-CD3 degradation [63]. In a recent study, Song *et al*. [64] reported that *RNF128* promotes lysine-63-linked ubiquitination and activation of a critical kinase TBK1, thereby augmenting the induction of type I interferon antiviral cytokines that curb viral replication. The authors' *in vivo* experiments further showed that *Rnf128* deficient mice were more susceptible to vesicular stomatitis virus (an RNA virus) and herpes simplex virus (a DNA virus). *MUC5B* (mucin 5, subtype B, tracheobronchial), encodes a member of the mucin family of proteins, and is associated with idiopathic pulmonary fibrosis in humans [65]. Overexpression of this gene in mice causes mucociliary dysfunction, and enhances lung fibrosis [66]. It was reported to be required for airway defense in another study [67]. *TMPRSS2* (transmembrane protease, serine 2) encodes a protein that belongs to the serine protease family. *Tmprss2* knockout mice show reduced lung inflammation with IAVs (H1N1, H3N2, or H7N9) infection and exhibit decreased susceptibility to virus-induced morbidity/mortality [68]. Studies also demonstrated that SARS coronavirus engages *ACE2* as the entry receptor on the cell surface [8, 9] and employs the *TMPRSS2* for Spike protein priming, which facilitates viral entry and infection [69, 70]. *CCDC40* (coiled-coil domain containing 40) encodes a protein that is essential for motile cilia function. According to the OMIM database, this gene is associated with recurrent respiratory infections (HP:0002205) and abnormal axonemal organization of respiratory motile cilia (HP:0012258). Malfunction of *Ccdc40* in mice resulted in left pulmonary isomerism and lung situs inversus [71]. In addition, *Ulk4*, *Sox11*, and *Tff2* are associated with abnormal respiratory

motile cilium [72], pulmonary hypoplasia [73], and abnormal adaptive immunity [74], respectively.

Genetic causal pathways for the host responses to infection

The innate immune system plays a crucial role in the early recognition and subsequent triggering of proinflammatory responses. Our Bayesian network model suggests that this response may be modulated in part by TNF signaling pathway related genes (*Atf4*, *Csf2*, *Cxcl2*, *lif*, and *Traf3*), particularly *Atf4 and Lif*, two mediators for body weight loss at 2 and 3 dpi. *Atf4* encodes a transcription factor that was originally identified as a widely expressed mammalian DNA binding protein that could bind a tax-responsive enhancer element in the LTR of HTLV-1. Coronavirus replication is structurally and functionally associated with the endoplasmic reticulum (ER). The over-expression of the spike protein of SARS-CoV, MHV, and HCoV-HKU1 has been shown to induce potent ER stress in cell culture [75-78]. In response to ER stress, phosphorylated eIF2α induces the expression of *ATF4* [79]. A previous study has demonstrated the protective effect of Ang 1–7 against Ang II induced ER stress and endothelial dysfunction [80]. It indicates that the expression levels of *Ace2* and *Atf4* show a negative correlation, which is consistent with the results of our analysis. Furthermore, as an ER sensor, *ATF4* defends lungs via induction of heme oxygenase 1 and its dependent responsiveness to ER stress is significantly impaired in the elderly [81]. *Lif* (leukemia inhibitory factor) encodes a pleiotropic cytokine with roles in several different systems (http://www.informatics.jax.org/marker/MGI:96787). A study has shown that LIF is expressed in the airspace of pneumonic lungs and the endogenous LIF facilitates tissue protection during pneumonia. In addition, The LIF-STAT3 axis has been identified as a key determinant of lung injury [82]. The proactive role of *Lif* on lungs during infection was also demonstrated by another study [83].Therefore, SM Metcalfe proposed to use LIF to protect the lungs and reduce disease severity caused by SARS-CoV-2 [84].

Immune responses not only act to control and eliminate infections, but often times inflict collateral damage of host lungs and other tissues. A diversity of molecules, metabolites, and cell types are involved including some of genes implicated in host defense against pathogens (*Atf4*, *Cxcl2*, *Lif*, *Muc5b*, *Reg3g*, *Ripk3*, and *Traf3*) in the Bayesian network. The key genetic driver of this damage in the BXD family is a locus on Chr X at 164 Mb, precisely the position of *Ace2*. This root causal path to body weight loss is mediated in part by variation in *Ace2* and *Reg3g expression* (regenerating islet-derived 3 γ). The protein encoded by this gene is an antimicrobial lectin with activity against Gram-positive bacteria. *Reg3g* is a critical STAT3 target in lung epithelium, and is also highly expressed in gastrointestinal epithelium [85]. Our previous study revealed that *Reg3g* was significantly up-regulated in B6 but not in D2 after the H1N1 infection. *Reg3g* knockout mice in the B6 background showed a decrease in body weight at 4-6 dpi. [20].

STAT3-mediated induction of the antimicrobial protein REG3G is required for host defense against methicillin-resistant *Staphylococcus aureus* pneumonia [85]. A study has shown that IL22 and IL6 influence *Reg3g* expression in the gut and lungs, respectively. Gastrointestinal delivery of recombinant REG3G decreased lung inflammatory gene expression and protected *Il22*$^{-/-}$ mice from weight-loss during infection [86].

Implications for COVID-19

The ongoing outbreak of the COVID-19 caused by SARS-CoV-2 poses a global public health threat [87-89]. SARS-CoV-2 entry into host cells is partly dependent on *ACE2* [10], the receptor for SARS-CoV [8, 9]. How ACE2 interacts with other proteins involved in the progression of SARS-CoV-2-induced respiratory diseases remains to be determined. The first report based on autopsy samples demonstrated that the pathological characteristics of COVID-19 are similar to those of SARS-CoV and MERS-CoV infected patients [90]. We therefore focused most attention on 31 prioritized genes involved in cilium function (**Table 1**) that are co-expressed with *Ace2* after H1N1 infection in mouse and in SARS-CoV-infected human HAE cells. Twenty out of these 31 transcripts are consistently up- or down-regulated, suggesting these two viruses share common *Ace2* networks that participate in the development and severity of lung pathology. In addition, our Bayesian network model also suggests several genes could be targeted for lung protection during SARS-CoV-2 infection, such as *Atf4, Lif,* and *Reg3g*.

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Author Contributions

LL, KS, RWW and RSB conceived the study; SB and ACS conducted the experiments; FX, KS and RWW performed data analysis; LL, FX, KS, RWW, and JG wrote the manuscript. FX, KS, and JG prepared the figures and tables; RWW, KL, DGA, CBJ edited the manuscript; all authors read and approved the final version of the manuscript for publication.

Conflicts of Interest

The authors declare no conflicts of interests.

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From: Lu, Lu[llu@uthsc.edu]
Sent: Tue 9/8/2020 10:59:14 AM (UTC-07:00)
To: Ashbrook, David[dashbroo@uthsc.edu]
Cc: Silke Bergmann[silke.bergmann@gmx.net]; Sims, Amy C[amy.sims@pnnl.gov]; Baric, Ralph S[rbaric@email.unc.edu]; Cui, Yan[ycui2@uthsc.edu]; Jonsson, Colleen Beth[cjonsson@uthsc.edu]; Williams, Robert W[rwilli10@uthsc.edu]; Klaus x Klaus Schughart[klaus.schughart@helmholtz-hzi.de]; Xu, Fuyi[fxu10@uthsc.edu]; Li, Kui[kli1@uthsc.edu]; JUN GAO; **5 U.S.C. § 552(b)(6)**
Subject: Re: Ace2

Dear David:
Thank you for your editing. We will accept and address them.

Lu Lu
Professor
Department of Genetics, Genomics and Informatics
University of Tennessee Health Science Center
71 S. Manassas St., Room 410K
Memphis, TN 38163
Tel: (901) 448-7557 (O)
Fax: (901) 448-3500 (Dept)

On Sep 8, 2020, at 12:25 PM, Ashbrook, David <dashbroo@uthsc.edu> wrote:

Dear Lu,

Please find attached my edited version, just minor things.

Best,
David

David Ashbrook
Assistant Professor

The University of Tennessee Health Science Center
Department of Genetics, Genomics and Informatics
Translational Science Research Building, Room 410H
71 S Manassas St
Memphis, TN 38103

dashbrook@UTHSC.edu
https://davidashbrook.wordpress.com/

From: Lu, Lu <llu@uthsc.edu>
Sent: Sunday, September 6, 2020 7:35 PM
To: Silke Bergmann <silke.bergmann@gmx.net>; Sims, Amy C <amy.sims@pnnl.gov>; Ashbrook, David

<dashbroo@uthsc.edu>; Baric, Ralph S <rbaric@email.unc.edu>; Cui, Yan <ycui2@uthsc.edu>; Jonsson, Colleen Beth <cjonsson@uthsc.edu>
Cc: Williams, Robert W <rwilli10@uthsc.edu>; Klaus Schughart <klaus.schughart@helmholtz-hzi.de>; Xu, Fuyi <fxu10@uthsc.edu>; Li, Kui <kli1@uthsc.edu>; JUN GAO **5 U.S.C. § 552(b)(6)**
Subject: Ace2

Dear all authors:
Here is the revised version of Ace2 paper based on new analysis and some of new data. We plan to submit it at coming week. Please review it and feel free to edit, and send it back to me before end of September 10 if you has modification. Thanks.

Lu Lu
Professor
Department of Genetics, Genomics and Informatics
University of Tennessee Health Science Center
71 S. Manassas St., Room 410K
Memphis, TN 38163
Tel: (901) 448-7557 (O)
Fax: (901) 448-3500 (Dept)

<Ace2_V19_082820_DA.docx>

From: Rauscher, Madison Hayes[mrausch@unc.edu]
Sent: Wed 9/9/2020 9:59:53 AM (UTC-07:00)
To: Ames, Amber A[Amber.Ames@pnnl.gov]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]; Sheahan, Timothy Patrick[sheahan@email.unc.edu]; Moore, Victoria L[victoria_moore@unc.edu]; Burkhart, Carol J.[carol_burkhart@unc.edu]
Subject: RE: Contract No. 528372, IPF 20-5613

Good Afternoon Amber,

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Thank you,
Madison

Madison Rauscher
Sponsored Projects Specialist
Office of Sponsored Research
The University of North Carolina at Chapel Hill
104 Airport Drive, Suite 2200
Chapel Hill, NC 27599-1350
919-962-4692

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Thursday, August 27, 2020 6:44 PM
To: OSR Research Admin <resadminosr@unc.edu>; Mina, Alexie Christine <amina93@live.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Subject: Contract No. 528372, IPF 20-5613

Dear Alexie,

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Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Ames, Amber A[Amber.Ames@pnnl.gov]
Sent: Wed 9/9/2020 10:09:34 AM (UTC-07:00)
To: Rauscher, Madison Hayes[mrausch@unc.edu]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]; Sheahan, Timothy Patrick[sheahan@email.unc.edu]; Moore, Victoria L[victoria_moore@unc.edu]; Burkhart, Carol J.[carol_burkhart@unc.edu]
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Let me know if this answers your questions.

Kind regards,

Amber

From: Rauscher, Madison Hayes <mrausch@unc.edu>
Sent: Wednesday, September 09, 2020 10:00 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sheahan, Timothy Patrick <sheahan@email.unc.edu>; Moore, Victoria L <victoria_moore@unc.edu>; Burkhart, Carol J. <carol_burkhart@unc.edu>
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Sent: Thursday, August 27, 2020 6:44 PM
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Dear Alexie,

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Kind regards,

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Pacific Northwest
NATIONAL LABORATORY

From: Rauscher, Madison Hayes[mrausch@unc.edu]
Sent: Wed 9/9/2020 11:09:45 AM (UTC-07:00)
To: Ames, Amber A[Amber.Ames@pnnl.gov]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]; Sheahan, Timothy Patrick[sheahan@email.unc.edu]; Moore, Victoria L[victoria_moore@unc.edu]; Burkhart, Carol J.[carol_burkhart@unc.edu]
Subject: RE: Contract No. 528372, IPF 20-5613

Thank you for your quick response! I appreciate this information and I'll return the signed document as soon as possible.

Madison Rauscher
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From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Wednesday, September 9, 2020 1:10 PM
To: Rauscher, Madison Hayes <mrausch@unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sheahan, Timothy Patrick <sheahan@email.unc.edu>; Moore, Victoria L <victoria_moore@unc.edu>; Burkhart, Carol J. <carol_burkhart@unc.edu>
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Kind regards,

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Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov



From: Leist, Sarah Rebecca[leist@email.unc.edu]
Sent: Wed 9/9/2020 1:16:58 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Hello and a little help please

Hi Amy,
Sorry for the delay…
I found many different p11's and I found p11-GFP (from TPS).
Is this what you'll need?
Should I just let Ben know where it is and he handles it from there?

Hope you're doing fine!

Thanks,
Sarah

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Wednesday, August 26, 2020 at 11:28 AM
To: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Subject: Re: Hello and a little help please

Hi Sarah,

Moving is super exciting! I hope you like your new place and that they love cats! That would be awesome and hopefully not too long of a freezer dive in Little Switzerland. Thank you very much!! I appreciate you making time to respond! Thank you again, Amy

---

From: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Date: Wednesday, August 26, 2020 at 6:30 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Hello and a little help please

Hi Amy,
I can have a look later this week.
I'm moving right now.

Sorry for the delay!

Hope you're doing fine!

Sarah

Sent from my iPhone

> On Aug 20, 2020, at 12:41 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:
>
> Hi Sarah!

I hope you and your kitty clan are doing well! I hope the boys transitioned to the US well and that everyone is getting along nicely! And that there is still somewhere for you to sleep in your apartment.

I know you are crazy busy but I am hoping you can help me with something that maybe won't take too long.

Could you help Ben with finding a few vials of the NL63 stocks from the experiment you and I worked on previously? I am asking to get the wild type (with the S point mutation) and the one with GFP. If you can't find these please let me know.
I really appreciate it as I know you are totally slammed. Congratulations on the publications! That is really great!

Thank you very much! I miss getting to catch up with you and I really hope you are getting a little down time to enjoy life! Amy

From: Rauscher, Madison Hayes[mrausch@unc.edu]
Sent: Thur 9/10/2020 11:14:36 AM (UTC-07:00)
To: Ames, Amber A[Amber.Ames@pnnl.gov]
Cc: Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]; Sheahan, Timothy Patrick[sheahan@email.unc.edu]; Moore, Victoria L[victoria_moore@unc.edu]; Burkhart, Carol J.[carol_burkhart@unc.edu]
Subject: RE: Contract No. 528372, IPF 20-5613
Attachment: Fully_Exe_PO528372.pdf

Amber,

Please find the fully executed agreement attached and reach out if you need anything else.

Best,
Madison

Madison Rauscher
Sponsored Projects Specialist
Office of Sponsored Research
The University of North Carolina at Chapel Hill
104 Airport Drive, Suite 2200
Chapel Hill, NC 27599-1350
919-962-4692

From: Rauscher, Madison Hayes
Sent: Wednesday, September 9, 2020 2:10 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sheahan, Timothy Patrick <sheahan@email.unc.edu>; Moore, Victoria L <victoria_moore@unc.edu>; Burkhart, Carol J. <carol_burkhart@unc.edu>
Subject: RE: Contract No. 528372, IPF 20-5613

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Madison Rauscher
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919-962-4692

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Sent: Wednesday, September 9, 2020 1:10 PM
To: Rauscher, Madison Hayes <mrausch@unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sheahan, Timothy Patrick <sheahan@email.unc.edu>; Moore, Victoria L <victoria_moore@unc.edu>; Burkhart, Carol J. <carol_burkhart@unc.edu>
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To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sheahan, Timothy Patrick <sheahan@email.unc.edu>; Moore, Victoria L <victoria_moore@unc.edu>; Burkhart, Carol J. <carol_burkhart@unc.edu>
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Pacific Northwest NATIONAL LABORATORY
Proudly Operated by Battelle Since 1965

Battelle Memorial Institute, Pacific Northwest Division
Acting Under Contract DE-AC05-76RL01830
With the U.S. Department of Energy
Operating the Pacific Northwest National Laboratory (PNNL) (www.pnnl.gov)

Schedule - Contract No. 528372

Issued by:	**Name and Address of Contractor:**
Battelle Battelle Boulevard, K9-15 P.O. Box 999 Richland, WA 99352-0999 USA Contracts Specialist: Amber A. Ames Telephone Number: (509) 371-7050 Email: amber.ames@pnnl.gov	University of North Carolina at Chapel Hill Office of Sponsored Research 104 Airport Drive, Suite 2200 Campus Box 1350 Chapel Hill, NC 27599-1350 USA Contractor Contact: David Paul Telephone Number: (919) 966-3411 Email: resadminosr@unc.edu
Payment Terms: Net 30	**Contract Type:** Cost Reimbursement
Submit Invoices and Invoice/Payment Inquiries to ap.invoices@pnnl.gov. **Note:** Invoices must list location(s) of service (US: City, State; Foreign: Country).	**Total Contract Amount:** $(b) (4)
Contract Period of Performance: July 27, 2020 through May 31, 2021	
Award Battelle hereby agrees to award this Contract to the Contractor subject to acceptance. The rights and obligations of the parties to this Contract are subject to and governed by this document and any documents attached or incorporated by reference.	**Contractor Agreement** Contractor accepts and agrees to furnish and deliver the items or perform services to the extent stated in this document for the consideration stated in this contract. The rights and obligations of the parties to this contract are subject to and governed by this document and any documents attached or incorporated by reference.

Battelle Memorial Institute Pacific Northwest Division	**Contractor shall sign and return a copy of this document**
Signature of person authorized to sign Digitally signed by Amber A. Ames ~~Date: 2020.08.27 15:38:32 -07'00'~~	**Signature of person authorized to sign** JoAnne E. Shanklin Digitally signed by JoAnne E. Shanklin Date: 2020.09.10 13:27:33 -04'00'
Name Amber A. Ames	**Name** on behalf of Terry Magnuson, PH.D.
Title Contracts Specialist	Title Vice Chancellor for Research
Date	Date 09/10/2020

IMPORTANT NOTE: Any domestic and foreign travel associated with this contract (including contractor travel within a country of presence) shall be approved in writing by the Battelle Contracts Representative in advance of travel arrangements being finalized. Without the advance approval of the Battelle Contracts Representative for any such travel, any invoiced costs related to such travel will not be paid.

Statement of Work

Contractor agrees to perform the scope outlined in the attached Statement of Work dated July 16, 2020.

Indirect Rates

The following indirect cost rates are hereby established until and unless changed by mutual agreement:

Category	Rate	Base	Type	Effective
Indirect Costs	55.5%	On Campus Organized Research MTDC*	Provisional	From 07/01/2020 Through Until amended

*Modified Total Direct Costs

Fringe Benefits: *The fringe benefits are specifically identified to each employee and are charged individually as direct costs.*

The provisional rate(s) specific above may be prospectively or retroactively revised by mutual agreement, at either Battelle or the Contractor's request, to prevent substantial overpayment.

Upon establishment/approval of finalized, or final rates, for any period consistent with the period of performance, the Contractor agrees to supply such approval to Battelle, within 30 days or receipt of approval from the cognizant agency.

Technical Oversight Representative

All technical questions should be directed to the Technical Oversight Representative, Pamela M. Kinsey at (509) 375-6848 or pamela.kinsey@pnnl.gov. The Technical Oversight Representative cannot modify this agreement.

Battelle Contracts Representative

All contractual questions should be directed to the Battelle Contracts Representative, Amber A. Ames at (509) 371-7050 or amber.ames@pnnl.gov.

Approval of Subcontracts

Subcontracts require the prior written approval of the Battelle Contracts Representative.

Contract Contents

In addition to this Schedule, the Contract consists of:

- Representations and Certifications dated July 27, 2020
- The General Provisions Applicable for Educational Institutions and Nonprofit Organizations, Form A-409.25-Ed/NP dated October 2019, apply and may be viewed at http://www.pnnl.gov/contracts/contractdocuments.aspx
- Precontract Cost Authorization Letter dated July 24, 2020
- Statement of Work dated July 16, 2020

Alterations to General Provisions

- **Insurance – Liability to Third Persons (cl. 378b – Mar 1996)** This clause is hereby deleted and replaced with:

  "Contractor is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."
- **Disputes (cl. 331-Nov 2014)** This clause is hereby deleted and replaced with the following: "Except as otherwise provided or agreed, any dispute relating to this contract which is not disposed of by agreement shall be decided by litigation in a court of competent jurisdiction upon filing of a legal action by the aggrieved party. During the pendency of any dispute, the Contractor shall proceed diligently with the performance of the contract and in accordance with the direction of Battelle."

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- **Laws and Regulations, DOE Directives, and Indemnification (cl. 3121 -Mar 2014)** Delete the word "indemnification" in the title and all of Section C."
- **FAR 52.227-3 Patent Indemnity (Apr 1984)** This clause is self-deleting because work being performed under this contract does not include the delivery of commercial items.
- **FAR 52.227-10 Filing of Patent Applications-Classified Subject Matter (DEC 2007)** This clause is self-deleting because this contract is not expected to result in a patent application containing classified subject matter.
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Integration

This Contract contains the entire understanding between the parties, and there are no understandings or representations not set forth or incorporated by reference herein. No subsequent modifications of this Contract shall be of any force or effect unless in writing signed by the party claimed to be bound thereby. No communications, written or oral, by other than a Battelle Contracts Representative shall be effective to modify or otherwise affect the provisions of this Contract.

From: Ames, Amber A [Amber.Ames@pnnl.gov]
Sent: 9/10/2020 11:34:06 AM
To: Koltz, Diane M [dkoltz@email.unc.edu]
CC: Fulcher, Leslie [leslie_fulcher@med.unc.edu]; Sandoval, Norma I [Norma.Sandoval@pnnl.gov]; Sims, Amy C [amy.sims@pnnl.gov]; Kinsey, Pamela M [Pamela.Kinsey@pnnl.gov]
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form
Attachments: GP-A-409.24-FP_October 2019.pdf; MLI Order Form Oct2019 (002).docx; PO 521567.xml; Fully_Exe_PO528372.pdf

Dear Diane,

Attached please find a fully executed contract that was placed with OSP. It seems these negotiated changes should be acceptable university-wide so I am hopeful we can move this forward?

Thank you,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Ames, Amber A
Sent: Friday, July 24, 2020 3:28 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

Thank you in advance for any update you can provide.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Ames, Amber A
Sent: Thursday, July 16, 2020 1:26 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Diane,

Just checking in to see if you have an update.

Kind regards,

Amber

From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Wednesday, July 08, 2020 11:03 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I am working with my manager on reviewing the General Terms and Conditions and hope to be back with you by the end of the week.

Thanks for your patience,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Wednesday, July 8, 2020 1:22 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

Just checking in for a status update.

Kind regards,

Amber

From: Ames, Amber A
Sent: Monday, June 29, 2020 10:25 AM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

I have been advised that we would like to pursue UNC as the source of the HBE cells. I have attached our purchase order template in word. We do not customize the General Provisions so those are a .pdf. All changes will be listed in the purchase order as an alteration to the GPs—sample below. We have a long history of contracting with UNC so I have copied the Alterations we have negotiated for previous awards. Unfortunately, as a DOE M&O contractor we are also very limited on what we can negotiate. DOE requires their terms control. We understand universities cannot grant indemnity and we are confident we will be able to negotiate changes that will be acceptable to UNC and DOE.

Alterations to General Provisions

1. Permits and Responsibilities (cl. 358—Nov 1991) is hereby deleted and replaced with:

5 U.S.C. § 552(b)(4)

2. Insurance—Liability to Third Persons (cl. 378b—Mar 1996) is hereby deleted and replaced with:

5 U.S.C. § 552(b)(4)

3. Disputes (cl. 331—Nov 2014)

Delete in its entirety.

4. Insurance Requirements (cl. 378—Nov 2014) is hereby deleted and replaced with:

5 U.S.C. § 552(b)(4)

I note I have been advised we will have another order with a budget of 5 U.S.C. § 552(b)(4) so it is critical we resolve the terms and conditions.

Thank you for your assistance with this matter.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Thursday, June 18, 2020 11:06 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I received your changes for review and upon a first look, UNC cannot agree to all of the supplemental terms contained in the online documents you want to include. As a state institution, we are somewhat limited. The order form contains the minimal terms UNC requires in its contracts and we typically do not agree to changes. Is there any possibility that we could make UNC's agreement control, or not reference the terms at all, since much of what is contained in the online "purchase agreements" won't apply to what we are providing. If this is not possible, please provide me word versions of the online agreements so I can outline our requested edits and comments. Also, please note that review of the documents will take time.

Thanks,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Thursday, June 18, 2020 12:58 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Just checking in to see if there is a response to our requested changes to the order form terms.

Thanks so much!

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Wednesday, June 10, 2020 3:04 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Good Morning Amber,
Yes, once the contract is executed, Amy will be able to order as needed up to the dollar amount on the contract and during the 1 year period. I am including our contract specialist who can look at your suggested changes and she will be in touch with you soon.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 9:02 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Thanks, Leslie. The project would like to be able to order up to 10 ALI medium and 26 Normal HBE Cells from now until September 30, 2021. Are they able to order on an as-needed basis? I can incorporate a signed version of the attached into the PO for the project to use? Once I sign it, they won't be able to edit it. Perhaps we need to do a purchase order per order?

I note I provided redlines on the attached. Please advise if UNCC is able to work with the redlines.

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 5:29 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,
Thanks for emailing back, but to complete the contract, I need the agreement signed and returned to me prior to ordering. As for payment options, a check is fine, but we do have an account that funds could be wired. If that works for you, I can share that information.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 5:09 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

Attached please find Purchase Order No. 521567 to purchase up to the quantities I had listed below. Per the PO, we will place orders via the ordering website. There is no need to sign the PO—if you can acknowledge receipt and that this will work for ordering/payment purposes, that would be helpful.

I'm guessing the MLI Tissue Procurement and Cell Culture Core Facility will want a paper check mailed to the 125 Mason Farm Road address instead of paid by ACH to UNCC's main Bank of America account?

Amy, the shipping address in PES is 331 Building, Room 70. Even if a different shipping address is input in the UNCC online ordering system, any orders associated with PO 521567 will ship to 331/70. If you need a different ship to, let me know.

Thanks!

Amber A. Ames
Senior Contracts Specialist
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Pacific Northwest Division
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Richland, WA 99352
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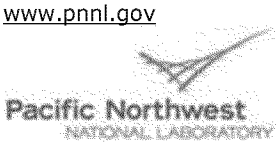

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 12:36 PM

To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,

As long as the contract is signed, the dollar amount is entered, and the period is in place there will be no rate increase.
You don't need to select the quantity of any item, but if your project you will use the quantity listed below, entering in the dollar amount is sufficient. I may suggest adding a little wiggle room in the dollar amount because once the dollar amount is reached, even before the term is up, we will need to renew the contract.

Also, once the contract is executed, you would just log onto our ordering website and order what you need.
Please let me know if you have any questions.

Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 9, 2020 1:19 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

I have a requisition to issue a Purchase Order to UNCC for a fixed unit rate contract for the following:

Description	Price	Maximum Quantity Expected	Extended Price
BEGM MEDIUM	$360		
ALI MEDIUM	$360		
VALI MEDIUM	$525		
Normal HBE Cells	$800		
Diseased HBE Cells	$800		
Cystic Fibrosis HBE Cells	$2,225		
Normal Microvascular Cells	$800		
Normal Fibroblast Cells	$800		

5 U.S.C. § 552(b)(4)

Total Not to Exceed Amount	5 U.S.C. § 552(b)(4)

The project would like to use the purchase order for payment of requirements on an as-needed basis through September 30, 2021.

My question is how long the pricing in Exhibit A of the attached is valid? Are the prices updated annually?

Do you have any concerns with this approach?

Kind regards,

Amber A. Ames
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Pacific Northwest Division
902 Battelle Blvd.
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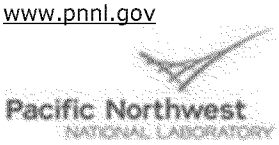

Pacific Northwest
NATIONAL LABORATORY
Proudly Operated by **Battelle** *Since 1965*

Battelle Memorial Institute, Pacific Northwest Division
Acting Under Contract DE-AC05-76RL01830
With the U.S. Department of Energy
Operating the Pacific Northwest National Laboratory (PNNL) (www.pnnl.gov)

Schedule - Contract No. 528372

Issued by:	**Name and Address of Contractor:**
Battelle Battelle Boulevard, K9-15 P.O. Box 999 Richland, WA 99352-0999 USA	University of North Carolina at Chapel Hill Office of Sponsored Research 104 Airport Drive, Suite 2200 Campus Box 1350 Chapel Hill, NC 27599-1350 USA
[redacted]	
Payment Terms: Net 30	**Contract Type:** Cost Reimbursement
Submit Invoices and Invoice/Payment Inquiries to ap.invoices@pnnl.gov. **Note:** Invoices must list location(s) of service (US: City, State; Foreign: Country).	**Total Contract Amount** 5 U.S.C. § 552(b)(4)
Contract Period of Performance: July 27, 2020 through May 31, 2021	
Award Battelle hereby agrees to award this Contract to the Contractor subject to acceptance. The rights and obligations of the parties to this Contract are subject to and governed by this document and any documents attached or incorporated by reference.	**Contractor Agreement** Contractor accepts and agrees to furnish and deliver the items or perform services to the extent stated in this document for the consideration stated in this contract. The rights and obligations of the parties to this contract are subject to and governed by this document and any documents attached or incorporated by reference.

Battelle Memorial Institute **Pacific Northwest Division**	**Contractor shall sign and return a copy of this document**
Signature of person authorized to sign. Digitally signed by Amber A. Ames Date: 2020.08.27 15:38:32 -07'00'	**Signature of person authorized to sign** JoAnne E. Shanklin Digitally signed by JoAnne E. Shanklin Date: 2020.09.10 13:27:33 -04'00'
Name Amber A. Ames	**Name** on behalf of Terry Magnuson, PH.D.
Title Contracts Specialist	Title Vice Chancellor for Research
Date	Date 09/10/2020

IMPORTANT NOTE: Any domestic and foreign travel associated with this contract (including contractor travel within a country of presence) shall be approved in writing by the Battelle Contracts Representative in advance of travel arrangements being finalized. Without the advance approval of the Battelle Contracts Representative for any such travel, any invoiced costs related to such travel will not be paid.

Statement of Work

Contractor agrees to perform the scope outlined in the attached Statement of Work dated July 16, 2020.

Indirect Rates

The following indirect cost rates are hereby established until and unless changed by mutual agreement:

Category	Rate	Base	Type	Effective
Indirect Costs	55.5%	On Campus Organized Research MTDC*	Provisional	From 07/01/2020 Through Until amended

*Modified Total Direct Costs

Fringe Benefits: *The fringe benefits are specifically identified to each employee and are charged individually as direct costs.*

The provisional rate(s) specific above may be prospectively or retroactively revised by mutual agreement, at either Battelle or the Contractor's request, to prevent substantial overpayment.

Upon establishment/approval of finalized, or final rates, for any period consistent with the period of performance, the Contractor agrees to supply such approval to Battelle, within 30 days or receipt of approval from the cognizant agency.

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  "Contractor is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."
- **Laws and Regulations, DOE Directives, and Indemnification (cl. 3121 -Mar 2014)** Delete the word "indemnification" in the title and all of Section C."
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- **FAR 52.227-10 Filing of Patent Applications-Classified Subject Matter (DEC 2007)** This clause is self-deleting because this contract is not expected to result in a patent application containing classified subject matter.
- **FAR 52.246-5 Inspection Service - Cost Reimbursement (Apr 1984)** and **FAR 52.246-8 Inspection of Research and Development—Cost Reimbursement (May 2001)** are hereby deleted and replaced with **52.246-9 Inspection of Research and Development (Short Form) (Apr 1984)**.
- **DEAR 970.5229-1 State and Local Taxes (Dec 2000)** This clause is deleted.

Integration

This Contract contains the entire understanding between the parties, and there are no understandings or representations not set forth or incorporated by reference herein. No subsequent modifications of this Contract shall be of any force or effect unless in writing signed by the party claimed to be bound thereby. No communications, written or oral, by other than a Battelle Contracts Representative shall be effective to modify or otherwise affect the provisions of this Contract.

From:	Sims, Amy C[amy.sims@pnnl.gov]
Attendees:	Fritch, Ethan James
Location:	Phone call or we could try Teams if you want
Subject:	Catch up with Ethan
Importance:	Normal
Start Time:	Thur 9/17/2020 1:00:00 PM (UTC-07:00)
End Time:	Thur 9/17/2020 2:30:00 PM (UTC-07:00)
Required Attendees:	Fritch, Ethan James

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Mon 9/14/2020 7:06:06 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: RE: Adding NL63?

What address should I use for the NL63 virus?

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, September 2, 2020 12:31 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: Adding NL63?

Sounds great. Sarah Leist should have stocks of both of the NL63 viruses and she already knows you will be asking for them.

Thank you, Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Wednesday, September 2, 2020 at 9:26 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Adding NL63?

Amy,

I just sent an email to Boyd, Tim, and Lisa to start getting an idea of the availability of these viruses and when we could realistically expect to have them ready to ship. I will keep you updated.

I've been sending out the SARS2 viruses non-stop so those will be easy. And I just sent some NL63-GFP today, so I can definitely get that one sent easily and soon. Assuming I can track down the spike point mutation version, I'll aim to send the two NL63 viruses the week of Sept 14th.

I will also submit a request to amend the MTA right now, to add the NL63 viruses.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, September 2, 2020 11:37 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Cc: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Re: Adding NL63?

Hi Ben,

Yes this is still the list. Please add both the wild type NL63 plus spike point mutation and NL63 expressing GFP to the MTA. I appreciate it.

I appreciate the offer to ship next week but Monday is a holiday and you won't have access to dry ice. It would be best to wait until the week of Sept. 14th.

If you could send me the two NL63 strains then that would be amazing. Let me know when you would like the address etc.

The BL3 strains will have to be shipped in a couple of different shipments and will need to go to the lab in Seattle which will require more coordination especially for the select agent transfer of the 2003 strain of SARS-CoV.

We can discuss this further once we can agree on shipping dates. Thank you very much. Amy

---

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, September 1, 2020 at 11:12 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Adding NL63?

- wild type infectious clone derived Middle East Respiratory syndrome coronavirus (MERS-CoV)
- MERS-CoV expressing the red fluorescent protein gene
- MERS-CoV expressing the nanoluciferase protein gene
- MERS-CoV delta open reading frame 3 to 5 (MERS-CoV delta 3-5)
- Wild type infectious clone derived severe acute respiratory syndrome coronavirus 2002-2003 outbreak** select agent (SARS-CoV)
- Wild type infectious clone derived SARS-CoV 2
- SARS-CoV 2 expressing the green fluorescent protein gene
- SARS-CoV 2 expressing the nanoluciferase protein gene

Is this still the full list? Plus the NL63?

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, September 1, 2020 2:02 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: FW: Adding NL63?

Hi Ben,

Just wanted to make sure you saw this! Thank you, Amy

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Thursday, August 20, 2020 at 9:34 AM
To: "McGlaughon, Ben" <benmcg@email.unc.edu>
Cc: "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: Adding NL63?

Ben,

I hope you are doing well and transitioning to working in the Baric laboratory in the weirdness of the pandemic.

Can you please talk to Ralph about adding human coronavirus NL63 to our existing MTA?

I would like both the current wild type strain (should contain a point mutation in spike following tissue culture adaptation) and the virus expressing green fluorescent protein GFP. Sarah Leist should have stocks of these at BSL2.

I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 9/14/2020 7:42:55 AM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]; Leist, Sarah Rebecca[leist@email.unc.edu]
Subject: Re: Adding NL63?

Hi Ben and Sarah,

Sorry I owe you and Sarah email responses. I have a presentation in a few minutes for a conference being held on Zoom.

I will catch up on emails this afternoon. Do you mind waiting to ship until Tuesday or Wednesday of this week?

Thank you very much! Amy

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To: Sims, Amy C
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What address should I use for the NL63 virus?

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To: Sims, Amy C[amy.sims@pnnl.gov]; Leist, Sarah Rebecca[leist@email.unc.edu]
Subject: RE: Adding NL63?

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Thank you very much, Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 9/14/2020 9:21:26 AM (UTC-07:00)
To: Leist, Sarah Rebecca[leist@email.unc.edu]
Subject: Re: Hello and a little help please

Hi Sarah,

I figured given how well the virus grew in the experiments you and I did together if you could send me some of that stock it would do nicely.

Is that possible? A couple of tubes each of the wild type, p11 and GFP virus would be amazing if possible.

Does that make sense? Ben is ready to ship this week if that works for you. Thank you! Amy

PS Hope the move was uneventful! We are doing okay but have had some very smokey days here due to all of the wild fires.

From: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Date: Wednesday, September 9, 2020 at 1:17 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Hello and a little help please

Hi Amy,
Sorry for the delay…
I found many different p11's and I found p11-GFP (from TPS).
Is this what you'll need?
Should I just let Ben know where it is and he handles it from there?

Hope you're doing fine!

Thanks,
Sarah

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Wednesday, August 26, 2020 at 11:28 AM
To: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Subject: Re: Hello and a little help please

Hi Sarah,

Moving is super exciting! I hope you like your new place and that they love cats! That would be awesome and hopefully not too long of a freezer dive in Little Switzerland. Thank you very much!! I appreciate you making time to respond! Thank you again, Amy

---

From: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Date: Wednesday, August 26, 2020 at 6:30 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Hello and a little help please

Hi Amy,

I can have a look later this week.
I'm moving right now.

Sorry for the delay!

Hope you're doing fine!

Sarah

Sent from my iPhone

On Aug 20, 2020, at 12:41 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:

Hi Sarah!

I hope you and your kitty clan are doing well! I hope the boys transitioned to the US well and that everyone is getting along nicely! And that there is still somewhere for you to sleep in your apartment.

I know you are crazy busy but I am hoping you can help me with something that maybe won't take too long.

Could you help Ben with finding a few vials of the NL63 stocks from the experiment you and I worked on previously? I am asking to get the wild type (with the S point mutation) and the one with GFP. If you can't find these please let me know.
I really appreciate it as I know you are totally slammed. Congratulations on the publications! That is really great!

Thank you very much! I miss getting to catch up with you and I really hope you are getting a little down time to enjoy life! Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Mon 9/14/2020 6:51:22 PM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]; Leist, Sarah Rebecca[leist@email.unc.edu]
Subject: Re: Adding NL63?

Dear Ben and Sarah,

In true 2020 fashion I am going to have to ask you to delay the shipment of NL63 to PNNL. The lab was closed today and will be closed again tomorrow due to the hazardous levels of smoke in the air from all of the wild fires burning on the west coast.

We thought things were going to clear up today but that has not happened and may not happen for a few more days and I wanted to make sure I am there to get the box.

Right now we most likely will need to push the shipment back until the week of October 5th. Please let me know if that will work for you.

Thank you for your patience. I am very ready for this year to end! Thank you both very much! Best wishes, Amy

---

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Monday, September 14, 2020 at 7:51 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "Leist, Sarah Rebecca" <leist@email.unc.edu>
Subject: RE: Adding NL63?

I was planning for tomorrow at the earliest, so not a problem.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, September 14, 2020 10:43 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>; Leist, Sarah Rebecca <leist@email.unc.edu>
Subject: Re: Adding NL63?

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Thank you very much! Amy

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What address should I use for the NL63 virus?

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Sent: Mon 9/14/2020 7:05:01 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Cc: McGlaughon, Ben[benmcg@email.unc.edu]
Subject: Re: Adding NL63?

Hi Amy,
No problem - it actually works better for me.
That'll actually work better for me - I still need to look up the exact stocks that we used back then.
Just give me one or two days lead time and we should be fine.

Stay safe - those fires are scary (at least for a German!).

Best,
Sarah

Sent from my iPhone

On Sep 14, 2020, at 9:51 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:

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Subject: Re: Adding NL63?

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We can discuss this further once we can agree on shipping dates. Thank you very much. Amy

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From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, September 1, 2020 at 11:12 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Adding NL63?

- wild type infectious clone derived Middle East Respiratory syndrome coronavirus (MERS-CoV)

- MERS-CoV expressing the red fluorescent protein gene
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- SARS-CoV 2 expressing the green fluorescent protein gene
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Is this still the full list? Plus the NL63?

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, September 1, 2020 2:02 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: FW: Adding NL63?

Hi Ben,

Just wanted to make sure you saw this! Thank you, Amy

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Thursday, August 20, 2020 at 9:34 AM
To: "McGlaughon, Ben" <benmcg@email.unc.edu>
Cc: "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: Adding NL63?

Ben,

I hope you are doing well and transitioning to working in the Baric laboratory in the weirdness of the pandemic.

Can you please talk to Ralph about adding human coronavirus NL63 to our existing MTA?

I would like both the current wild type strain (should contain a point mutation in spike following tissue culture adaptation) and the virus expressing green fluorescent protein GFP. Sarah Leist should have stocks of these at BSL2.

I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Tue 9/15/2020 12:53:21 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]; Leist, Sarah Rebecca[leist@email.unc.edu]
Subject: RE: Adding NL63?

Sorry, Amy! I hope you're able to stay safe/healthy. This year really does suck. Just keep us posted on feasible shipping dates. I still have a lot of the BSL3 viruses left to locate anyway, this will give me more time to work on that.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, September 14, 2020 9:51 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>; Leist, Sarah Rebecca <leist@email.unc.edu>
Subject: Re: Adding NL63?

Dear Ben and Sarah,

In true 2020 fashion I am going to have to ask you to delay the shipment of NL63 to PNNL. The lab was closed today and will be closed again tomorrow due to the hazardous levels of smoke in the air from all of the wild fires burning on the west coast.

We thought things were going to clear up today but that has not happened and may not happen for a few more days and I wanted to make sure I am there to get the box.

Right now we most likely will need to push the shipment back until the week of October 5th. Please let me know if that will work for you.

Thank you for your patience. I am very ready for this year to end! Thank you both very much! Best wishes, Amy

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From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Monday, September 14, 2020 at 7:51 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "Leist, Sarah Rebecca" <leist@email.unc.edu>
Subject: RE: Adding NL63?

I was planning for tomorrow at the earliest, so not a problem.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, September 14, 2020 10:43 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>; Leist, Sarah Rebecca <leist@email.unc.edu>
Subject: Re: Adding NL63?

Hi Ben and Sarah,

Sorry I owe you and Sarah email responses. I have a presentation in a few minutes for a conference being held on Zoom.

I will catch up on emails this afternoon. Do you mind waiting to ship until Tuesday or Wednesday of this week?

Thank you very much! Amy

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Subject: RE: Adding NL63?

What address should I use for the NL63 virus?

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Sent: Wednesday, September 2, 2020 12:31 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
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Thank you, Amy

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Amy,

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I've been sending out the SARS2 viruses non-stop so those will be easy. And I just sent some NL63-GFP today, so I can definitely get that one sent easily and soon. Assuming I can track down the spike point mutation version, I'll aim to send the two NL63 viruses the week of Sept 14th.

I will also submit a request to amend the MTA right now, to add the NL63 viruses.

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Sent: Tue 9/15/2020 1:39:51 PM (UTC-07:00)
To: McGlaughon, Ben[benmcg@email.unc.edu]; Leist, Sarah Rebecca[leist@email.unc.edu]
Subject: Re: Adding NL63?

Hi Ben and Sarah,

This just one more thing to add to the crazy list. At least this will leave more rapidly than the crazy hurricane heading for my relatives in AL!

I will keep you posted on dates that will work! Hope you both are doing well too! Thank you for getting back to me! Amy

---

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, September 15, 2020 at 12:55 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "Leist, Sarah Rebecca" <leist@email.unc.edu>
Subject: RE: Adding NL63?

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Thank you very much, Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 9/17/2020 8:44:03 AM (UTC-07:00)
To: Belsito, Erica L[Erica.Belsito@pnnl.gov]; UNC Office of Tech Dev MTA[mta@unc.edu]
Cc: ^PNNL NDA Specialist[ndaspecialist@pnnl.gov]; benmcg@email.unc.edu[benmcg@email.unc.edu]
Subject: Re: REVISION OF 529913_MTA_Battelle_University of North Carolina. FW: Amendment to MO-16244

Thank you, Erica. I appreciate it. Amy

From: "Belsito, Erica L" <Erica.Belsito@pnnl.gov>
Date: Thursday, September 17, 2020 at 8:43 AM
To: UNC Office of Tech Dev MTA <mta@unc.edu>
Cc: ^PNNL NDA Specialist <ndaspecialist@pnnl.gov>, "Sims, Amy C" <amy.sims@pnnl.gov>, "benmcg@email.unc.edu" <benmcg@email.unc.edu>
Subject: FW: REVISION OF 529913_MTA_Battelle_University of North Carolina. FW: Amendment to MO-16244

Good morning Dr. Whitman,
Please find attached Battelle's signed version of the Amendment. Thank you.

Erica Belsito
IP Specialist
Intellectual Property Legal Services
Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999, MSIN K1-53
Richland, WA 99354
Tel: 509-375-6518
Fax: 509-375-4487
erica.belsito@pnnl.gov

From: UNC Office of Tech Dev MTA <mta@unc.edu>
Date: Thursday, September 3, 2020 at 9:06 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Cc: "McGlaughon, Ben" <benmcg@email.unc.edu>, UNC Office of Tech Dev MTA <mta@unc.edu>
Subject: RE: Amendment to MO-16244

Thanks, Ben.

Amy, please find attached a draft amendment that adds the below mentioned material to the original MTA. Let me know there are any questions or if PNNL requests any revisions.

Thanks,
Nate

Nathan Whitman, PhD
Licensing Fellow

THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
INNOVATION, ENTREPRENEURSHIP AND ECONOMIC DEVELOPMENT – INNOVATE CAROLINA
Office of Technology Commercialization

Campus Box 4105
109 Church Street | Chapel Hill, NC 27516
T: 919.962.6369 | F: 919.962.0646
Email: nathan.whitman@unc.edu | Twitter: @innovateunc | Facebook: @InnovateUNC
Web: otc.unc.edu | innovate.unc.edu

From: McGlaughon, Ben <benmcg@email.unc.edu>
Sent: Wednesday, September 2, 2020 12:37 PM
To: UNC Office of Tech Dev MTA <mta@unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>
Subject: Amendment to MO-16244

Nate,

I'd like to amend MO-16244 to add a couple more viruses, if possible. I have copied Amy Sims who should be able to coordinate on behalf of the recipients.

We would like to add:

- wild type human coronavirus NL63 plus spike point mutation
- human coronavirus NL63 expressing GFP

Let me know if you need any further information from me. Thanks!

Ben

Ben McGlaughon, MS
Baric Lab Manager | UNC-Chapel Hill
(919) 966-7991
benmcg@unc.edu

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 9/17/2020 5:22:18 PM (UTC-07:00)
To: Fritch, Ethan James[ejfritch@email.unc.edu]; Dinnon, Kenneth Harold[kdinnon@email.unc.edu]
Subject: Neutral red help please

Hi guys,

I have powdered neutral red and I need to make 10X stock. Can you remind me of how much neutral red powder and sodium chloride I need to add for a liter?

Thank you! Was awesome to catch up with you both! Amy

From: Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]
Sent: Thur 9/17/2020 5:49:34 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Cc: Fritch, Ethan James[ejfritch@email.unc.edu]
Subject: Re: Neutral red help please

No problem!

8.5g NaCl
5g Neutral Red
1L water

Yeah I'm glad we could catch up!

KD3

On Sep 17, 2020, at 8:22 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:

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Sent: Thur 9/17/2020 6:05:47 PM (UTC-07:00)
To: Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]
Cc: Fritch, Ethan James[ejfritch@email.unc.edu]
Subject: Re: Neutral red help please

Thank you! Last one! Can you send me the recipe for 2X media for plaque assays?? Thank you! Amy

---

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Date: Thursday, September 17, 2020 at 5:49 PM
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Cc: "Fritch, Ethan James" <ejfritch@email.unc.edu>
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To: Sims, Amy C[amy.sims@pnnl.gov]
Cc: Fritch, Ethan James[ejfritch@email.unc.edu]
Subject: Re: Neutral red help please

I use 2X DMEM, supplemented to 10% FCII and 2X anti/anti (for a final of 5% FCII and 1X anti/anti) and make 2X agarose at 1.6% for a final of 0.8%.

Some others in the lab use 20% (final 10%) FCII for their plaque assays, not sure which camp you were in.

Kenny

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Thursday, September 17, 2020 at 9:05 PM
To: "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu>
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From: Fritch, Ethan James[ejfritch@email.unc.edu]
Sent: Fri 9/18/2020 6:16:48 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]; Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]
Subject: Re: Neutral red help please

To make 1L 2x Media:

940 mL Autoclaved DI H2O
2 Packets Gibco DMEM powder
60 mL Gibco Sodium Bicarbonate

Vacuum Filter

From: Sims, Amy C <amy.sims@pnnl.gov>
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To: Fritch, Ethan James[ejfritch@email.unc.edu]; Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]
Subject: Re: Neutral red help please

Thank you guys! I really appreciate it. Have a great Friday and weekend!! Amy

Get Outlook for iOS

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Thank you very much. Best wishes, Amy Sims

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Date: Friday, September 18, 2020 at 1:48 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "Belsito, Erica L" <Erica.Belsito@pnnl.gov>, UNC Office of Tech Dev MTA <mta@unc.edu>
Cc: ^PNNL NDA Specialist <ndaspecialist@pnnl.gov>, "McGlaughon, Ben" <benmcg@email.unc.edu>
Subject: RE: REVISION OF 529913_MTA_Battelle_University of North Carolina. FW: Amendment to MO-16244

Hi all,

Please find attached a copy of the fully executed agreement for your records. Let us know if we can provide any further assistance.

Best,
Nate

Nathan Whitman, PhD
Licensing Fellow

THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
INNOVATION, ENTREPRENEURSHIP AND ECONOMIC DEVELOPMENT – INNOVATE CAROLINA
Office of Technology Commercialization
Campus Box 4105
109 Church Street | Chapel Hill, NC 27516
T: 919.962.6369 | F: 919.962.0646
Email: nathan.whitman@unc.edu | Twitter: @innovateunc | Facebook: @InnovateUNC
Web: otc.unc.edu | innovate.unc.edu

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Thursday, September 17, 2020 11:44 AM
To: Belsito, Erica L <Erica.Belsito@pnnl.gov>; UNC Office of Tech Dev MTA <mta@unc.edu>
Cc: ^PNNL NDA Specialist <ndaspecialist@pnnl.gov>; McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: REVISION OF 529913_MTA_Battelle_University of North Carolina. FW: Amendment to MO-16244

Thank you, Erica. I appreciate it. Amy

From: "Belsito, Erica L" <Erica.Belsito@pnnl.gov>
Date: Thursday, September 17, 2020 at 8:43 AM
To: UNC Office of Tech Dev MTA <mta@unc.edu>
Cc: ^PNNL NDA Specialist <ndaspecialist@pnnl.gov>, "Sims, Amy C" <amy.sims@pnnl.gov>, "benmcg@email.unc.edu" <benmcg@email.unc.edu>
Subject: FW: REVISION OF 529913_MTA_Battelle_University of North Carolina. FW: Amendment to MO-16244

Good morning Dr. Whitman,
Please find attached Battelle's signed version of the Amendment. Thank you.

Erica Belsito
IP Specialist
Intellectual Property Legal Services
Pacific Northwest National Laboratory
902 Battelle Boulevard
P.O. Box 999, MSIN K1-53
Richland, WA 99354
Tel: 509-375-6518
Fax: 509-375-4487
erica.belsito@pnnl.gov

From: UNC Office of Tech Dev MTA <mta@unc.edu>
Date: Thursday, September 3, 2020 at 9:06 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Cc: "McGlaughon, Ben" <benmcg@email.unc.edu>, UNC Office of Tech Dev MTA <mta@unc.edu>
Subject: RE: Amendment to MO-16244

Thanks, Ben.

Amy, please find attached a draft amendment that adds the below mentioned material to the original MTA. Let me know there are any questions or if PNNL requests any revisions.

Thanks,
Nate

Nathan Whitman, PhD
Licensing Fellow

THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
INNOVATION, ENTREPRENEURSHIP AND ECONOMIC DEVELOPMENT – INNOVATE CAROLINA
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Campus Box 4105
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T: 919.962.6369 | F: 919.962.0646
Email: nathan.whitman@unc.edu | Twitter: @innovateunc | Facebook: @InnovateUNC
Web: otc.unc.edu | innovate.unc.edu

From: McGlaughon, Ben <benmcg@email.unc.edu>
Sent: Wednesday, September 2, 2020 12:37 PM
To: UNC Office of Tech Dev MTA <mta@unc.edu>
Cc: Sims, Amy C <amy.sims@pnnl.gov>
Subject: Amendment to MO-16244

Nate,

I'd like to amend MO-16244 to add a couple more viruses, if possible. I have copied Amy Sims who should be able to coordinate on behalf of the recipients.

We would like to add:

- wild type human coronavirus NL63 plus spike point mutation
- human coronavirus NL63 expressing GFP

Let me know if you need any further information from me. Thanks!

Ben

Ben McGlaughon, MS
Baric Lab Manager | UNC-Chapel Hill
(919) 966-7991
benmcg@unc.edu

From: Baric, Ralph S [rbaric@email.unc.edu]
Sent: 9/22/2020 8:26:20 AM
To: Sims, Amy C [amy.sims@pnnl.gov]
CC: Edwards, Caitlin E [caitedw@unc.edu]
Subject: RE: Reminder to renew DEA registration

Wrong email address, this is the right one

From: Baric, Ralph S
Sent: Tuesday, September 22, 2020 11:25 AM
To: Sims, Amy C <sims0018@email.unc.edu>
Cc: Edwards, Caitlin E <caitedw@unc.edu>
Subject: RE: Reminder to renew DEA registration

Hi Amy, Hi—hope you all aren't burning up in the PNW. Looks bad out there. The SADS PNAS paper proofs are here. Do you want us to change affiliation to Pacific Northwest Natl Labs? If so, send your address/contact info to Caitlin. Hope your doing well. Ralph

---

From: Sims, Amy C <sims0018@email.unc.edu>
Sent: Wednesday, February 12, 2020 8:07 PM
To: Sheahan, Timothy Patrick <sheahan@email.unc.edu>; Baric, Ralph S <rbaric@email.unc.edu>
Subject: Fw: Reminder to renew DEA registration

Hope you guys are already on this.

Email will likely die tomorrow. Thank you. Amy

From: DEA <DEA.Validation@usdoj.gov>
Sent: Wednesday, February 12, 2020 7:51:33 PM
To: Sims, Amy C <sims0018@email.unc.edu>
Subject: Reminder to renew DEA registration

Dear Registrant (DEA Number(s) **5 U.S.C. § 552(b)(6)**

Your DEA Certificate of Registration will expire at the end of this month. It is recommended you complete your renewal application online at **5 U.S.C. § 552(b)(6)** Please read all instructions before logging in to begin the renewal process.

Federal law prohibits you from handling controlled substances or List 1 chemicals once the DEA registration has expired and it is in a retired status.

Please do not respond to this email as it is not monitored. If you have questions, send an email to DEA.Registration.Help@usdoj.gov

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 9/22/2020 8:42:47 AM (UTC-07:00)
To: Baric, Ralph S[rbaric@email.unc.edu]
Cc: Edwards, Caitlin E[caitedw@unc.edu]
Subject: Re: Reminder to renew DEA registration

Hi Ralph,

We didn't have any actual fires in the area but on Labor Day and then again for more than a week a few days later we had so much smoke and ash in the sky that the air was too hazardous to breath. PNNL closed for 2.5 days and our dog Maddie got hives! Just another non-magical thing to add to the 2020 list.

Hi Caitlin! Congratulations! You have had an amazing year for publications! Of course. You can list my affiliation as the following.

Current address: Chemical and Biological Signatures Division, Pacific Northwest National Laboratory, Richland, WA USA.

Thank you very much for including me! Sorry I didn't contribute more during the submission process.

Have a great rest of the week. Thank you! Amy

From: "Baric, Ralph S" <rbaric@email.unc.edu>
Date: Tuesday, September 22, 2020 at 8:27 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Cc: "Edwards, Caitlin E" <caitedw@unc.edu>
Subject: RE: Reminder to renew DEA registration

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From: Baric, Ralph S
Sent: Tuesday, September 22, 2020 11:25 AM
To: Sims, Amy C <sims0018@email.unc.edu>
Cc: Edwards, Caitlin E <caitedw@unc.edu>
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From: Edwards, Caitlin E [caitedw@unc.edu]
Sent: 9/22/2020 9:26:23 AM
To: Sims, Amy C [amy.sims@pnnl.gov]; Baric, Ralph S [rbaric@email.unc.edu]
Subject: Re: Reminder to renew DEA registration

Thanks, Amy! Glad to hear that you haven't had to face fires in the area, but definitely sorry to hear the air has been so bad. Fingers crossed that things start to clear up soon.

I will update your affiliation as I go through the proofs. Thanks for your help!

I hope you're doing awesome despite the craziness that is 2020 – we miss you!!

Cait

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Tuesday, September 22, 2020 at 11:42 AM
To: "Baric, Ralph S" <rbaric@email.unc.edu>
Cc: "Edwards, Caitlin E" <caitedw@unc.edu>
Subject: Re: Reminder to renew DEA registration

Hi Ralph,

We didn't have any actual fires in the area but on Labor Day and then again for more than a week a few days later we had so much smoke and ash in the sky that the air was too hazardous to breath. PNNL closed for 2.5 days and our dog Maddie got hives! Just another non-magical thing to add to the 2020 list.

Hi Caitlin! Congratulations! You have had an amazing year for publications! Of course. You can list my affiliation as the following.

Current address: Chemical and Biological Signatures Division, Pacific Northwest National Laboratory, Richland, WA USA.

Thank you very much for including me! Sorry I didn't contribute more during the submission process.

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Please do not respond to this email as it is not monitored. If you have questions, send an email to DEA.Registration.Help@usdoj.gov

From: Baric, Ralph S[rbaric@email.unc.edu]

Sent: Wed 9/23/2020 7:56:21 AM (UTC-07:00)

To: Subbarao, Kanta[kanta.subbarao@influenzacentre.org]

Cc: Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]; Leist, Sarah Rebecca[leist@email.unc.edu]; Sims, Amy C[amy.sims@pnnl.gov]; McGlaughon, Ben[benmcg@email.unc.edu]

Subject: RE: MA SARS-CoV-2 and NL63

Hi Kanta, nice to hear from you. The mouse adapted paper is in press in Cell and I will send along a copy of the proof when we receive it. We have recombinant NL63 (PMC2583659), and selected a variant which has a mutation or two and grows better in primary human airway cells and in Vero cells (If I remember correctly). Sarah/Amy, do you remember where those mutations are and for that matter how we selected it-HAE or continuous cells in culture? Amy Sims also has some primate data showing the new virus grew in primates better than wildtype (Amy this right? we haven't published on it yet). Ralph

-----Original Message-----
From: Subbarao, Kanta <kanta.subbarao@influenzacentre.org>
Sent: Friday, September 18, 2020 12:01 AM
To: Baric, Ralph S <rbaric@email.unc.edu>
Subject: MA SARS-CoV-2 and NL63

Hi Ralph-

I have two questions for you-

1. On the SARS-CoV-2 front, it was great hearing the progress you have made with the p10 MA virus. I am keen to try and get that virus from you but we will have to get high level approval from the Gene Therapy Regulatory Authority here. I have the Dinnon preprint. Do you have a follow up paper in preprint form describing the passage? Can you put me in touch with someone in your lab who can work with my postdoc who is putting together our application? It will take weeks/months to get approval!
2. We are working on developing a human challenge infection model for NL63 and got a virus from Lia van der Hoek but we are not sure it will grow in Vero cells. Do you have any thoughts on NL63 (WT or reverse genetics derived) growth in Vero cells?

Thanks
Kanta

[cid:image001.png@01D3588B.7A1FF710]<https://protect2.fireeye.com/v1/url?k=8ca86387-d01d5c3e-8ca84992-0cc47adc5fce-525bf17b22158080&q=1&e=f0326a8f-ed37-47db-bfbc-4103a7b0b131&u=http%3A%2F%2Fwww.influenzacentre.org%2F>

Kanta Subbarao | Director
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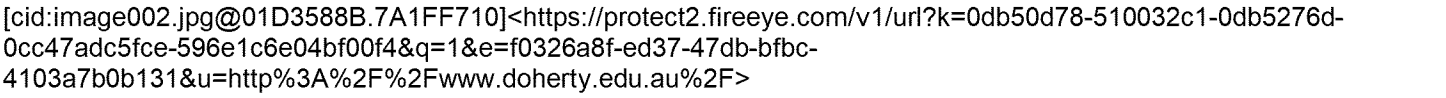
F +61 (0) 3 9342 9329

WHO Collaborating Centre for Reference and Research on Influenza The Peter Doherty Institute for Infection and Immunity
792 Elizabeth Street | Melbourne | Victoria | Australia | 3000
https://protect2.fireeye.com/v1/url?k=da8cde0b-8639e1b2-da8cf41e-0cc47adc5fce-cf847eeb65e0c183&q=1&e=f0326a8f-ed37-47db-bfbc-4103a7b0b131&u=http%3A%2F%2Fwww.influenzacentre.org%2F<https://protect2.fireeye.com/v1/url?k=a54a22f9-f9ff1d40-a54a08ec-0cc47adc5fce-d745ced5af585e41&q=1&e=f0326a8f-ed37-47db-bfbc-4103a7b0b131&u=http%3A%2F%2Fwww.influenzacentre.org%2F> https://protect2.fireeye.com/v1/url?k=64d03cff-38650346-64d016ea-0cc47adc5fce-f93797a6e618e5ac&q=1&e=f0326a8f-ed37-47db-bfbc-4103a7b0b131&u=http%3A%2F%2Fwww.doherty.edu.au%2F<https://protect2.fireeye.com/v1/url?k=aa6a6421-f6df5b98-aa6a4e34-0cc47adc5fce-f575a45ae1bbe061&q=1&e=f0326a8f-ed37-47db-bfbc-4103a7b0b131&u=http%3A%2F%2Fwww.doherty.edu.au%2F>

Professor, Department of Microbiology and Immunology, The University of Melbourne E

kanta.subbarao@unimelb.edu.au<mailto:kanta.subbarao@influenzacentre.org>



From: Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]

Sent: Wed 9/23/2020 11:15:32 AM (UTC-07:00)

To: Baric, Ralph S[rbaric@email.unc.edu]; Subbarao, Kanta[kanta.subbarao@influenzacentre.org]

Cc: Leist, Sarah Rebecca[leist@email.unc.edu]; Sims, Amy C[amy.sims@pnnl.gov]; McGlaughon, Ben[benmcg@email.unc.edu]

Subject: Re: MA SARS-CoV-2 and NL63

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I am working on rederiving the plaque purified virus from a clone now, and there is a good chance that is what we will have available to share in a few months. I am not sure the regulations for you on recombinant versus not (though the parental MA virus is recombinant derived). Feel free to bug me for any information you may need.

As for NL63, Amy is definitely the key person for that info, but we culture NL63 in LLCMK2 cells, and more successfully in LLCMK2 cells (rhesus mcacque kidney epithelial cell line) that we have engineered to overexpress TMPRSS2. Our standard strain of NL63 in lab is the one Ralph alluded to which I believe (Amy please correct me!) was temperature selected at 32* in LLCMK2 cells to mimic upper respiratory tract temperature. I am not familiar with any data on trying to grow NL63 in Vero cells (my guess is it doesn't work based on our use of LLCMK2 cells instead) or in HAEs.

Best,
Kenny

On 9/23/20, 10:56 AM, "Baric, Ralph S" <rbaric@email.unc.edu> wrote:

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Kanta

[cid:image001.png@01D3588B.7A1FF710]<http://www.influenzacentre.org/>

Kanta Subbarao | Director
T +61 (0) 3 9342 9310 | E kanta.subbarao@influenzacentre.org<mailto:kanta.subbarao@influenzacentre.org>

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WHO Collaborating Centre for Reference and Research on Influenza The Peter Doherty Institute for Infection and Immunity
792 Elizabeth Street | Melbourne | Victoria | Australia | 3000
www.influenzacentre.org<http://www.influenzacentre.org/> www.doherty.edu.au<http://www.doherty.edu.au/>

Professor, Department of Microbiology and Immunology, The University of Melbourne E kanta.subbarao@unimelb.edu.au<mailto:kanta.subbarao@influenzacentre.org>

From: Subbarao, Kanta[kanta.subbarao@influenzacentre.org]

Sent: Wed 9/23/2020 3:55:25 PM (UTC-07:00)

To: Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]; Baric, Ralph S[rbaric@email.unc.edu]

Cc: Leist, Sarah Rebecca[leist@email.unc.edu]; Sims, Amy C[amy.sims@pnnl.gov]; McGlaughon, Ben[benmcg@email.unc.edu]; Jessica Neil[jessica.neil@unimelb.edu.au]

Subject: Re: MA SARS-CoV-2 and NL63

Thank you very much, Kenny and Ralph.
I am copying Jessica in- she will start working on the paperwork for the MA SARS-CoV-2. We will need to do a fair bit of paperwork because it starts with an RG virus that increased host range. But we'll get there!

I will follow up with you separately about NL 63- any additional information from Amy/Sarah about Vero cell growth would be welcome. I will be talking with NIAID in the next week or so.

Best wishes,
Kanta

On 24/9/20, 4:15 am, "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu> wrote:

Hello Kanta,

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Thanks

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Professor, Department of Microbiology and Immunology, The University of Melbourne E kanta.subbarao@unimelb.edu.au<mailto:kanta.subbarao@influenzacentre.org>

[cid:image002.jpg@01D3588B.7A1FF710]<http://www.doherty.edu.au/>

WARNING: This message originated from outside the Northern/Melbourne/Western Health e-mail network. The sender cannot be validated. Caution is advised. Contact IT Services for more information.

From: Sims, Amy C[amy.sims@pnnl.gov]

Sent: Wed 9/23/2020 5:02:48 PM (UTC-07:00)

To: Subbarao, Kanta[kanta.subbarao@influenzacentre.org]; Dinnon, Kenneth Harold III[kdinnon@email.unc.edu]; Baric, Ralph S[rbaric@email.unc.edu]

Cc: Leist, Sarah Rebecca[leist@email.unc.edu]; McGlaughon, Ben[benmcg@email.unc.edu]; Jessica Neil[jessica.neil@unimelb.edu.au]

Subject: Re: MA SARS-CoV-2 and NL63

Hi Kanta,

Good to hear from you even if it is indirectly.

As Kenny mentioned NL63 prefers to grow in LLCMK2 cells. I believe we may have tried it in Vero cells ages ago but as we continued to grow it exclusively in LLCMK2 cells I am going to say it did not work.

We typically grow NL63 at 32C so the passage adaptation was also done at that temperature in LLCMK2 cells. Passage adapted virus did grow better in NHP. I need to get that paper submitted as well.

I hope this is helpful. I will send you more details soon.

Thank you, Amy

On 9/23/20, 3:56 PM, "Subbarao, Kanta" <kanta.subbarao@influenzacentre.org> wrote:

Thank you very much, Kenny and Ralph.
I am copying Jessica in- she will start working on the paperwork for the MA SARS-CoV-2. We will need to do a fair bit of paperwork because it starts with an RG virus that increased host range. But we'll get there!

I will follow up with you separately about NL 63- any additional information from Amy/Sarah about Vero cell growth would be welcome. I will be talking with NIAID in the next week or so.

Best wishes,
Kanta

On 24/9/20, 4:15 am, "Dinnon, Kenneth Harold III" <kdinnon@email.unc.edu> wrote:

Hello Kanta,

Happy to help get you info on the virus to get paperwork started. Like Ralph said, the Cell pre-proof of the MA10 paper is out today (https://doi.org/10.1016/j.cell.2020.09.050). The virus sequence is uploaded to NCBI under accession number MT952602, but it looks like that is still embargoed and may take a day or two to become live. But I am happy to send you and/or your postdoc a sequence file too.

I am working on rederiving the plaque purified virus from a clone now, and there is a good chance that is what we will have available to share in a few months. I am not sure the regulations for you on recombinant versus not (though the parental MA virus is recombinant derived). Feel free to bug me for any information you may need.

As for NL63, Amy is definitely the key person for that info, but we culture NL63 in LLCMK2 cells, and more successfully in LLCMK2 cells (rhesus mcacque kidney epithelial cell line) that we have engineered to overexpress TMPRSS2. Our standard strain of NL63 in lab is the one Ralph alluded to which I believe (Amy please correct me!) was temperature selected at 32* in LLCMK2 cells to mimic upper respiratory tract temperature. I am not familiar with any data on trying to grow NL63 in Vero cells (my guess is it doesn't work based on our use of LLCMK2 cells instead) or in HAEs.

Best,
Kenny

On 9/23/20, 10:56 AM, "Baric, Ralph S" <rbaric@email.unc.edu> wrote:

Hi Kanta, nice to hear from you. The mouse adapted paper is in press in Cell and I will send along a copy of the proof when we receive it. We have recombinant NL63 (PMC2583659), and selected a variant which has a mutation or two and grows better in primary human airway cells and in Vero cells (If I remember correctly). Sarah/Amy, do you remember where those mutations are and for that matter how we selected it-HAE or continuous cells in culture? Amy Sims also has some primate data showing the new virus grew in primates better than wildtype (Amy this right? we haven't published on it yet). Ralph

-----Original Message-----
From: Subbarao, Kanta <kanta.subbarao@influenzacentre.org>
Sent: Friday, September 18, 2020 12:01 AM
To: Baric, Ralph S <rbaric@email.unc.edu>
Subject: MA SARS-CoV-2 and NL63

Hi Ralph-

I have two questions for you-

1. On the SARS-CoV-2 front, it was great hearing the progress you have made with the p10 MA virus. I am keen to try and get that virus from you but we will have to get high level approval from the Gene Therapy Regulatory Authority here. I have the Dinnon preprint. Do you have a follow up paper in preprint form describing the passage? Can you put me in touch with someone in your lab who can work with my postdoc who is putting together our application? It will take weeks/months to get approval!
2. We are working on developing a human challenge infection model for NL63 and got a virus from Lia van der Hoek but we are not sure it will grow in Vero cells. Do you have any thoughts on NL63 (WT or reverse genetics derived) growth in Vero cells?

Thanks
Kanta

[cid:image001.png@01D3588B.7A1FF710]<http://www.influenzacentre.org/>

Kanta Subbarao | Director
T +61 (0) 3 9342 9310 | E kanta.subbarao@influenzacentre.org<mailto:kanta.subbarao@influenzacentre.org>

F +61 (0) 3 9342 9329

WHO Collaborating Centre for Reference and Research on Influenza The Peter Doherty Institute for Infection and Immunity
792 Elizabeth Street | Melbourne | Victoria | Australia | 3000
www.influenzacentre.org<http://www.influenzacentre.org/> www.doherty.edu.au<http://www.doherty.edu.au/>

Professor, Department of Microbiology and Immunology, The University of Melbourne E kanta.subbarao@unimelb.edu.au<mailto:kanta.subbarao@influenzacentre.org>

[cid:image002.jpg@01D3588B.7A1FF710]<http://www.doherty.edu.au/>

WARNING: This message originated from outside the Northern/Melbourne/Western Health e-mail network. The sender cannot be validated. Caution is advised. Contact IT Services for more information.

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 9/24/2020 2:02:27 PM (UTC-07:00)
To: Leist, Sarah Rebecca[leist@email.unc.edu]
Cc: McGlaughon, Ben[benmcg@email.unc.edu]
Subject: Re: Adding NL63?

Hello again!

My schedule continues to be frustratingly fluid these days!

Is there any way you could ship me NL63 virus stocks Tuesday, September 29th or Wednesday, September 30th?

I may be out of town the week of October 5th now.

Is this sufficient time? If not let me know. Thank you very much! Also Ben, would it be possible to toss in a few tubes of LLCMK2 cells? I am not sure I thought to ask for those previously.

Thank you! Amy

From: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Date: Monday, September 14, 2020 at 7:05 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Cc: "McGlaughon, Ben" <benmcg@email.unc.edu>
Subject: Re: Adding NL63?

Hi Amy,
No problem - it actually works better for me.
That'll actually work better for me - I still need to look up the exact stocks that we used back then.
Just give me one or two days lead time and we should be fine.

Stay safe - those fires are scary (at least for a German!).

Best,
Sarah

Sent from my iPhone

> On Sep 14, 2020, at 9:51 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:
>
> Dear Ben and Sarah,
>
> In true 2020 fashion I am going to have to ask you to delay the shipment of NL63 to PNNL. The lab was closed today and will be closed again tomorrow due to the hazardous levels of smoke in the air from all of the wild fires burning on the west coast.
>
> We thought things were going to clear up today but that has not happened and may not happen for a few more days and I wanted to make sure I am there to get the box.

Right now we most likely will need to push the shipment back until the week of October 5th. Please let me know if that will work for you.

Thank you for your patience. I am very ready for this year to end! Thank you both very much! Best wishes, Amy

---

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Monday, September 14, 2020 at 7:51 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "Leist, Sarah Rebecca" <leist@email.unc.edu>
Subject: RE: Adding NL63?

I was planning for tomorrow at the earliest, so not a problem.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, September 14, 2020 10:43 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>; Leist, Sarah Rebecca <leist@email.unc.edu>
Subject: Re: Adding NL63?

Hi Ben and Sarah,

Sorry I owe you and Sarah email responses. I have a presentation in a few minutes for a conference being held on Zoom.

I will catch up on emails this afternoon. Do you mind waiting to ship until Tuesday or Wednesday of this week?

Thank you very much! Amy

Get Outlook for iOS

From: McGlaughon, Ben <benmcg@email.unc.edu>
Sent: Monday, September 14, 2020 7:07 AM
To: Sims, Amy C
Subject: RE: Adding NL63?

What address should I use for the NL63 virus?

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, September 2, 2020 12:31 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: Adding NL63?

Sounds great. Sarah Leist should have stocks of both of the NL63 viruses and she already knows you will be asking for them.

Thank you, Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Wednesday, September 2, 2020 at 9:26 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Adding NL63?

Amy,

I just sent an email to Boyd, Tim, and Lisa to start getting an idea of the availability of these viruses and when we could realistically expect to have them ready to ship. I will keep you updated.

I've been sending out the SARS2 viruses non-stop so those will be easy. And I just sent some NL63-GFP today, so I can definitely get that one sent easily and soon. Assuming I can track down the spike point mutation version, I'll aim to send the two NL63 viruses the week of Sept 14th.

I will also submit a request to amend the MTA right now, to add the NL63 viruses.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, September 2, 2020 11:37 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Cc: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Re: Adding NL63?

Hi Ben,

Yes this is still the list. Please add both the wild type NL63 plus spike point mutation and NL63 expressing GFP to the MTA. I appreciate it.

I appreciate the offer to ship next week but Monday is a holiday and you won't have access to dry ice. It would be best to wait until the week of Sept. 14th.

If you could send me the two NL63 strains then that would be amazing. Let me know when you would like the address etc.

The BL3 strains will have to be shipped in a couple of different shipments and will need to go to the lab in Seattle which will require more coordination especially for the select agent transfer of the 2003 strain of SARS-CoV.

We can discuss this further once we can agree on shipping dates. Thank you very much. Amy

---

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, September 1, 2020 at 11:12 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Adding NL63?

- wild type infectious clone derived Middle East Respiratory syndrome coronavirus (MERS-CoV)
- MERS-CoV expressing the red fluorescent protein gene
- MERS-CoV expressing the nanoluciferase protein gene
- MERS-CoV delta open reading frame 3 to 5 (MERS-CoV delta 3-5)
- Wild type infectious clone derived severe acute respiratory syndrome coronavirus 2002-2003 outbreak** select agent (SARS-CoV)

- Wild type infectious clone derived SARS-CoV 2
- SARS-CoV 2 expressing the green fluorescent protein gene
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Is this still the full list? Plus the NL63?

From: Sims, Amy C <amy.sims@pnnl.gov>
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Cc: "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: Adding NL63?

Ben,

I hope you are doing well and transitioning to working in the Baric laboratory in the weirdness of the pandemic.

Can you please talk to Ralph about adding human coronavirus NL63 to our existing MTA?

I would like both the current wild type strain (should contain a point mutation in spike following tissue culture adaptation) and the virus expressing green fluorescent protein GFP. Sarah Leist should have stocks of these at BSL2.

I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Thur 9/24/2020 2:04:07 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Cc: Leist, Sarah Rebecca[leist@email.unc.edu]
Subject: Re: Adding NL63?

If Sarah has the virus ready to go then I should be able to ship next week.

Ben

> On Sep 24, 2020, at 5:02 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:
>
> Hello again!
>
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Sent from my iPhone

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- SARS-CoV 2 expressing the nanoluciferase protein gene

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To: "McGlaughon, Ben" <benmcg@email.unc.edu>
Cc: "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: Adding NL63?

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Thank you very much, Amy

From: Sims, Amy C[amy.sims@pnnl.gov]

Sent: Fri 9/25/2020 11:02:54 AM (UTC-07:00)

To: rlgraham@email.unc.edu[rlgraham@email.unc.edu]; Sheahan, Timothy Patrick[sheahan@email.unc.edu]

Subject: IACUC protocol number for ethics statement

Hi,

Can either of you please send me the ethics statement for the MERS-CoV infections Tim and Adam did to collect lung samples for 'omics studies?

A group at PNNL used basically all of the previous 'omics datasets to test a new graphing method. Tim you and Adam are listed as authors. This is the one about hypergraphs.

Thank you! Hope all is well in your neck of the woods. Amy

From: Ames, Amber A [Amber.Ames@pnnl.gov]
Sent: 9/10/2020 11:34:06 AM
To: Koltz, Diane M [dkoltz@email.unc.edu]
CC: Fulcher, Leslie [leslie_fulcher@med.unc.edu]; Sandoval, Norma I [Norma.Sandoval@pnnl.gov]; Sims, Amy C [amy.sims@pnnl.gov]; Kinsey, Pamela M [Pamela.Kinsey@pnnl.gov]
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form
Attachments: GP-A-409.24-FP_October 2019.pdf; MLI Order Form Oct2019 (002).docx; PO 521567.xml; Fully_Exe_PO528372.pdf

Dear Diane,

Attached please find a fully executed contract that was placed with OSP. It seems these negotiated changes should be acceptable university-wide so I am hopeful we can move this forward?

Thank you,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Ames, Amber A
Sent: Friday, July 24, 2020 3:28 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

Thank you in advance for any update you can provide.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Ames, Amber A
Sent: Thursday, July 16, 2020 1:26 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Diane,

Just checking in to see if you have an update.

Kind regards,

Amber

From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Wednesday, July 08, 2020 11:03 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I am working with my manager on reviewing the General Terms and Conditions and hope to be back with you by the end of the week.

Thanks for your patience,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Wednesday, July 8, 2020 1:22 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

Just checking in for a status update.

Kind regards,

Amber

From: Ames, Amber A
Sent: Monday, June 29, 2020 10:25 AM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

I have been advised that we would like to pursue UNC as the source of the HBE cells. I have attached our purchase order template in word. We do not customize the General Provisions so those are a .pdf. All changes will be listed in the purchase order as an alteration to the GPs—sample below. We have a long history of contracting with UNC so I have copied the Alterations we have negotiated for previous awards. Unfortunately, as a DOE M&O contractor we are also very limited on what we can negotiate. DOE requires their terms control. We understand universities cannot grant indemnity and we are confident we will be able to negotiate changes that will be acceptable to UNC and DOE.

Alterations to General Provisions

1. Permits and Responsibilities (cl. 358—Nov 1991) is hereby deleted and replaced with:

5 U.S.C. § 552(b)(4)

2. Insurance—Liability to Third Persons (cl. 378b—Mar 1996) is hereby deleted and replaced with:

5 U.S.C. § 552(b)(4)

3. Disputes (cl. 331—Nov 2014)

Delete in its entirety.

4. Insurance Requirements (cl. 378—Nov 2014) is hereby deleted and replaced with:

5 U.S.C. § 552(b)(4)

I note I have been advised we will have another order with a budget of 5 U.S.C. § 552(b)(4) so it is critical we resolve the terms and conditions.

Thank you for your assistance with this matter.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Thursday, June 18, 2020 11:06 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I received your changes for review and upon a first look, UNC cannot agree to all of the supplemental terms contained in the online documents you want to include. As a state institution, we are somewhat limited. The order form contains the minimal terms UNC requires in its contracts and we typically do not agree to changes. Is there any possibility that we could make UNC's agreement control, or not reference the terms at all, since much of what is contained in the online "purchase agreements" won't apply to what we are providing. If this is not possible, please provide me word versions of the online agreements so I can outline our requested edits and comments. Also, please note that review of the documents will take time.

Thanks,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Thursday, June 18, 2020 12:58 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Just checking in to see if there is a response to our requested changes to the order form terms.

Thanks so much!

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Wednesday, June 10, 2020 3:04 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Good Morning Amber,
Yes, once the contract is executed, Amy will be able to order as needed up to the dollar amount on the contract and during the 1 year period. I am including our contract specialist who can look at your suggested changes and she will be in touch with you soon.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 9:02 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Thanks, Leslie. The project would like to be able to order up to 10 ALI medium and 26 Normal HBE Cells from now until September 30, 2021. Are they able to order on an as-needed basis? I can incorporate a signed version of the attached into the PO for the project to use? Once I sign it, they won't be able to edit it. Perhaps we need to do a purchase order per order?

I note I provided redlines on the attached. Please advise if UNCC is able to work with the redlines.

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 5:29 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,
Thanks for emailing back, but to complete the contract, I need the agreement signed and returned to me prior to ordering. As for payment options, a check is fine, but we do have an account that funds could be wired. If that works for you, I can share that information.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 5:09 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

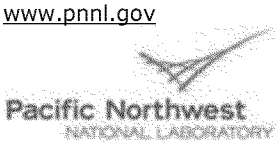
Attached please find Purchase Order No. 521567 to purchase up to the quantities I had listed below. Per the PO, we will place orders via the ordering website. There is no need to sign the PO—if you can acknowledge receipt and that this will work for ordering/payment purposes, that would be helpful.

I'm guessing the MLI Tissue Procurement and Cell Culture Core Facility will want a paper check mailed to the 125 Mason Farm Road address instead of paid by ACH to UNCC's main Bank of America account?

Amy, the shipping address in PES is 331 Building, Room 70. Even if a different shipping address is input in the UNCC online ordering system, any orders associated with PO 521567 will ship to 331/70. If you need a different ship to, let me know.

Thanks!

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov



From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 12:36 PM

To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,

As long as the contract is signed, the dollar amount is entered, and the period is in place there will be no rate increase.
You don't need to select the quantity of any item, but if your project you will use the quantity listed below, entering in the dollar amount is sufficient. I may suggest adding a little wiggle room in the dollar amount because once the dollar amount is reached, even before the term is up, we will need to renew the contract.

Also, once the contract is executed, you would just log onto our ordering website and order what you need.
Please let me know if you have any questions.

Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 9, 2020 1:19 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

I have a requisition to issue a Purchase Order to UNCC for a fixed unit rate contract for the following:

Description	Price	Maximum Quantity Expected	Extended Price
BEGM MEDIUM		5 U.S.C. § 552(b)(4)	
ALI MEDIUM			
VALI MEDIUM			
Normal HBE Cells			
Diseased HBE Cells			
Cystic Fibrosis HBE Cells			
Normal Microvascular Cells			
Normal Fibroblast Cells			

Total Not to Exceed Amount	5 U.S.C. § 552(b)(4)

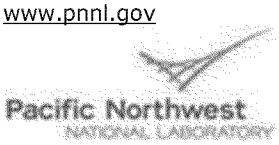
The project would like to use the purchase order for payment of requirements on an as-needed basis through September 30, 2021.

My question is how long the pricing in Exhibit A of the attached is valid? Are the prices updated annually?

Do you have any concerns with this approach?

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov



The University of North Carolina at Chapel Hill

MLI Tissue Procurement and Cell
Culture Core Facility
Recharge Core Agreement

The University of North Carolina at Chapel Hill
MLI Tissue Procurement and Cell Culture Core Facility
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Road
Room 1119 Marsico Hall, CB 7248
Chapel Hill, NC 27599-7361

Make checks payable to: The University of North Carolina at Chapel Hill

Remit payment to:
University of North Carolina - Chapel Hill
MLI Tissue Procurement and Cell Culture Core Facility
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Road
Room 1119 Marsico Hall, CB 7248
Tax ID#: 56-600-1393

Client
Client Name: _____Contact Name: _____

Mailing Address: _____
_____
_____
_____

Phone Number: _____
Contact E-mail Address:_____

Send Invoice to: (if different from above):
Name:_____Email

Address:
_____
_____

Payment Terms: Net 30 days upon receipt of invoice

Not to Exceed Cost: $ _____

Start Date:_____End Date: _____

Payment Method: PO_____Credit Card _____

Description of Services):
Specialized services related to provision of human primary lung cells and custom media in accordance with Exhibit A attached hereto.

Terms and Conditions

1) Services. The University of North Carolina at Chapel Hill ("University") possesses expertise and related technologies and equipment through its MLI Tissue Procurement and Cell Culture Core Facility ("Facility"). Client has instructed University to undertake the specific services described above (the "Services"). In consideration of Client's payment to the Facility in accordance with the terms stated herein, the Facility shall perform the Services.

2) Reports. Facility shall provide Client with a report regarding the data obtained in the course of the Services. The report shall be maintained as confidential pursuant to Section 3 below. Client recognizes that the results of the Services which do not disclose Confidential Information provided hereunder may be deemed publishable by University, and that the University employees engaged in the Services shall be free to publish these results, consistent with the obligations imposed in Section 3 of this Agreement.

3) Confidentiality. Any confidential or proprietary information disclosed by Client to University ("Confidential Information") shall be disclosed in writing and designated as confidential and/or proprietary, or if disclosed orally, shall be confirmed in writing and designated confidential and/or proprietary within thirty (30) days of such disclosure. University shall use the Confidential Information only for the purpose of this Agreement and further agrees that it will not disclose or publish such Confidential Information except that the foregoing restrictions shall not apply to: (a) Confidential Information which is or becomes publicly known through no breach of this agreement by University; (b) Confidential Information learned from a third party entitled to disclose such information; (c) Confidential Information already known to or developed by University prior to receipt hereunder, or information independently developed at any time by University personnel not privy to the Confidential Information, as shown by University's written records; or (d) Confidential Information required to be disclosed by operation of law (including, but not limited to, the North Carolina Public Records Act) or court order. The obligation of confidentiality imposed by this Section shall expire three (3) years following the expiration or termination of this Agreement. University will use a reasonable degree of care to prevent the inadvertent, accidental, unauthorized, or mistaken disclosure or use by its employees of Confidential Information. For avoidance of doubt, data, information, results, materials, or products of the Services shall be considered Confidential Information for the purposes of this Agreement.

4) Intellectual Property. It is not anticipated that intellectual property will arise in University's performance of the Services. However, in the event of an invention by at least one employee of University the intellectual property shall be owned as follows: a) Inventions which involve the use of, composition of, or improvement to Client-provided materials or information, or a derivative, analogue thereof shall belong to Client; and b) Inventions which cover a scientific or analytical measurement process, technique, procedure, medium, device or other process which is not unique to characterizing, testing, or fabricating Client's proprietary materials or does not derive from Client-provided materials or Client's Confidential Information shall be owned by University.

5) Publicity. Neither party will use the name of the other party in any publicity, advertising, or news release without the prior written approval of the authorized representative of the other party.

6) Termination. Either party may terminate this Agreement upon prior written notice to the other party. All reasonable costs and non-cancelable obligations incurred by University at the time of said termination shall be reimbursed by Client. At the request of Client, all unused Client-provided materials at the time of termination shall either be returned to Client or destroyed by University as negotiated with the Client.

7) Independent Contractor. In the performance of the Services, University shall be deemed to be and shall be an independent contractor.

8) No Warranties and Indemnity. University makes no warranties, express or implied, regarding the quality of product produced under this Agreement. University shall use its reasonable efforts to perform the Services. University does not warrant or guarantee any results from a given project. University shall not be liable for Client's use of the report or other information provided by University.

9) Export Control. University will not accept export-controlled materials or technical information under this Agreement. Client hereby represents and warrants that materials and technical information provided to University do not require any license from the U.S. government before being exported.

10) Hazardous Materials. All materials provided by Client must be accompanied by the appropriate environmental and safety information for those materials as required by law.

11) Governing Law. This Agreement shall be governed and construed in accordance with the laws of the State of North Carolina.

12) Entire Agreement. The terms and conditions of Purchase Order No. 521567 supplement this agreement.

Check one:

_____No Client employees will work in University facilities in connection with this Agreement

_____Client employees will be performing work related to this Agreement in University facilities.

By Authorized Official of The University of North Carolina at Chapel Hill	By Authorized Official of Client
By:_____	By: _____
Name: acting on behalf of Terry Magnuson, PhD	Name: _____
Title: Vice Chancellor for Research	Title: _____
Date: _____	Date: _____

EXHIBIT A

MARSICO LUNG INSTITUTE

Tissue Procurement and Cell Culture Core

EXTERNAL PRICING

MEDIA	
BEGM MEDIUM	(b) (4)
ALI MEDIUM	$269/Liter (b) (4)
VALI MEDIUM	(b) (4)
HUMAN BRONCHIAL EPITHELIAL CELLS	
Normal HBE Cells	(b) (4)
Diseased HBE Cells	(b) (4)
Cystic Fibrosis HBE Cells	(b) (4)
OTHER HUMAN LUNG CELLS	
Normal Microvascular Cells	(b) (4)
Normal Fibroblast Cells	(b) (4)

DESCRIPTIONS

MEDIA	
BEGM MEDIUM	Bronchial epithelial growth media for expansion of cells on plastic
ALI MEDIUM	Air-Liquid interface media for differentiation of cells on porous supports
VALI MEDIUM	Vertex-ALI for differentiation of cells on porous supports (contains Ultroser G)

HUMAN BRONCHIAL EPITHELIAL CELLS	
Normal Donors	No history of prior chronic lung disease, smoker or non-smoker
Diseased Donors	History of prior chronic lung disease— (COPD, asthma)
Cystic Fibrosis Donors	Homozygous severe CFTR mutation— (F508del/F508del)
Cystic Fibrosis Donors	Heterozygous F508del/second severe CFTR mutation— (F508del/Other)
Cystic Fibrosis Donors	Non F508del CFTR mutations— (Other CF/Other CF)

OTHER HUMAN LUNG CELLS	
Normal Microvascular Cells	No history of prior chronic lung disease
Normal Fibroblast Cells	No history of prior chronic lung disease

Pacific Northwest
NATIONAL LABORATORY

Proudly Operated by **Battelle** *Since 1965*

Battelle Memorial Institute, Pacific Northwest Division
Acting Under Contract DE-AC05-76RL01830
With the U.S. Department of Energy
Operating the Pacific Northwest National Laboratory (PNNL) (www.pnnl.gov)

Schedule - Contract No. 528372

Issued by:	**Name and Address of Contractor:**
Battelle Battelle Boulevard, K9-15 P.O. Box 999 Richland, WA 99352-0999 USA Contracts Specialist: Amber A. Ames Telephone Number: (509) 371-7050 Email: amber.ames@pnnl.gov	University of North Carolina at Chapel Hill Office of Sponsored Research 104 Airport Drive, Suite 2200 Campus Box 1350 Chapel Hill, NC 27599-1350 USA Contractor Contact: David Paul Telephone Number: (919) 966-3411 Email: resadminosr@unc.edu
Payment Terms: Net 30	**Contract Type:** Cost Reimbursement
Submit Invoices and Invoice/Payment Inquiries to ap.invoices@pnnl.gov. **Note:** Invoices must list location(s) of service (US: City, State; Foreign: Country).	**Total Contract Amount:** $60,000.00
Contract Period of Performance: July 27, 2020 through May 31, 2021	
Award Battelle hereby agrees to award this Contract to the Contractor subject to acceptance. The rights and obligations of the parties to this Contract are subject to and governed by this document and any documents attached or incorporated by reference.	**Contractor Agreement** Contractor accepts and agrees to furnish and deliver the items or perform services to the extent stated in this document for the consideration stated in this contract. The rights and obligations of the parties to this contract are subject to and governed by this document and any documents attached or incorporated by reference.

Battelle Memorial Institute Pacific Northwest Division	**Contractor shall sign and return a copy of this document**
Signature of person authorized to sign Digitally signed by Amber A. Ames Date: 2020.08.27 15:38:32 -07'00'	**Signature of person authorized to sign** JoAnne E. Shanklin Digitally signed by JoAnne E. Shanklin Date: 2020.09.10 13:27:33 -04'00'
Name Amber A. Ames	**Name** on behalf of Terry Magnuson, PH.D.
Title Contracts Specialist	Title Vice Chancellor for Research
Date	Date 09/10/2020

IMPORTANT NOTE: Any domestic and foreign travel associated with this contract (including contractor travel within a country of presence) shall be approved in writing by the Battelle Contracts Representative in advance of travel arrangements being finalized. Without the advance approval of the Battelle Contracts Representative for any such travel, any invoiced costs related to such travel will not be paid.

Statement of Work

Contractor agrees to perform the scope outlined in the attached Statement of Work dated July 16, 2020.

Indirect Rates

The following indirect cost rates are hereby established until and unless changed by mutual agreement:

Category	Rate	Base	Type	Effective
Indirect Costs	55.5%	On Campus Organized Research MTDC*	Provisional	From 07/01/2020 Through Until amended

*Modified Total Direct Costs

Fringe Benefits: *The fringe benefits are specifically identified to each employee and are charged individually as direct costs.*

The provisional rate(s) specific above may be prospectively or retroactively revised by mutual agreement, at either Battelle or the Contractor's request, to prevent substantial overpayment.

Upon establishment/approval of finalized, or final rates, for any period consistent with the period of performance, the Contractor agrees to supply such approval to Battelle, within 30 days or receipt of approval from the cognizant agency.

Technical Oversight Representative

All technical questions should be directed to the Technical Oversight Representative, Pamela M. Kinsey at (509) 375-6848 or pamela.kinsey@pnnl.gov. The Technical Oversight Representative cannot modify this agreement.

Battelle Contracts Representative

All contractual questions should be directed to the Battelle Contracts Representative, Amber A. Ames at (509) 371-7050 or amber.ames@pnnl.gov.

Approval of Subcontracts

Subcontracts require the prior written approval of the Battelle Contracts Representative.

Contract Contents

In addition to this Schedule, the Contract consists of:

- Representations and Certifications dated July 27, 2020
- The General Provisions Applicable for Educational Institutions and Nonprofit Organizations, Form A-409.25-Ed/NP dated October 2019, apply and may be viewed at http://www.pnnl.gov/contracts/contractdocuments.aspx
- Precontract Cost Authorization Letter dated July 24, 2020
- Statement of Work dated July 16, 2020

Alterations to General Provisions

- **Insurance – Liability to Third Persons (cl. 378b – Mar 1996)** This clause is hereby deleted and replaced with:

  "Contractor is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."
- **Disputes (cl. 331-Nov 2014)** This clause is hereby deleted and replaced with the following: "Except as otherwise provided or agreed, any dispute relating to this contract which is not disposed of by agreement shall be decided by litigation in a court of competent jurisdiction upon filing of a legal action by the aggrieved party. During the pendency of any dispute, the Contractor shall proceed diligently with the performance of the contract and in accordance with the direction of Battelle."

- **Insurance Requirements (cl. 378 - April 2017)** This clause is hereby deleted and replaced with:

  "Contractor is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."
- **Laws and Regulations, DOE Directives, and Indemnification (cl. 3121 -Mar 2014)** Delete the word "indemnification" in the title and all of Section C."
- **FAR 52.227-3 Patent Indemnity (Apr 1984)** This clause is self-deleting because work being performed under this contract does not include the delivery of commercial items.
- **FAR 52.227-10 Filing of Patent Applications-Classified Subject Matter (DEC 2007)** This clause is self-deleting because this contract is not expected to result in a patent application containing classified subject matter.
- **FAR 52.246-5 Inspection Service - Cost Reimbursement (Apr 1984)** and **FAR 52.246-8 Inspection of Research and Development—Cost Reimbursement (May 2001)** are hereby deleted and replaced with **52.246-9 Inspection of Research and Development (Short Form) (Apr 1984)**.
- **DEAR 970.5229-1 State and Local Taxes (Dec 2000)** This clause is deleted.

Integration

This Contract contains the entire understanding between the parties, and there are no understandings or representations not set forth or incorporated by reference herein. No subsequent modifications of this Contract shall be of any force or effect unless in writing signed by the party claimed to be bound thereby. No communications, written or oral, by other than a Battelle Contracts Representative shall be effective to modify or otherwise affect the provisions of this Contract.

The University of North Carolina at Chapel Hill

MLI Tissue Procurement and Cell
Culture Core Facility
Recharge Core Agreement

The University of North Carolina at Chapel Hill
MLI Tissue Procurement and Cell Culture Core Facility
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Road
Room 1119 Marsico Hall, CB 7248
Chapel Hill, NC 27599-7361

Make checks payable to: The University of North Carolina at Chapel Hill

Remit payment to:
University of North Carolina - Chapel Hill
MLI Tissue Procurement and Cell Culture Core Facility
Marsico Lung Institute/CF Research & Treatment Center
125 Mason Farm Road
Room 1119 Marsico Hall, CB 7248
Tax ID#: 56-600-1393

Payment Terms: Net 30 days upon receipt of invoice

Not to Exceed Cost: $ _____

Start Date:_____End Date: _____

Payment Method: PO_____Credit Card _____

Client
Client Name: _____Contact Name: _____

Mailing Address: _____
_____
_____
_____

Phone Number: _____
Contact E-mail Address:_____

Send Invoice to: (if different from above):
Name:_____Email

Address:
_____
_____

Description of Services):
Specialized services related to provision of human primary lung cells and custom media in accordance with Exhibit A attached hereto.

Terms and Conditions

1) Services. The University of North Carolina at Chapel Hill ("University") possesses expertise and related technologies and equipment through its MLI Tissue Procurement and Cell Culture Core Facility ("Facility"). Client has instructed University to undertake the specific services described above (the "Services"). In consideration of Client's payment to the Facility in accordance with the terms stated herein, the Facility shall perform the Services.

2) Reports. Facility shall provide Client with a report regarding the data obtained in the course of the Services. The report shall be maintained as confidential pursuant to Section 3 below. Client recognizes that the results of the Services which do not disclose Confidential Information provided hereunder may be deemed publishable by University, and that the University employees engaged in the Services shall be free to publish these results, consistent with the obligations imposed in Section 3 of this Agreement.

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9) Export Control. University will not accept export-controlled materials or technical information under this Agreement. Client hereby represents and warrants that materials and technical information provided to University do not require any license from the U.S. government before being exported.

10) Hazardous Materials. All materials provided by Client must be accompanied by the appropriate environmental and safety information for those materials as required by law.

11) Governing Law. This Agreement shall be governed and construed in accordance with the laws of the State of North Carolina.

12) Entire Agreement. The terms and conditions of Purchase Order No. 521567 supplement this agreement.

Check one:

_____No Client employees will work in University facilities in connection with this Agreement

_____Client employees will be performing work related to this Agreement in University facilities.

By Authorized Official of The University of North Carolina at Chapel Hill	By Authorized Official of Client
By:_____	By: _____
Name: acting on behalf of Terry Magnuson, PhD	Name: _____
Title: Vice Chancellor for Research	Title: _____
Date: _____	Date: _____

EXHIBIT A

MARSICO LUNG INSTITUTE

Tissue Procurement and Cell Culture Core

EXTERNAL PRICING

MEDIA	
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Normal HBE Cells	(b) (4)
Diseased HBE Cells	(b) (4)
Cystic Fibrosis HBE Cells	(b) (4)
OTHER HUMAN LUNG CELLS	
Normal Microvascular Cells	(b) (4)
Normal Fibroblast Cells	(b) (4)

DESCRIPTIONS

MEDIA	
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ALI MEDIUM	Air-Liquid interface media for differentiation of cells on porous supports
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Cystic Fibrosis Donors	Homozygous severe CFTR mutation— (F508del/F508del)
Cystic Fibrosis Donors	Heterozygous F508del/second severe CFTR mutation— (F508del/Other)
Cystic Fibrosis Donors	Non F508del CFTR mutations— (Other CF/Other CF)

OTHER HUMAN LUNG CELLS	
Normal Microvascular Cells	No history of prior chronic lung disease
Normal Fibroblast Cells	No history of prior chronic lung disease

From: Graham, Rachel[rlgraham@ad.unc.edu]
Sent: Fri 9/25/2020 1:42:58 PM (UTC-07:00)
To: Sheahan, Timothy Patrick[sheahan@email.unc.edu]; Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: IACUC protocol number for ethics statement

I'm guessing on the IACUC protocol somewhat because I can't quite remember when Adam left, but this one should be good:

All experiments were performed with prior approval and in accordance with the guidelines outlined by the Institutional Animal Care and Use Committee of the University of North Carolina at Chapel Hill (approval number 16-251).

Hope you're doing well and staying out of the fire and particulates!

Rachel

~~~~~~~~~~~~
Rachel Graham, Ph.D.
Assistant Professor
Baric Lab | UNC-Chapel Hill
(919) 966-4689
On Sep 25, 2020, 2:03 PM -0400, Sims, Amy C <amy.sims@pnnl.gov>, wrote:

> Hi,
>
> Can either of you please send me the ethics statement for the MERS-CoV infections Tim and Adam did to collect lung samples for 'omics studies?
>
> A group at PNNL used basically all of the previous 'omics datasets to test a new graphing method. Tim you and Adam are listed as authors. This is the one about hypergraphs.
>
> Thank you! Hope all is well in your neck of the woods. Amy
~~~~~~~~~~~~

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Fri 9/25/2020 1:53:17 PM (UTC-07:00)
To: Graham, Rachel[rlgraham@ad.unc.edu]; Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Subject: Re: IACUC protocol number for ethics statement

Perfect. Thank you very much! The air cleared last Friday which was a huge help! I appreciate it. Thank you again, Amy

---

From: "Graham, Rachel" <rlgraham@ad.unc.edu>
Date: Friday, September 25, 2020 at 1:44 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>, "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: IACUC protocol number for ethics statement

I'm guessing on the IACUC protocol somewhat because I can't quite remember when Adam left, but this one should be good:

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Rachel
~~~~~~~~~~~~
Rachel Graham, Ph.D.
Assistant Professor
Baric Lab | UNC-Chapel Hill
(919) 966-4689
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A group at PNNL used basically all of the previous 'omics datasets to test a new graphing method. Tim you and Adam are listed as authors. This is the one about hypergraphs.

Thank you! Hope all is well in your neck of the woods. Amy
~~~~~~~~~~~~

From: McGlaughon, Ben[benmcg@email.unc.edu]
Sent: Mon 9/28/2020 7:18:43 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Cc: Leist, Sarah Rebecca[leist@email.unc.edu]
Subject: Re: Adding NL63?

Amy can we get shipping info please?

Ben

On Sep 24, 2020, at 5:02 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:

Hello again!

My schedule continues to be frustratingly fluid these days!

Is there any way you could ship me NL63 virus stocks Tuesday, September 29th or Wednesday, September 30th?

I may be out of town the week of October 5th now.

Is this sufficient time? If not let me know. Thank you very much! Also Ben, would it be possible to toss in a few tubes of LLCMK2 cells? I am not sure I thought to ask for those previously.

Thank you! Amy

From: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Date: Monday, September 14, 2020 at 7:05 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Cc: "McGlaughon, Ben" <benmcg@email.unc.edu>
Subject: Re: Adding NL63?

Hi Amy,
No problem - it actually works better for me.
That'll actually work better for me - I still need to look up the exact stocks that we used back then.
Just give me one or two days lead time and we should be fine.

Stay safe - those fires are scary (at least for a German!).

Best,
Sarah

Sent from my iPhone

On Sep 14, 2020, at 9:51 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:

Dear Ben and Sarah,

In true 2020 fashion I am going to have to ask you to delay the shipment of NL63 to PNNL. The lab was closed today and will be closed again tomorrow due to the hazardous levels of smoke in the air from all of the wild fires burning on the west coast.

We thought things were going to clear up today but that has not happened and may not happen for a few more days and I wanted to make sure I am there to get the box.

Right now we most likely will need to push the shipment back until the week of October 5th. Please let me know if that will work for you.

Thank you for your patience. I am very ready for this year to end! Thank you both very much! Best wishes, Amy

---

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Monday, September 14, 2020 at 7:51 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>, "Leist, Sarah Rebecca" <leist@email.unc.edu>
Subject: RE: Adding NL63?

I was planning for tomorrow at the earliest, so not a problem.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Monday, September 14, 2020 10:43 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>; Leist, Sarah Rebecca <leist@email.unc.edu>
Subject: Re: Adding NL63?

Hi Ben and Sarah,

Sorry I owe you and Sarah email responses. I have a presentation in a few minutes for a conference being held on Zoom.

I will catch up on emails this afternoon. Do you mind waiting to ship until Tuesday or Wednesday of this week?

Thank you very much! Amy

Get Outlook for iOS

From: McGlaughon, Ben <benmcg@email.unc.edu>
Sent: Monday, September 14, 2020 7:07 AM
To: Sims, Amy C
Subject: RE: Adding NL63?

What address should I use for the NL63 virus?

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, September 2, 2020 12:31 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: Re: Adding NL63?

Sounds great. Sarah Leist should have stocks of both of the NL63 viruses and she already knows you will be asking for them.

Thank you, Amy

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Wednesday, September 2, 2020 at 9:26 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Adding NL63?

Amy,

I just sent an email to Boyd, Tim, and Lisa to start getting an idea of the availability of these viruses and when we could realistically expect to have them ready to ship. I will keep you updated.

I've been sending out the SARS2 viruses non-stop so those will be easy. And I just sent some NL63-GFP today, so I can definitely get that one sent easily and soon. Assuming I can track down the spike point mutation version, I'll aim to send the two NL63 viruses the week of Sept 14th.

I will also submit a request to amend the MTA right now, to add the NL63 viruses.

Ben

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Wednesday, September 2, 2020 11:37 AM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Cc: Baric, Ralph S <rbaric@email.unc.edu>
Subject: Re: Adding NL63?

Hi Ben,

Yes this is still the list. Please add both the wild type NL63 plus spike point mutation and NL63 expressing GFP to the MTA. I appreciate it.

I appreciate the offer to ship next week but Monday is a holiday and you won't have access to dry ice. It would be best to wait until the week of Sept. 14th.

If you could send me the two NL63 strains then that would be amazing. Let me know when you would like the address etc.

The BL3 strains will have to be shipped in a couple of different shipments and will need to go to the lab in Seattle which will require more coordination especially for the select agent transfer of the 2003 strain of SARS-CoV.

We can discuss this further once we can agree on shipping dates. Thank you very much. Amy

---

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Tuesday, September 1, 2020 at 11:12 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: RE: Adding NL63?

- wild type infectious clone derived Middle East Respiratory syndrome coronavirus (MERS-CoV)
- MERS-CoV expressing the red fluorescent protein gene
- MERS-CoV expressing the nanoluciferase protein gene
- MERS-CoV delta open reading frame 3 to 5 (MERS-CoV delta 3-5)
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- Wild type infectious clone derived SARS-CoV 2
- SARS-CoV 2 expressing the green fluorescent protein gene
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Is this still the full list? Plus the NL63?

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, September 1, 2020 2:02 PM
To: McGlaughon, Ben <benmcg@email.unc.edu>
Subject: FW: Adding NL63?

Hi Ben,

Just wanted to make sure you saw this! Thank you, Amy

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Thursday, August 20, 2020 at 9:34 AM
To: "McGlaughon, Ben" <benmcg@email.unc.edu>
Cc: "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: Adding NL63?

Ben,

I hope you are doing well and transitioning to working in the Baric laboratory in the weirdness of the pandemic.

Can you please talk to Ralph about adding human coronavirus NL63 to our existing MTA?

I would like both the current wild type strain (should contain a point mutation in spike following tissue culture adaptation) and the virus expressing green fluorescent protein GFP. Sarah Leist should have stocks of these at BSL2.

I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 9/28/2020 7:39:23 PM
To: McGlaughon, Ben [benmcg@email.unc.edu]; Leist, Sarah Rebecca [leist@email.unc.edu]
Subject: Re: Adding NL63?

Perfect. For clarity this shipment should contain only the NL63 strains please. I will give you a different address for the BL3 strains once I get the logistics of receiving that shipment figured out.

I just emailed Sarah the NL63 strains I would like to have if she can find it so hopefully that will be helpful. The address is below.

Battelle for the US DOE
Attn: Amy Sims/331/33

5 U.S.C. § 552(b)(6)

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Hi Ben and Sarah,

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I will catch up on emails this afternoon. Do you mind waiting to ship until Tuesday or Wednesday of this week?

Thank you very much! Amy

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We can discuss this further once we can agree on shipping dates. Thank you very much. Amy

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I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 9/28/2020 7:42:23 PM
To: McGlaughon, Ben [benmcg@email.unc.edu]; Leist, Sarah Rebecca [leist@email.unc.edu]
Subject: Fwd: Adding NL63?

Ben and Sarah

I thought the email below went out last week. My apologies.

Microsoft is having major issues. Thank you. Amy

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From: Sims, Amy C <amy.sims@pnnl.gov>
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To: McGlaughon, Ben; Leist, Sarah Rebecca
Subject: Re: Adding NL63?

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Get Outlook for iOS

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- SARS-CoV 2 expressing the green fluorescent protein gene
- SARS-CoV 2 expressing the nanoluciferase protein gene

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To: "McGlaughon, Ben" <benmcg@email.unc.edu>
Cc: "Baric, Ralph S" <rbaric@email.unc.edu>
Subject: Adding NL63?

Ben,

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I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: Sims, Amy C [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CBA4C053EE8E4D48A0BC8A4E81D51935-SIMS, AMY C]
Sent: 9/28/2020 8:18:45 PM
To: McGlaughon, Ben [benmcg@email.unc.edu]
Subject: NL63 can ship category B

Hi Ben,

You can ship the NL63 category B UN3373 if that helps.

Thank you. Amy

PS my phone number is **5 U.S.C. § 552(b)(6)**

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From: McGlaughon, Ben [benmcg@email.unc.edu]
Sent: 9/28/2020 8:21:25 PM
To: Sims, Amy C [amy.sims@pnnl.gov]
Subject: Re: NL63 can ship category B

Sounds good, I'll get you tracking info once I have it.

Ben

> On Sep 28, 2020, at 11:18 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:
>
> Hi Ben,
>
> You can ship the NL63 category B UN3373 if that helps.
>
> Thank you. Amy
>
> PS my phone number is **5 U.S.C. § 552(b)(6)**
>
> Get Outlook for iOS

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Tue 9/29/2020 10:46:07 AM (UTC-07:00)
To: Schaefer, Alexandra[aschaefe@email.unc.edu]
Subject: Time to catch up

Hi Alex,

I hope you are doing well. I would like to find a time to meet in the next week or so to discuss next steps on the R21.

Let me know which days are best for you and we will figure out a time that will work.

Thank you, Amy

From: Sheahan, Timothy Patrick[sheahan@email.unc.edu]
Sent: Tue 9/29/2020 12:32:50 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: IACUC protocol number for ethics statement

hey stranger. how's life? keeping busy? HA!

T

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Friday, September 25, 2020 4:53 PM
To: Graham, Rachel <rlgraham@ad.unc.edu>; Sheahan, Timothy Patrick <sheahan@email.unc.edu>
Subject: Re: IACUC protocol number for ethics statement

Perfect. Thank you very much! The air cleared last Friday which was a huge help! I appreciate it. Thank you again, Amy

---

From: "Graham, Rachel" <rlgraham@ad.unc.edu>
Date: Friday, September 25, 2020 at 1:44 PM
To: "Sheahan, Timothy Patrick" <sheahan@email.unc.edu>, "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: IACUC protocol number for ethics statement

I'm guessing on the IACUC protocol somewhat because I can't quite remember when Adam left, but this one should be good:

All experiments were performed with prior approval and in accordance with the guidelines outlined by the Institutional Animal Care and Use Committee of the University of North Carolina at Chapel Hill (approval number 16-251).

Hope you're doing well and staying out of the fire and particulates!

Rachel
~~~~~~~~~~~~
Rachel Graham, Ph.D.
Assistant Professor
Baric Lab | UNC-Chapel Hill
(919) 966-4689
On Sep 25, 2020, 2:03 PM -0400, Sims, Amy C <amy.sims@pnnl.gov>, wrote:

Hi,

Can either of you please send me the ethics statement for the MERS-CoV infections Tim and Adam did to collect lung samples for 'omics studies?

A group at PNNL used basically all of the previous 'omics datasets to test a new graphing method. Tim you and Adam are listed as authors. This is the one about hypergraphs.

Thank you! Hope all is well in your neck of the woods. Amy
~~~~~~~~~~~~

From: Leist, Sarah Rebecca[leist@email.unc.edu]
Sent: Tue 9/29/2020 3:30:21 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Hello and a little help please

Hi Amy,
I'm trying to collect your viruses.
Do you want p11 or Dp11?
Also, we used a couple of different stocks over time… I selected the ones that I'm assuming we used for the big growth curve – no 100% guarantee.
I have a GFP stock and Casey's old Dp11 stock – still hunting for the icNL63 WT stock.
If I can't find it should we send the GFP and Dp11 anyway?

Thanks,
Sarah

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Monday, September 14, 2020 at 12:22 PM
To: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Subject: Re: Hello and a little help please

Hi Sarah,

I figured given how well the virus grew in the experiments you and I did together if you could send me some of that stock it would do nicely.

Is that possible? A couple of tubes each of the wild type, p11 and GFP virus would be amazing if possible.

Does that make sense? Ben is ready to ship this week if that works for you. Thank you! Amy

PS Hope the move was uneventful! We are doing okay but have had some very smokey days here due to all of the wild fires.

From: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Date: Wednesday, September 9, 2020 at 1:17 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Hello and a little help please

Hi Amy,
Sorry for the delay…
I found many different p11's and I found p11-GFP (from TPS).
Is this what you'll need?
Should I just let Ben know where it is and he handles it from there?

Hope you're doing fine!

Thanks,
Sarah

From: "Sims, Amy C" <amy.sims@pnnl.gov>

Date: Wednesday, August 26, 2020 at 11:28 AM
To: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Subject: Re: Hello and a little help please

Hi Sarah,

Moving is super exciting! I hope you like your new place and that they love cats! That would be awesome and hopefully not too long of a freezer dive in Little Switzerland. Thank you very much!! I appreciate you making time to respond! Thank you again, Amy

---

From: "Leist, Sarah Rebecca" <leist@email.unc.edu>
Date: Wednesday, August 26, 2020 at 6:30 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Hello and a little help please

Hi Amy,
I can have a look later this week.
I'm moving right now.

Sorry for the delay!

Hope you're doing fine!

Sarah

Sent from my iPhone

> On Aug 20, 2020, at 12:41 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:
>
> Hi Sarah!
>
> I hope you and your kitty clan are doing well! I hope the boys transitioned to the US well and that everyone is getting along nicely! And that there is still somewhere for you to sleep in your apartment.
>
> I know you are crazy busy but I am hoping you can help me with something that maybe won't take too long.
>
> Could you help Ben with finding a few vials of the NL63 stocks from the experiment you and I worked on previously? I am asking to get the wild type (with the S point mutation) and the one with GFP. If you can't find these please let me know.
> I really appreciate it as I know you are totally slammed. Congratulations on the publications! That is really great!
>
> Thank you very much! I miss getting to catch up with you and I really hope you are getting a little down time to enjoy life! Amy

From: Leist, Sarah Rebecca[leist@email.unc.edu]
Sent: Tue 9/29/2020 3:46:37 PM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]; McGlaughon, Ben[benmcg@email.unc.edu]
Subject: Re: Adding NL63?

Hi,
I have:

- 2x "STOCK NL63 Dp.11 P-1 6-16-09"
- 5x "hCoV NL63 GFP Pass 7 20150921 tps from MEB p6 11-21-08"

Kenny will look for his icNL63 WT stock tomorrow morning.

@Ben: Right now I have the 7 tubes in a little plastic bag on the second shelf from the bottom in Lil' Swiss. It is not in a box but in the "open space" on the far right side.

Please let me know if you'll need anything else.
I will most likely not be in lab tomorrow.

Thanks,
Sarah

From: "Sims, Amy C" <amy.sims@pnnl.gov>
Date: Monday, September 28, 2020 at 10:42 PM
To: "McGlaughon, Ben" <benmcg@email.unc.edu>, "Leist, Sarah Rebecca" <leist@email.unc.edu>
Subject: Fwd: Adding NL63?

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Battelle for the US DOE
Attn: Amy Sims/331/33
(919) 225-7664
Collaborator samples, no PO

790 6th Street
Richland, WA 99354

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Date: Monday, September 14, 2020 at 7:51 AM
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Can you please talk to Ralph about adding human coronavirus NL63 to our existing MTA?

I would like both the current wild type strain (should contain a point mutation in spike following tissue culture adaptation) and the virus expressing green fluorescent protein GFP. Sarah Leist should have stocks of these at BSL2.

I am also close to needing you to ship me the list of BL3 viruses. Can you please tell me a reasonable timeframe in which you could ship?

Thank you very much, Amy

From: Schaefer, Alexandra[aschaefe@email.unc.edu]
Sent: Thur 10/1/2020 5:15:34 AM (UTC-07:00)
To: Sims, Amy C[amy.sims@pnnl.gov]
Subject: Re: Time to catch up

Hi Amy,

Yes, I am doing fine- hope you are too!

I am not available next week, but the week after would be good- it looks afternoons would works best for.

How about you give some slots that work for you (10/12- 10/16) and we make a plan?

Thanks,
Alex

Get Outlook for iOS

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, September 29, 2020 1:46:06 PM
To: Schaefer, Alexandra <aschaefe@email.unc.edu>
Subject: Time to catch up

Hi Alex,

I hope you are doing well. I would like to find a time to meet in the next week or so to discuss next steps on the R21.

Let me know which days are best for you and we will figure out a time that will work.

Thank you, Amy

From: Sims, Amy C[amy.sims@pnnl.gov]
Sent: Thur 10/1/2020 8:30:37 AM (UTC-07:00)
To: Schaefer, Alexandra[aschaefe@email.unc.edu]
Subject: Re: Time to catch up

Hi Alex,

I am glad to hear that all is well and I hope the work pace is getting a little more reasonable.

That is unfortunate that next week won't work for you as most likely the week of the 12th is going to be bad for me. If that changes I will get back in touch with you to choose a time that week.

For now give me a day or two that would work the week of October 18th please and we will set something up then.

In between now and then can you please send me an update on what you've been able to do to date and any data that you might have? I would really appreciate it.

Thank you very much! Amy

From: "Schaefer, Alexandra" <aschaefe@email.unc.edu>
Date: Thursday, October 1, 2020 at 5:16 AM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: Time to catch up

Hi Amy,

Yes, I am doing fine- hope you are too!

I am not available next week, but the week after would be good- it looks afternoons would works best for.

How about you give some slots that work for you (10/12- 10/16) and we make a plan?

Thanks,
Alex

Get Outlook for iOS

From: Sims, Amy C <amy.sims@pnnl.gov>
Sent: Tuesday, September 29, 2020 1:46:06 PM
To: Schaefer, Alexandra <aschaefe@email.unc.edu>
Subject: Time to catch up

Hi Alex,

I hope you are doing well. I would like to find a time to meet in the next week or so to discuss next steps on the R21.

Let me know which days are best for you and we will figure out a time that will work.

Thank you, Amy

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 10/1/2020 4:27:57 PM
To: McGlaughon, Ben [benmcg@email.unc.edu]; Leist, Sarah Rebecca [leist@email.unc.edu]
Subject: Re: NL63 can ship category B

The box arrived. I have not unpacked it but I will soon. Thank you both!! Amy

---

From: "McGlaughon, Ben" <benmcg@email.unc.edu>
Date: Monday, September 28, 2020 at 8:21 PM
To: "Sims, Amy C" <amy.sims@pnnl.gov>
Subject: Re: NL63 can ship category B

Sounds good, I'll get you tracking info once I have it.

Ben

> On Sep 28, 2020, at 11:18 PM, Sims, Amy C <amy.sims@pnnl.gov> wrote:
>
> Hi Ben,
>
> You can ship the NL63 category B UN3373 if that helps.
>
> Thank you. Amy
>
> PS my phone number is **5 U.S.C. § 552(b)(6)**
>
> Get Outlook for iOS

From: Sims, Amy C [amy.sims@pnnl.gov]
Sent: 10/2/2020 10:44:53 AM
To: Caldwell, Chandra [ccaldwel@email.unc.edu]
CC: Sandoval, Norma I [Norma.Sandoval@pnnl.gov]
Subject: ERA commons assistance pleaes

Hi Chandra,

I know we spoke about this earlier and I think you did it but for some reason when PNNL administrative people look at ERA Commons I am still affiliated with UNC.

I believe I updated my profile to say I had moved to PNNL so please let me know if this is an issue with what I did.

I hope you are doing well and staying safe.

Thank you so much! I really appreciate. Amy

Cell phone number is 5 U.S.C. § 552(b)(6)

From: Koltz, Diane M[dkoltz@email.unc.edu]
Sent: Tue 10/6/2020 7:56:34 AM (UTC-07:00)
To: Ames, Amber A[Amber.Ames@pnnl.gov]
Cc: Fulcher, Leslie[leslie_fulcher@med.unc.edu]; Sandoval, Norma I[Norma.Sandoval@pnnl.gov]; Sims, Amy C[amy.sims@pnnl.gov]; Kinsey, Pamela M[Pamela.Kinsey@pnnl.gov]
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form
Attachment: PNNL Revised Agmt 06Oct2020.docx
Attachment: MLI External Exhibit A UPDATED 05Oct2020.pdf

Hi Amber,

I have received the Core's updated rates and we are ready to move forward. I can accept the changes you propose in the agreement you provided, however, the PO document will need to reflect the alterations made in the prior PO you provided. In addition, UNC has updated their agreements to include the new language in Section 1. I have attached the further revised agreement and the new Exhibit A. If the new language is acceptable and you are amenable to modifying the PO, please provide me finalized copies of each for final review and signature. Should you have questions, please feel free to contact me.

Thanks,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Thursday, September 10, 2020 2:34 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

Attached please find a fully executed contract that was placed with OSP. It seems these negotiated changes should be acceptable university-wide so I am hopeful we can move this forward?

Thank you,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov



From: Ames, Amber A
Sent: Friday, July 24, 2020 3:28 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

Thank you in advance for any update you can provide.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Ames, Amber A
Sent: Thursday, July 16, 2020 1:26 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Diane,

Just checking in to see if you have an update.

Kind regards,

Amber

From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Wednesday, July 08, 2020 11:03 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I am working with my manager on reviewing the General Terms and Conditions and hope to be back with you by the end of the week.
Thanks for your patience,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Wednesday, July 8, 2020 1:22 PM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

Just checking in for a status update.

Kind regards,

Amber

From: Ames, Amber A
Sent: Monday, June 29, 2020 10:25 AM
To: Koltz, Diane M <dkoltz@email.unc.edu>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Diane,

I have been advised that we would like to pursue UNC as the source of the HBE cells. I have attached our purchase order template in word. We do not customize the General Provisions so those are a .pdf. All changes will be listed in the purchase order as an alteration to the GPs—sample below. We have a long history of contracting with UNC so I have copied the Alterations we have negotiated for previous awards. Unfortunately, as a DOE M&O contractor we are also very limited on what we can negotiate. DOE requires their terms control. We understand universities cannot grant indemnity and we are confident we will be able to negotiate changes that will be acceptable to UNC and DOE.

> **Alterations to General Provisions**
> **1. Permits and Responsibilities (cl. 358—Nov 1991)** is hereby deleted and replaced with:
> "The Contractor is an independent contractor, not an agent or employee of Battelle. The Contractor shall, without additional expense to Battelle or the Government, be responsible for obtaining any necessary licenses and permits, and for complying with any Federal, State, and municipal laws, codes, and regulations applicable to the performance of the work. The Contractor shall also be responsible for all damages to persons or property that occurs as a result of the Contractor's fault or negligence only in the manner and to the extent permitted under North Carolina law, including but not limited to the NC Tort Claims Act, GS 143-291, et seq., and without waiver of its sovereign immunity."
> **2. Insurance—Liability to Third Persons (cl. 378b—Mar 1996)** is hereby deleted and replaced with:
> "University of North Carolina is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."
> **3. Disputes (cl. 331—Nov 2014)**
> Delete in its entirety.
> **4. Insurance Requirements (cl. 378—Nov 2014)** is hereby deleted and replaced with:
> "University of North Carolina is self-insured through the State of North Carolina and its requirements and will not be required to provide an insurance certificate or modify its coverage terms."

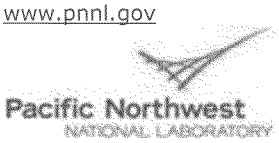
I note I have been advised we will have another order with a budget of [5 U.S.C. § 552(b)(4)] so it is critical we resolve the terms and conditions.

Thank you for your assistance with this matter.

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352

Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov



From: Koltz, Diane M <dkoltz@email.unc.edu>
Sent: Thursday, June 18, 2020 11:06 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hi Amber,

I received your changes for review and upon a first look, UNC cannot agree to all of the supplemental terms contained in the online documents you want to include. As a state institution, we are somewhat limited. The order form contains the minimal terms UNC requires in its contracts and we typically do not agree to changes. Is there any possibility that we could make UNC's agreement control, or not reference the terms at all, since much of what is contained in the online "purchase agreements" won't apply to what we are providing. If this is not possible, please provide me word versions of the online agreements so I can outline our requested edits and comments. Also, please note that review of the documents will take time.

Thanks,
Diane

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Thursday, June 18, 2020 12:58 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Just checking in to see if there is a response to our requested changes to the order form terms.

Thanks so much!

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Wednesday, June 10, 2020 3:04 AM
To: Ames, Amber A <Amber.Ames@pnnl.gov>; Koltz, Diane M <dkoltz@email.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Good Morning Amber,
Yes, once the contract is executed, Amy will be able to order as needed up to the dollar amount on the contract and during the 1 year period. I am including our contract specialist who can look at your suggested changes and she will be in touch with you soon.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 9:02 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Thanks, Leslie. The project would like to be able to order up to 10 ALI medium and 26 Normal HBE Cells from now until September 30, 2021. Are they able to order on an as-needed basis? I can incorporate a signed version of the attached into the PO for the project to use? Once I sign it, they won't be able to edit it. Perhaps we need to do a purchase order per order?

I note I provided redlines on the attached. Please advise if UNCC is able to work with the redlines.

Amber

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 5:29 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,
Thanks for emailing back, but to complete the contract, I need the agreement signed and returned to me prior to ordering. As for payment options, a check is fine, but we do have an account that funds could be wired. If that works for you, I can share that information.
Thank you,
Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 09, 2020 5:09 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Kinsey, Pamela M <Pamela.Kinsey@pnnl.gov>; Sims, Amy C <amy.sims@pnnl.gov>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

Attached please find Purchase Order No. 521567 to purchase up to the quantities I had listed below. Per the PO, we will place orders via the ordering website. There is no need to sign the PO—if you can acknowledge receipt and that this will work for ordering/payment purposes, that would be helpful.

I'm guessing the MLI Tissue Procurement and Cell Culture Core Facility will want a paper check mailed to the 125 Mason Farm Road address instead of paid by ACH to UNCC's main Bank of America account?

Amy, the shipping address in PES is 331 Building, Room 70. Even if a different shipping address is input in the UNCC online ordering system, any orders associated with PO 521567 will ship to 331/70. If you need a different ship to, let me know.

Thanks!

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
amber.ames@pnnl.gov
www.pnnl.gov

Pacific Northwest
NATIONAL LABORATORY

From: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Sent: Tuesday, June 09, 2020 12:36 PM
To: Ames, Amber A <Amber.Ames@pnnl.gov>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>; Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Subject: RE: Request for Proposal No. 588659 - MLI Academic Order Form

Hello Amber,

As long as the contract is signed, the dollar amount is entered, and the period is in place there will be no rate increase.
You don't need to select the quantity of any item, but if your project you will use the quantity listed below, entering in the dollar amount is sufficient. I may suggest adding a little wiggle room in the dollar amount because once the dollar amount is reached, even before the term is up, we will need to renew the contract.

Also, once the contract is executed, you would just log onto our ordering website and order what you need.
Please let me know if you have any questions.

Leslie

From: Ames, Amber A <Amber.Ames@pnnl.gov>
Sent: Tuesday, June 9, 2020 1:19 PM
To: Fulcher, Leslie <leslie_fulcher@med.unc.edu>
Cc: Sandoval, Norma I <Norma.Sandoval@pnnl.gov>
Subject: Request for Proposal No. 588659 - MLI Academic Order Form

Dear Leslie,

I have a requisition to issue a Purchase Order to UNCC for a fixed unit rate contract for the following:

Description	Price	Maximum Quantity Expected	Extended Price
BEGM MEDIUM	5 U.S.C. § 552(b)(4)	0	5 U.S.C. § 552(b)(4)

ALI MEDIUM		5 U.S.C. § 552(b)(4)	10	5 U.S.C. § 552(b)(4)
VALI MEDIUM			0	
Normal HBE Cells			26	
Diseased HBE Cells			0	
Cystic Fibrosis HBE Cells			0	
Normal Microvascular Cells			0	
Normal Fibroblast Cells			0	
Total Not to Exceed Amount				

The project would like to use the purchase order for payment of requirements on an as-needed basis through September 30, 2021.

My question is how long the pricing in Exhibit A of the attached is valid? Are the prices updated annually?

Do you have any concerns with this approach?

Kind regards,

Amber A. Ames
Senior Contracts Specialist
Battelle Memorial Institute
Pacific Northwest Division
902 Battelle Blvd.
Richland, WA 99352
Tel: (509) 371-7050
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