From: Lauer, Michael (NIH/OD) [E]
To: Hallett, Adrienne (NIH/OD) [E]
Cc: Lauer, Michael (NIH/OD) [E]; Tabak, Lawrence (NIH/OD) [E]
Subject: FW: FOR SIGNATURE - SST/E&C Letter to Sec Azar
Date: Sunday, August 16, 2020 11:06:14 AM
Attachments: 06.26.20 SST EC Letter to HHS[1][1].pdf
ATT00001.htm
Eco Health Lab letter July 8.pdf
ATT00002.htm
SST and EC EcoHealth Alliance response.docx
ATT00003.htm

Hi Adrienne – given the new developments discussed on Friday (that is, the letter received late Thursday from EcoHealth Alliance Counsel), I'm standing by.

Thanks, Mike

From: "LaMontagne, Karen (NIH/OD) [E]" (b) (6)
Date: Friday, August 14, 2020 at 12:40 PM
To: "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: "Lohmann, Larry (NIH/OD) [E]" (b) (6), "Showe, Melanie (NIH/OD) [E]" (b) (6)
Subject: FOR SIGNATURE - SST/E&C Letter to Sec Azar

Hi, Dr. Lauer,

I'm not sure if Adrienne reached out to you about this separately, but OGC is trying to get signature on the attached final response (re: WIV) to send to the Hill today. Will you let us know if you have any concerns and, if not, let us know if you can provide a signature so that HHS can transmit? Happy to help however needed.

Thanks, and let me know if you have any questions.
Karen

Begin forwarded message:

From: "Honig, Esther (HHS/ASL)" (b) (6)
Date: August 14, 2020 at 12:07:30 PM EDT
To: "Lohmann, Larry (NIH/OD) [E]" (b) (6), "Hallett, Adrienne (NIH/OD) [E]" (b) (6), "LaMontagne, Karen (NIH/OD) [E]" (b) (6)
Cc: "Brosnan, Kyle (HHS/OGC)" (b) (6)
Subject: RE: SST/E&C Letter to Sec Azar

Checking back in on this.

From: Honig, Esther (HHS/ASL)
Sent: Friday, August 14, 2020 9:35 AM
To: Lohmann, Larry (NIH/OD) [E] (b) (6); Hallett, Adrienne (NIH/OD) [E] (b) (6); LaMontagne, Karen (NIH/OD) [E] (b) (6)
Cc: Brosnan, Kyle (HHS/OGC) (b) (6)
Subject: SST/E&C Letter to Sec Azar

Good morning,

Attached is the cleared letter, ready for signature. We are hoping to transmit this today. Please let me know if you have any comments or concerns.

Thank you,
Esther

Congress of the United States
House of Representatives
Washington, DC 20515

June 26, 2020

The Honorable Alex M. Azar II
Secretary
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Dear Secretary Azar,

We write with strong concerns surrounding the Administration's termination of the National Institutes of Health (NIH) grant to EcoHealth Alliance on April 24, 2020.[1] In the letter communicating the grant's termination, NIH Deputy Director for Extramural Research, Dr. Michael Lauer, wrote that "At this time, NIH does not believe the current project outcomes align with the program goals and agency priorities."[2] However, press reports indicate that the grant was canceled because a small portion of the funding was to be given to the Wuhan Institute of Virology for on-the-ground sample collection and analysis.[3] Given the potential for this study to inform our knowledge of coronavirus disease 2019 (COVID-19) transmission, it is deeply concerning that it may have been canceled for political reasons in the midst of the current pandemic.

It is always important that federal research priorities are driven by science-based decisions. This is especially true in a time that requires unparalleled investment in research that may help bring an end to this public health crisis. It is therefore troubling that this abrupt grant cancellation came just a week after President Trump announced that the Administration was looking into "grants going to that area" and continued that "we will end that grant very quickly."[4] This was in response to a reporter referencing false claims that COVID-19 "likely

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[2] Nurith Aizenman, "Why The U.S. Government Stopped Funding A Research Project On Bats And Coronaviruses," *NPR*, May 1, 2020, accessed here: https://www.npr.org/sections/goatsandsoda/2020/04/29/847948272/why-the-u-s-government-stopped-funding-a-research-project-on-bats-and-coronaviru
[3] *Id.*
[4] Clip of President Trump with Coronavirus Task Force Briefing, *CSPAN*, April 17, 2020, accessed here: https://www.c-span.org/video/?c4869590/user-clip-us-2015-grant-wuhan-lab-question

came from a Level 4 lab in Wuhan."[5] The Administration has been pushing this theory[6] despite scientific experts saying this path of transmission would be virtually impossible given what is known about the virus and lab safety protocols.[7] If this theory is the basis for the grant termination, it would be an egregious example of the Administration politicizing scientific decision making in order to further a politically convenient narrative.

EcoHealth Alliance's grant was renewed in 2019 after an initial five-year grant on the same topic. The grant it received was extremely competitive – only 22 percent of proposals were funded in 2019.[8] The July 2019 project proposal was titled, "Understanding the Risk of Bat Coronavirus Emergence."[9] In the midst of the COVID-19 pandemic that has taken over 115,000 American lives, it is inconceivable that this project would no longer "align with the program goals and agency priorities" of NIH. Any termination of a grant that has gone through NIH's rigorous scientific review process must be adequately justified on a scientific basis – particularly a grant which would appear to be so relevant to understanding our current health crisis.

As the Committees of jurisdiction over public health and science, we need to better understand the decision to terminate EcoHealth Alliance's NIH grant. We are especially concerned given Dr. Anthony Fauci's, Director of NIH's National Institute of Allergy and Infectious Diseases, assertion at a Committee on Energy and Commerce hearing on June 23 that "the grant was canceled because NIH was told to cancel it."[10] In order to understand how this decision was reached, we request a briefing to be delivered by July 15, 2020. At this briefing, we ask that you be prepared to address the following questions:

1. When the decision was made to terminate the grant to EcoHealth Alliance;

2. Who at HHS was involved in the decision to terminate the grant;

3. Whether entities outside HHS, including but not limited to the White House, the State Department, the National Security Council, and intelligence agencies, were involved in this decision;

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[8] Research Grants: Competing Applications, Awards, and Success Rates, National Institutes of Health, January 2020, accessed here: https://report nih.gov/nihdatabook/category/6

[9] "Understanding the Risk of Bat Coronavirus Emergence," National Institutes of Health Research Portfolio Online Reporting Tools, July 2019, accessed here: https://projectreporter.nih.gov/project_info_description.cfm?aid=9819304&icde=49752569

[10] House Committee on Energy and Commerce, Testimony of Anthony S. Fauci, M.D., Director, National Institute for Allergy and Infectious Diseases, *Oversight of the Trump Administration's Response to the COVID-19 Pandemic*, 116th Cong. (Jun. 23, 2020).

4. The analysis conducted to determine that the EcoHealth Alliance grant's project outcomes did not align with program goals and NIH priorities;

5. Any analysis conducted to determine EcoHealth Alliance's alleged improper disbursal of NIH funds to the Wuhan Institute of Virology;

6. Any other decision NIH has made to terminate grants since January 1, 2020; and

7. Any further action NIH is considering taking regarding EcoHealth Alliance or any other grant holder regarding alleged relationships with international laboratories.

In addition to the briefing, we request the following materials be provided to the Committees no later than July 10, 2020. Please provide these materials in a searchable electronic format.

1. All documents and communications relating to the cancellation of EcoHealth Alliance's grant, including the notification to and any response from EcoHealth Alliance;

2. All documents and communications regarding any potential direction from outside entities, including the White House or other Agencies or Departments, to terminate grants based on suspicion of collaboration with international laboratories;

3. All documentation of audits or other analyses conducted to determine improper disbursement of federal grant money from grant-holding institutions to other entities; and

4. The criteria that NIH used to assess the EcoHealth Alliance grant and determine that such grant merited cancelation, and documentation thereof.

Any decision to terminate a research grant should be conducted in a deliberative and transparent process that adheres to the highest standards of scientific integrity. Especially in this unprecedented time, it is important that our public health and science agencies remain free from political pressure and be allowed to pursue federally-funded research based on scientific merit.

Thank you for your attention to this matter. We look forward to speaking with you and reviewing the relevant materials.

Sincerely,

Eddie Bernice Johnson
Chairwoman
Committee on Science, Space,
and Technology

Frank Pallone, Jr.
Chairman
Committee on Energy and Commerce

Bill Foster
Chairman
Subcommittee on Investigations and Oversight

Diana DeGette
Chair
Subcommittee on Oversight and Investigations

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

8 July 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

In follow-up to my previous letter of April 24, 2020, I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS), has withdrawn its termination of grant R01AI110964, which supports the project *Understanding the Risk of Bat Coronavirus Emergence*. Accordingly, the grant is reinstated.

However, as you are aware, the NIH has received reports that the Wuhan Institute of Virology (WIV), a subrecipient of EcoHealth Alliance under R01AI110964, has been conducting research at its facilities in China that pose serious bio-safety concerns and, as a result, create health and welfare threats to the public in China and other countries, including the United States. Grant award R01AI110964 is subject to biosafety requirements set forth in the NIH Grants Policy Statement (e.g., NIH GPS, Section 4.1.24 "Public Health Security") and the Notice of Award (e.g., requiring that "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]."). Moreover, NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients. 45 C.F.R. § 75.101.

As the grantee, EcoHealth Alliance was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). We have concerns that WIV has not satisfied safety requirements under the award, and that EcoHealth Alliance has not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance.

Moreover, as we have informed you through prior Notices of Award, this award is subject to the Transparency Act subaward and executive compensation reporting requirement of 2 C.F.R. Part

170. To date you have not reported any subawards in the Federal Subaward Reporting System.

Therefore, effective the date of this letter, July 8, 2020, NIH is suspending all activities related to R01AI110964, until such time as these concerns have been addressed to NIH's satisfaction. This suspension is taken in accordance with 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable in accordance with 42 C.F.R. § 50.404 and the NIH GPS Section 8.7, Grant Appeals Procedures. However, EcoHealth Alliance has the opportunity to provide information and documentation demonstrating that WIV and EcoHealth Alliance have satisfied the above-mentioned requirements.

Specifically, to address the NIH's concerns, EcoHealth must provide the NIH with the following information and materials, which must be complete and accurate:

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.
3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.
4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.
5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.
6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.
7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

During this period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further asses compliance by EcoHealth Alliance and WIV, including compliance with other terms and conditions of award that may be implicated. Additionally, during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the

recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. Once the original award is reinstated, NIH will take additional steps to restrict all funding in the HHS Payment Management System in the amount of $369,819. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 CFR Part 75, including, but not limited to, terminating the grant award. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

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Sincerely,

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy
Ms. Emily Linde

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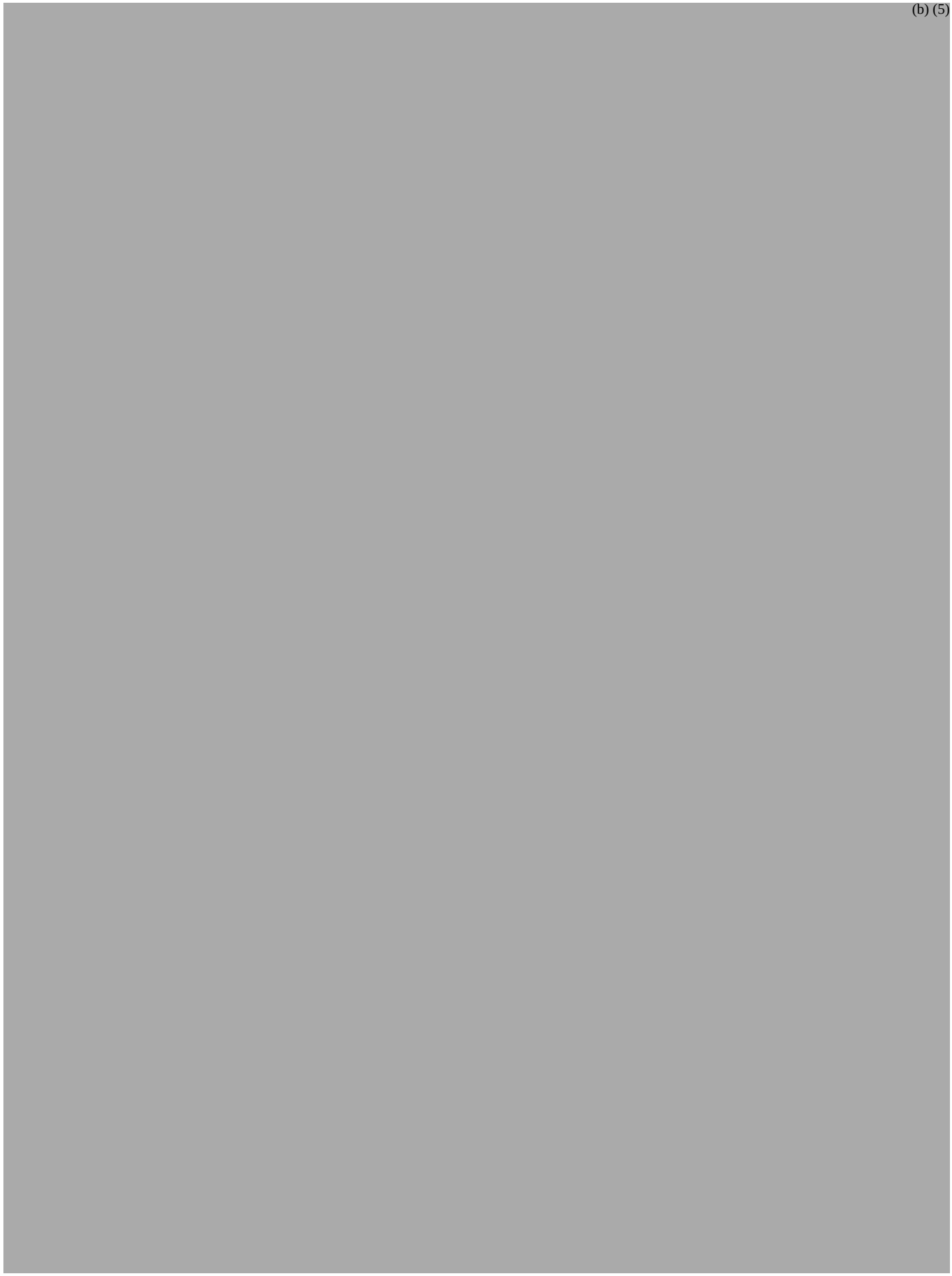

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From:	Lauer, Michael (NIH/OD) [E]
To:	Hallett, Adrienne (NIH/OD) [E]; Collins, Francis (NIH/OD) [E]; Tabak, Lawrence (NIH/OD) [E]
Cc:	Allen-Gifford, Patrice (NIH/OD) [E]; LaMontagne, Karen (NIH/OD) [E]; Lauer, Michael (NIH/OD) [E]
Subject:	Re: EcoHealth Response Letter
Date:	Friday, August 14, 2020 1:59:06 PM
Attachments:	06.26.20 SST EC Letter to HHS[1][1].pdf Eco Health Lab letter July 8.pdf SST and EC EcoHealth Alliance response[1].docx

Hi Francis, Larry, and Adrienne – late yesterday we received a "response" from EcoHealth Alliance counsel. Briefly, they are refusing to answer the questions. I've forwarded the materials to OGC for their review. Since EcoHealth Alliance has not responded to our questions, I think the ASL letter is accurate.

Thanks, Mike

From: "Hallett, Adrienne (NIH/OD) [E]" (b) (6)
Date: Friday, August 14, 2020 at 12:44 PM
To: "Collins, Francis (NIH/OD) [E]" (b) (6), "Tabak, Lawrence (NIH/OD) [E]" (b) (6), "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: "Allen-Gifford, Patrice (NIH/OD) [E]" (b) (6), "LaMontagne, Karen (NIH/OD) [E]" (b) (6)
Subject: EcoHealth Response Letter

FC,

Well, we finally got a draft back from ASL. It is attached.

Please let me know if you have any concerns.
Adrienne

Congress of the United States
House of Representatives
Washington, DC 20515

June 26, 2020

The Honorable Alex M. Azar II
Secretary
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Dear Secretary Azar,

We write with strong concerns surrounding the Administration's termination of the National Institutes of Health (NIH) grant to EcoHealth Alliance on April 24, 2020.[1] In the letter communicating the grant's termination, NIH Deputy Director for Extramural Research, Dr. Michael Lauer, wrote that "At this time, NIH does not believe the current project outcomes align with the program goals and agency priorities."[2] However, press reports indicate that the grant was canceled because a small portion of the funding was to be given to the Wuhan Institute of Virology for on-the-ground sample collection and analysis.[3] Given the potential for this study to inform our knowledge of coronavirus disease 2019 (COVID-19) transmission, it is deeply concerning that it may have been canceled for political reasons in the midst of the current pandemic.

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came from a Level 4 lab in Wuhan."[5] The Administration has been pushing this theory[6] despite scientific experts saying this path of transmission would be virtually impossible given what is known about the virus and lab safety protocols.[7] If this theory is the basis for the grant termination, it would be an egregious example of the Administration politicizing scientific decision making in order to further a politically convenient narrative.

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4. The criteria that NIH used to assess the EcoHealth Alliance grant and determine that such grant merited cancelation, and documentation thereof.

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Thank you for your attention to this matter. We look forward to speaking with you and reviewing the relevant materials.

Sincerely,

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Subcommittee on Investigations and Oversight

Diana DeGette
Chair
Subcommittee on Oversight and Investigations

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

8 July 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

In follow-up to my previous letter of April 24, 2020, I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS), has withdrawn its termination of grant R01AI110964, which supports the project *Understanding the Risk of Bat Coronavirus Emergence*. Accordingly, the grant is reinstated.

However, as you are aware, the NIH has received reports that the Wuhan Institute of Virology (WIV), a subrecipient of EcoHealth Alliance under R01AI110964, has been conducting research at its facilities in China that pose serious bio-safety concerns and, as a result, create health and welfare threats to the public in China and other countries, including the United States. Grant award R01AI110964 is subject to biosafety requirements set forth in the NIH Grants Policy Statement (e.g., NIH GPS, Section 4.1.24 "Public Health Security") and the Notice of Award (e.g., requiring that "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]."). Moreover, NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients. 45 C.F.R. § 75.101.

As the grantee, EcoHealth Alliance was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). We have concerns that WIV has not satisfied safety requirements under the award, and that EcoHealth Alliance has not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance.

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7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

During this period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further asses compliance by EcoHealth Alliance and WIV, including compliance with other terms and conditions of award that may be implicated. Additionally, during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the

recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. Once the original award is reinstated, NIH will take additional steps to restrict all funding in the HHS Payment Management System in the amount of $369,819. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 CFR Part 75, including, but not limited to, terminating the grant award. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

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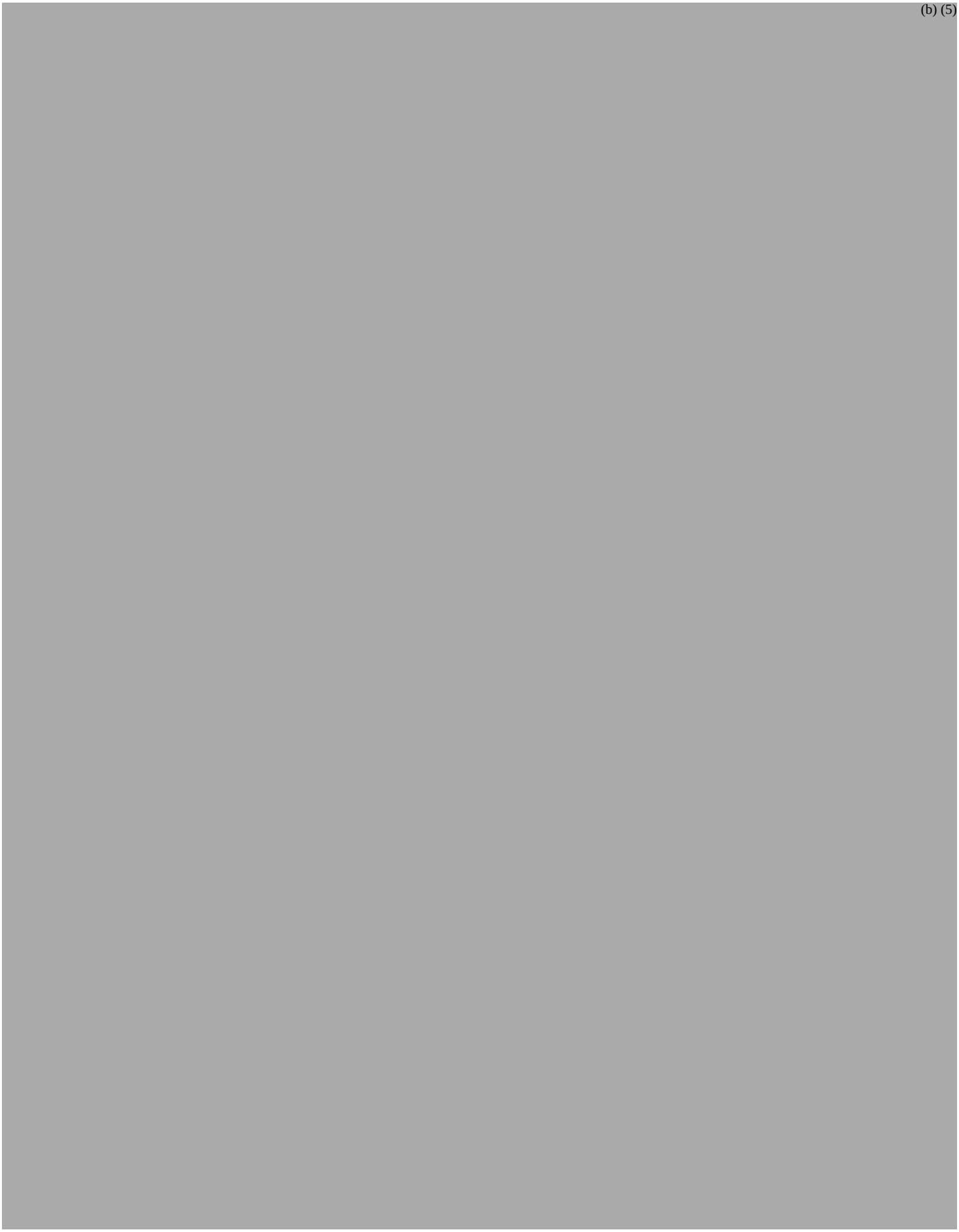
Sincerely,

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy
Ms. Emily Linde



From: Lauer, Michael (NIH/OD) [E]
To: Tabak, Lawrence (NIH/OD) [E]
Cc: Lauer, Michael (NIH/OD) [E]
Subject: FW: EcoHealth Response Letter
Date: Friday, August 14, 2020 1:21:29 PM
Attachments: 06.26.20 SST EC Letter to HHS[1][1].pdf
Eco Health Lab letter July 8.pdf
SST and EC EcoHealth Alliance response.docx

Hi Larry – we did get a response from EcoHealth Alliance yesterday, but I would call it a non-response since they are refusing to answer the questions. So this letter is still technically accurate.

Thanks, Mike

From: "Hallett, Adrienne (NIH/OD) [E]" (b) (6)
Date: Friday, August 14, 2020 at 12:44 PM
To: "Collins, Francis (NIH/OD) [E]" (b) (6), "Tabak, Lawrence (NIH/OD) [E]" (b) (6), "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: "Allen-Gifford, Patrice (NIH/OD) [E]" (b) (6), "LaMontagne, Karen (NIH/OD) [E]" (b) (6)
Subject: EcoHealth Response Letter

FC,

Well, we finally got a draft back from ASL. It is attached.

Please let me know if you have any concerns.
Adrienne

Congress of the United States
House of Representatives
Washington, DC 20515

June 26, 2020

The Honorable Alex M. Azar II
Secretary
U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Dear Secretary Azar,

We write with strong concerns surrounding the Administration's termination of the National Institutes of Health (NIH) grant to EcoHealth Alliance on April 24, 2020.[1] In the letter communicating the grant's termination, NIH Deputy Director for Extramural Research, Dr. Michael Lauer, wrote that "At this time, NIH does not believe the current project outcomes align with the program goals and agency priorities."[2] However, press reports indicate that the grant was canceled because a small portion of the funding was to be given to the Wuhan Institute of Virology for on-the-ground sample collection and analysis.[3] Given the potential for this study to inform our knowledge of coronavirus disease 2019 (COVID-19) transmission, it is deeply concerning that it may have been canceled for political reasons in the midst of the current pandemic.

It is always important that federal research priorities are driven by science-based decisions. This is especially true in a time that requires unparalleled investment in research that may help bring an end to this public health crisis. It is therefore troubling that this abrupt grant cancellation came just a week after President Trump announced that the Administration was looking into "grants going to that area" and continued that "we will end that grant very quickly."[4] This was in response to a reporter referencing false claims that COVID-19 "likely

[1] Sharah Owermohle, "Trump cuts U.S. research on bat-human virus transmission over China ties," *Politico*, April 27, 2020, accessed here: https://www.politico.com/news/2020/04/27/trump-cuts-research-bat-human-virus-china-213076
[2] Nurith Aizenman, "Why The U.S. Government Stopped Funding A Research Project On Bats And Coronaviruses," *NPR*, May 1, 2020, accessed here: https://www.npr.org/sections/goatsandsoda/2020/04/29/847948272/why-the-u-s-government-stopped-funding-a-research-project-on-bats-and-coronaviru
[3] *Id.*
[4] Clip of President Trump with Coronavirus Task Force Briefing, *CSPAN*, April 17, 2020, accessed here: https://www.c-span.org/video/?c4869590/user-clip-us-2015-grant-wuhan-lab-question

came from a Level 4 lab in Wuhan."[5] The Administration has been pushing this theory[6] despite scientific experts saying this path of transmission would be virtually impossible given what is known about the virus and lab safety protocols.[7] If this theory is the basis for the grant termination, it would be an egregious example of the Administration politicizing scientific decision making in order to further a politically convenient narrative.

EcoHealth Alliance's grant was renewed in 2019 after an initial five-year grant on the same topic. The grant it received was extremely competitive – only 22 percent of proposals were funded in 2019.[8] The July 2019 project proposal was titled, "Understanding the Risk of Bat Coronavirus Emergence."[9] In the midst of the COVID-19 pandemic that has taken over 115,000 American lives, it is inconceivable that this project would no longer "align with the program goals and agency priorities" of NIH. Any termination of a grant that has gone through NIH's rigorous scientific review process must be adequately justified on a scientific basis – particularly a grant which would appear to be so relevant to understanding our current health crisis.

As the Committees of jurisdiction over public health and science, we need to better understand the decision to terminate EcoHealth Alliance's NIH grant. We are especially concerned given Dr. Anthony Fauci's, Director of NIH's National Institute of Allergy and Infectious Diseases, assertion at a Committee on Energy and Commerce hearing on June 23 that "the grant was canceled because NIH was told to cancel it."[10] In order to understand how this decision was reached, we request a briefing to be delivered by July 15, 2020. At this briefing, we ask that you be prepared to address the following questions:

1. When the decision was made to terminate the grant to EcoHealth Alliance;

2. Who at HHS was involved in the decision to terminate the grant;

3. Whether entities outside HHS, including but not limited to the White House, the State Department, the National Security Council, and intelligence agencies, were involved in this decision;

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[5] *Id.*

[6] Mark Mazzetti, Julian E. Barnes, Edward Wong, and Adam Goldman, "Trump Officials Are Said to Press Spies to Link Virus and Wuhan Labs," *New York Times*, April 30, 2020, accessed here: https://www nytimes.com/2020/04/30/us/politics/trump-administration-intelligence-coronavirus-china html

[7] Geoff Brumfel and Emily Kwong, "Virus Researchers Cast Doubt On Theory Of Coronavirus Lab Accident," *NPR*, April 23, 2020, accessed here: https://www npr.org/sections/goatsandsoda/2020/04/23/841729646/virus-researchers-cast-doubt-on-theory-of-coronavirus-lab-accident

[8] Research Grants: Competing Applications, Awards, and Success Rates, National Institutes of Health, January 2020, accessed here: https://report nih.gov/nihdatabook/category/6

[9] "Understanding the Risk of Bat Coronavirus Emergence," National Institutes of Health Research Portfolio Online Reporting Tools, July 2019, accessed here: https://projectreporter.nih.gov/project_info_description.cfm?aid=9819304&icde=49752569

[10] House Committee on Energy and Commerce, Testimony of Anthony S. Fauci, M.D., Director, National Institute for Allergy and Infectious Diseases, *Oversight of the Trump Administration's Response to the COVID-19 Pandemic*, 116th Cong. (Jun. 23, 2020).

4. The analysis conducted to determine that the EcoHealth Alliance grant's project outcomes did not align with program goals and NIH priorities;

5. Any analysis conducted to determine EcoHealth Alliance's alleged improper disbursal of NIH funds to the Wuhan Institute of Virology;

6. Any other decision NIH has made to terminate grants since January 1, 2020; and

7. Any further action NIH is considering taking regarding EcoHealth Alliance or any other grant holder regarding alleged relationships with international laboratories.

In addition to the briefing, we request the following materials be provided to the Committees no later than July 10, 2020. Please provide these materials in a searchable electronic format.

1. All documents and communications relating to the cancellation of EcoHealth Alliance's grant, including the notification to and any response from EcoHealth Alliance;

2. All documents and communications regarding any potential direction from outside entities, including the White House or other Agencies or Departments, to terminate grants based on suspicion of collaboration with international laboratories;

3. All documentation of audits or other analyses conducted to determine improper disbursement of federal grant money from grant-holding institutions to other entities; and

4. The criteria that NIH used to assess the EcoHealth Alliance grant and determine that such grant merited cancelation, and documentation thereof.

Any decision to terminate a research grant should be conducted in a deliberative and transparent process that adheres to the highest standards of scientific integrity. Especially in this unprecedented time, it is important that our public health and science agencies remain free from political pressure and be allowed to pursue federally-funded research based on scientific merit.

Thank you for your attention to this matter. We look forward to speaking with you and reviewing the relevant materials.

Sincerely,

Eddie Bernice Johnson
Chairwoman
Committee on Science, Space,
and Technology

Frank Pallone, Jr.
Chairman
Committee on Energy and Commerce

Bill Foster
Chairman
Subcommittee on Investigations and Oversight

Diana DeGette
Chair
Subcommittee on Oversight and Investigations

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

8 July 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

In follow-up to my previous letter of April 24, 2020, I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS), has withdrawn its termination of grant R01AI110964, which supports the project *Understanding the Risk of Bat Coronavirus Emergence*. Accordingly, the grant is reinstated.

However, as you are aware, the NIH has received reports that the Wuhan Institute of Virology (WIV), a subrecipient of EcoHealth Alliance under R01AI110964, has been conducting research at its facilities in China that pose serious bio-safety concerns and, as a result, create health and welfare threats to the public in China and other countries, including the United States. Grant award R01AI110964 is subject to biosafety requirements set forth in the NIH Grants Policy Statement (e.g., NIH GPS, Section 4.1.24 "Public Health Security") and the Notice of Award (e.g., requiring that "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]."). Moreover, NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients. 45 C.F.R. § 75.101.

As the grantee, EcoHealth Alliance was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). We have concerns that WIV has not satisfied safety requirements under the award, and that EcoHealth Alliance has not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance.

Moreover, as we have informed you through prior Notices of Award, this award is subject to the Transparency Act subaward and executive compensation reporting requirement of 2 C.F.R. Part

170. To date you have not reported any subawards in the Federal Subaward Reporting System.

Therefore, effective the date of this letter, July 8, 2020, NIH is suspending all activities related to R01AI110964, until such time as these concerns have been addressed to NIH's satisfaction. This suspension is taken in accordance with 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable in accordance with 42 C.F.R. § 50.404 and the NIH GPS Section 8.7, Grant Appeals Procedures. However, EcoHealth Alliance has the opportunity to provide information and documentation demonstrating that WIV and EcoHealth Alliance have satisfied the above-mentioned requirements.

Specifically, to address the NIH's concerns, EcoHealth must provide the NIH with the following information and materials, which must be complete and accurate:

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.
3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.
4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.
5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.
6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.
7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

During this period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further asses compliance by EcoHealth Alliance and WIV, including compliance with other terms and conditions of award that may be implicated. Additionally, during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the

recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. Once the original award is reinstated, NIH will take additional steps to restrict all funding in the HHS Payment Management System in the amount of $369,819. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 CFR Part 75, including, but not limited to, terminating the grant award. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

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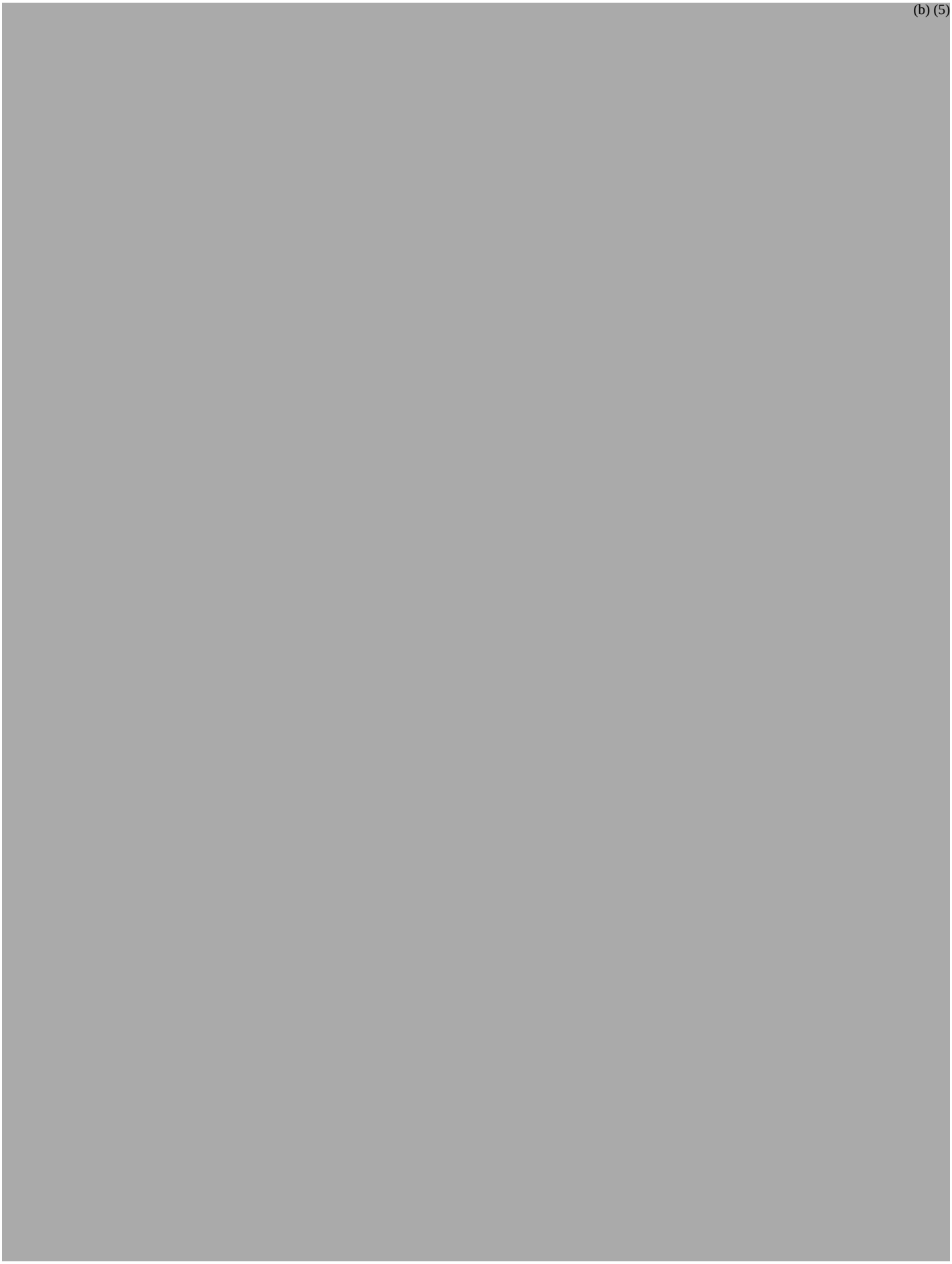
Sincerely,

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy
Ms. Emily Linde



From:	Lauer, Michael (NIH/OD) [E]
To:	Matthew R.Torsiello
Cc:	Linde, Emily (NIH/NIAID) [E]; Stemmy, Erik (NIH/NIAID) [E]; Andrew N. Krinsky; Nels T. Lippert; Black, Jodi (NIH/OD) [E]; Erbelding, Emily (NIH/NIAID) [E]; Bulls, Michelle G. (NIH/OD) [E]; Peter Daszak; Aleksei Chmura; Lauer, Michael (NIH/OD) [E]
Subject:	Re: EcoHealth Alliance re Suspension of NIH Grant No. 2R01 AI 110964-6
Date:	Friday, August 14, 2020 5:17:11 AM
Attachments:	image001.png EcoHealth Alliance - Letter to NIH re Grant Suspension 8-13-2020 (with Exhibits)[2].pdf

Dear Mr. Torsiello – letter received.

Thank you, Mike

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: (b) (6)
Email: (b) (6)

From: "Matthew R.Torsiello" (b) (6)
Date: Thursday, August 13, 2020 at 5:54 PM
To: "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: "Linde, Emily (NIH/NIAID) [E]" (b) (6), "Stemmy, Erik (NIH/NIAID) [E]" (b) (6), "Andrew N. Krinsky" (b) (6), "Nels T. Lippert" (b) (6), "Black, Jodi (NIH/OD) [E]" (b) (6), "Erbelding, Emily (NIH/NIAID) [E]" (b) (6), "Bulls, Michelle G. (NIH/OD) [E]" (b) (6), Peter Daszak (b) (6), Aleksei Chmura (b) (6), "Linde, Emily (NIH/NIAID) [E]" (b) (6)
Subject: EcoHealth Alliance re Suspension of NIH Grant No. 2R01 AI 110964-6

Dr. Lauer:

Please see the attached letter from Andrew Krinsky on behalf of EcoHealth Alliance, Inc., regarding the decision by NIH to suspend NIH Research Grant 2R01 AI 110964-6 on or about July 8, 2020.

Please confirm receipt. Thank you.

Best,

Matthew

Matthew R.Torsiello | Associate
D: (b) (6) | F: 212-216-8001
(b) (6) | Bio

Tarter Krinsky & Drogin LLP
1350 Broadway | New York | NY | 10018
www.tarterkrinsky.com | LinkedIn
COVID-19 RESOURCE CENTER

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212-216-8080, *Direct Dial*
akrinsky@tarterkrinsky.com

August 13, 2020

Via Email, Certified Mail, & FedEx
(b) (6)

Michael S. Lauer, MD
NIH Deputy Director for Extramural Research
National Institutes of Health
National Institute of Allergy and Infectious Diseases
1 Center Drive, Building 1, Room 144
Bethesda, Maryland 20892

Re: Suspension of NIH Grant 2R01 AI 110964-6

Dear Dr. Lauer:

This firm represents EcoHealth Alliance, Inc. ("EcoHealth Alliance"), in connection with the post-award decision by the National Institute of Allergy and Infectious Diseases ("NIAID"), an Institute within the National Institute of Health ("NIH"), under the Department of Health and Human Services ("HHS"), on July 8, 2020, to suspend grant 2R01 AI 110964-6 (the "Suspension:"), which funds the project *Understanding the Risk of Bat Coronavirus Emergence* (the "Project").

This letter constitutes EcoHealth Alliance's initial response to the Suspension, which was due to purported concerns regarding the safety of unspecified research being conducted at the Wuhan Institute of Virology ("WIV") and for EcoHealth Alliance's alleged failure to report certain subawards in connection with grant 2R01 AI 110964-6 (the "Grant").[1] As set forth in more detail below, the Suspension is unjustified as WIV has no connection to the Project or EcoHealth Alliance's current research and EcoHealth Alliance had not issued any subawards in connection with the Grant at the time of the Suspension. Moreover, NIAID is not authorized under 45 CFR §§ 75.371, 75.205, and 75.207, entitled *Specific Award Conditions*, to impose, *inter alia*, conditions that consist of demands for information regarding entities that are neither subrecipients of grant funds nor project affiliates.[2] Accordingly, EcoHealth Alliance hereby demands that the Suspension be withdrawn and all funding in the HHS Payment Management System be released immediately.

BACKGROUND

A. EcoHealth Alliance

EcoHealth Alliance is a prolific New York-based nonprofit institution dedicated to protecting the health of people, animals, and the environment from emerging zoonotic diseases. For more than a decade, EcoHealth Alliance has been conducting cutting edge scientific research

[1] A copy of my prior letter, dated May 22, 2020, regarding NIH's termination of the Grant, is attached hereto as Exhibit 1.
[2] Notwithstanding NIH's lack of authority to impose extraneous conditions on the Grant and Project, EcoHealth Alliance has made a good faith effort to respond to NIH's questions regarding WIV.

to identify hundreds of new coronaviruses ("CoVs") in bats and to study the capacity of these viruses to infect human cells. The purpose of this research is to identify high risk populations so international actors can leverage their resources to address potential pandemics. In cooperation with a global network of over seventy partners, including academic institutions, intergovernmental and governmental agencies, infectious disease surveillance laboratories, and other international and national organizations in over thirty countries, EcoHealth Alliance's work has led to numerous scientific papers published in high impact journals. These publications have been critical in raising awareness of the threat that CoVs pose to global health, the global economy, and U.S. National Security.

EcoHealth Alliance has a long history of successful cooperation with NIH including multiple Research Project Grant R01 awards. In particular, Peter Daszak, EcoHealth Alliance's President and Chief Scientist, has been the Principal Investigator on more than five multidisciplinary R01s. As demonstrated by Dr. Daszak's research, which produced the first ever global emerging disease "hotspots" map that identified locations in the world where viruses with pandemic potential are most likely to emerge, EcoHealth Alliance is uniquely qualified to assist in both identifying the origins of severe acute respiratory syndrome coronavirus 2 ("SARS-CoV-2") and developing and implementing strategies to combat coronavirus disease 2019 ("COVID-19").

Significantly, at this time, EcoHealth Alliance is working with several countries including, *inter alia*, Bangladesh, Côte d'Ivoire, Indonesia, Liberia, Malaysia, Republic of Congo, and Thailand to distribute PPE and provide critical reagents to test for and contain COVID-19. Notably, this effort is being supported by both the United States Department of State and the United States Agency for International Development. EcoHealth Alliance is also assisting the U.S. Geological Survey, the U.S. Fish & Wildlife Service, the International Union for Conservation of Nature, the World Health Organization, the World Organization for Animal Health, and the World Bank Group to place the COVID-19 pandemic in historical context, assess the risk of COVID-19 resurgence and spillover impacts, and determine best practices and cost-effective solutions to combat the virus. In sum, EcoHealth Alliance's research agenda is more consequential than ever.

B. NIH Issues EcoHealth Alliance A Five-Year Research Grant To Continue The Project

NIH issued EcoHealth Alliance an initial five-year research award for the Project in 2014. In 2019, EcoHealth Alliance submitted a renewal application to NIH through NIAID that contained a revised scope of work, research goals, and proposed collaborators and sought to extend the Project for an additional five years. Upon filing of its renewal application, the Project was ranked as an "extremely high priority" (in the top 3%) by NIAID during its external review process. In light of its success, the absence of any allegation that EcoHealth Alliance had violated the terms and conditions of its prior awards, and the importance of EcoHealth Alliance's continued research, on July 24, 2019, NIH reauthorized grant R01 AI 110964 and issued EcoHealth Alliance a notice of award in the amount of $733,750.00 funded under grant 2R01 AI 110964-6.[3]

[3] A copy of the notice of award, dated July 24, 2019, is attached hereto as Exhibit 1-A.

C. EcoHealth Alliance Informs HHS That WIV Is Not A Subrecipient Of Grant Funds And Agrees Not To Collaborate With WIV In Connection With The Project

On April 19, 2020, Michael S. Lauer, MD, NIH Deputy Director for Extramural Research, sent a letter to EcoHealth Alliance on behalf of NIH regarding WIV. The letter stated that, given allegations that COVID-19 "was precipitated by the release from WIV of the coronavirus responsible for COVID-19", NIH was pursuing suspension of WIV from participating in Federal programs. However, Dr. Lauer assured EcoHealth Alliance that "[t]his suspension of the sub-recipient does not affect the remainder of [EcoHealth Alliance's] grant assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension." [4]

On April 21, 2020, Dr. Daszak of EcoHealth Alliance responded by email to Dr. Lauer stating that he could "categorically state that no funds from [sic] 2R01 AI 110964-6 have been sent to Wuhan Institute of Virology, nor has any contract been signed." Dr. Daszak further represented that EcoHealth Alliance would comply with all NIAID requirements. Dr. Lauer acknowledged (1) that no monies from grant 2R01 AI 110964-6 had gone to WIV and no contract between EcoHealth Alliance and WIV had been signed and (2) EcoHealth Alliance's agreement that it would not provide any funds to WIV until and unless directed otherwise by NIH.[5]

D. NIH Unlawfully Terminates The Grant "For Convenience"

Notwithstanding NIH's representation that suspension of WIV would not affect EcoHealth Alliance's ongoing research, the Grant, or the Project, on April 24, 2020, NIH notified EcoHealth Alliance by letter that, effective immediately, the Grant and Project had been terminated (the "Termination"). The purported grounds for the Termination were: (1) convenience; (2) NIH's discretion not to award a grant, or to award a grant at a particular funding level; and (3) NIH's belief that the Project outcomes did not align with the program goals and agency priorities.[6] As a result of the Termination, EcoHealth Alliance was notified by HHS that it was required to submit a Final Research Performance Progress Report for the Project.

E. EcoHealth Alliance Files A First-Level Appeal Of The Termination

On May 22, 2020, by letter, EcoHealth Alliance filed a first-level appeal of the Termination on NIH, pursuant to NIH Grants Policy Statement Section 8.7 and 42 CFR 50, Subpart D (the "Appeal"). (Ex. 1). In its Appeal, EcoHealth Alliance argued, *inter alia*, that: (1) NIH research grants are not subject to termination for convenience; (2) NIH's discretion to award a grant at a particular funding level did not authorize NIH to issue a post-award decision to terminate a duly awarded grant during the budget period; (3) the research goals of the Project and the NIAID are substantially identical; and (4) there was no rational basis to terminate the Grant for cause.

[4] A copy of the NIAID's letter regarding WIV, dated April 19, 2020, is attached hereto as Exhibit 1-B.
[5] A copy of the email correspondence between NIH and EcoHealth Alliance is attached hereto as Exhibit 1-C.
[6] A copy of the NIAID's letter regarding the Termination, dated April 24, 2020, is attached hereto as Exhibit 1-D.

F. NIAID Withdraws The Termination But Suspends The Grant Due To Alleged Safety Concerns At WIV And For EcoHealth's Purported Failure To Report Subawards

Lacking a rational basis for its decision to terminate the Grant, on July 8, 2020, Dr. Lauer notified EcoHealth Alliance by letter that NIAID had withdrawn its termination of the Grant supporting the Project.[7] However, citing "bio-safety concerns" at WIV and EcoHealth Alliance's purported failure to report unspecified subawards, NIAID proceeded to immediately suspend the Grant and the Project, pursuant to 45 CFR § 75.371 and NIH Grants Policy Statement Section 8.5.2, leaving the status of the Project effectively unchanged. In addition, the Suspension seeks to impose on EcoHealth Alliance the outrageous obligation to provide NIH with information and materials in the custody and control of WIV and to somehow facilitate access by an USFG "inspection team" to WIV, as a condition for lifting the Suspension.[8]

ARGUMENT

In the Suspension, NIAID identifies two and only two grounds for its decision to suspend the Grant and the Project: (1) purported safety concerns regarding WIV; and (2) EcoHealth Alliance's purported failure to report unspecified subawards. As set forth in detail herein, EcoHealth Alliance is not conducting any research or otherwise collaborating with WIV in connection with the Project. Moreover, EcoHealth Alliance had not issued any subawards in connection with the Grant at the time of the Suspension. Accordingly, the Suspension should be withdrawn immediately.[9]

A. NIH's Purported Concern That WIV Poses A Threat To Public Health And Welfare Is Not A Basis To Suspend The Grant Or The Project As WIV Is Not A Current Subrecipient Of Grant Funds And Has No Connection To The Project

Under 45 CFR §§ 75.207, 75.205, and 75.371 and NIH Grants Policy Statement Section 8.5.2, NIAID may take one or more enforcement actions where a grant recipient has failed to materially comply with the terms and conditions of the award. Under 45 CFR 75.374, the HHS awarding agency must provide the non-Federal entity an opportunity to object and provide information challenging any suspension or termination action. Given the exclusion of WIV from the Project, and NIH's failure to identify any other safety concerns, there is no basis for NIAID to suspend the Grant or to impose additional conditions.

At all relevant times, EcoHealth Alliance has duly monitored the activities of its subrecipients as necessary to ensure that any subawards were used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward. Moreover, EcoHealth Alliance is not aware of any allegation that any subrecipient of grant 1R01 AI 110964 funds has ever used such funds for unauthorized purposes, or in violation of any Federal

[7] Please confirm that, due to the withdrawal of the Termination, EcoHealth Alliance is not required to submit a final Project report at this time.
[8] A copy of the NIAID's letter regarding the Suspension, dated July 8, 2020, is attached hereto as Exhibit 2.
[9] EcoHealth Alliance notes that the Suspension did not state any specific deadline for EcoHealth Alliance to respond to the Suspension or proposed additional conditions. Accordingly, this response is timely.

statutes, regulations, or the terms and conditions of the subject subaward. Furthermore, NIH has never accused EcoHealth Alliance of any act that posed a risk to public welfare and safety.

Significantly, WIV is the only organization identified in the Suspension as posing a risk to public welfare and safety. As stated in my prior letter on May 22, 2020, regarding the now admittedly unlawful termination of the Grant, at NIH's express request, no Grant funds have been distributed to WIV and no contract has been signed between EcoHealth Alliance and WIV in connection with the Project. Thus, the allegation that WIV's independent research at its facility poses unspecified bio-safety concerns should have no bearing on the Project, which was in strict compliance with NIH Grants Policy Statement §§ 4 and 4.1.24, and the terms and conditions of the Notice of Award (Ex. 1-A), at the time of the Suspension.

To reiterate, WIV is not a subrecipient of any Grant funds and will not be involved in the Project in any capacity. (*see* Ex. 1-C-7). Significantly, NIAID explicitly told EcoHealth Alliance that it could exclude WIV and continue the Project without jeopardizing the Grant so long as "no grant funds [were] provided to WIV." (Ex. 1-B).

B. EcoHealth Alliance Has Duly Reported All Issued Subawards And Was In Compliance With The Transparency Act At The Time Of The Suspension

Contrary to NIAID's assertion that EcoHealth Alliance failed to report unspecified subawards, EcoHealth Alliance did not issue or sign any subawards in connection with the 2019 Grant or before July 8, 2020. Accordingly, the reporting requirements of the Federal Funding Accountability and Transparency Act (the "FFATA") did not apply at the time of the Suspension.

Regarding the Project period between 2014 and 2019, EcoHealth Alliance duly complied with all NIAID-system-only financial reporting requirements. While EcoHealth Alliance had not entered the FFATA reporting information in the Federal Subaward Reporting System ("the FSRS"), all subawards issued in connection with the 2014 Project and the 2019 Project are now fully reported in the FSRS. Notably, no one at NIAID or NIH ever contacted or otherwise notified EcoHealth Alliance that it was not in compliance. As EcoHealth Alliance has taken appropriate corrective action that fully resolves its alleged non-compliance with the FFATA, pursuant to NIH Grants Policy Statement Section 8.5.2, the Suspension should be withdrawn.

C. HHS Has No Authority To Impose New Conditions That Are Wholly Unrelated To The Project And EcoHealth Alliance's Ongoing Research

Under 45 CFR § 75.207, NIAID may impose additional specific award conditions under the following circumstances: when the applicant or recipient has a history of failure to comply with the general or specific terms and conditions of a Federal award; when an applicant or recipients fails to meet expected performance goals; and when an applicant or recipient is not otherwise responsible. Allowed conditions include: (1) requiring payments as reimbursements rather than advance payments; (2) withholding authority to proceed to the next phase until receipt of evidence of acceptable performance within a given period of performance; (3) requiring additional, more detailed financial reports; (4) requiring additional project monitoring (5) requiring the non-Federal entity to obtain technical or management assistance; or (6) establishing additional

prior approvals. (45 CFR § 75.207[b]). The purpose of these additional conditions are to encourage the award recipients to comply with the original terms and conditions of the award, applicable statutes, and regulations.

There is no statute or NIH Grants Policy Statement provision that authorizes NIAID to impose additional conditions that consist of demands for information and materials regarding entities that are neither current subrecipients of grant funds nor connected to the research project funded by the subject grant. This makes sense, given that the purpose of imposing additional conditions is to ensure that research funded under a particular grant is conducted safely and in compliance with applicable laws.

Here, NIH's First, Second, Third, Fourth, Fifth, and Sixth proposed conditions, which require that EcoHealth Alliance, *inter alia*, provide information and materials regarding WIV, are wholly unrelated to the safety and efficacy of Project and EcoHealth Alliance's ongoing research as WIV is not a subrecipient of Grant funds (*see* Ex. 1-C-6, 7 and 8). Moreover, certain conditions, including the Sixth condition that "EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019" seek to impose impossible obligations. EcoHealth Alliance has no authority to grant NIAID access to the WIV lab facilities and is not conducting any research with WIV in connection with the Project. Whether or not EcoHealth Alliance is able to provide responses to the proposed conditions regarding WIV will not affect the safety of EcoHealth Alliance's current research, which will not involve WIV.

Without waiving any objections, in the interest of cooperation, EcoHealth Alliance has made a good faith effort to provide responses to the additional conditions (the "Requests") based on information now known to Peter Daszak, EcoHealth Alliance’s President and Chief Scientist.[10]

CONCLUSION

Every single outbreak of a novel virus has been accompanied by the allegation that the subject virus was created in a lab, including, *inter alia*, HIV, Ebola, and now SARS-CoV-2. There is no credible evidence to support these theories. By comparison, we know that seventy-five percent of new emerging diseases originate in wildlife. Every species of wildlife carry these viruses, an estimated 1.7 million of which are still unknown. While many of these viruses are benign, occasionally a lethal virus will emerge that can directly infect humans. EcoHealth Alliance is a valuable resource. The instant request to resume the Project funded by the Grant presents HHS with the opportunity to support proven research regarding the threat of zoonotic disease emergence and to support scientists who are working to determine whether certain vaccines and drugs can kill the SARS-CoV-2 virus to save our lives.

At this time, EcoHealth Alliance is in compliance with all of the terms and conditions of the award including the FFATA, there is no public health concern posed by EcoHealth Alliance's

[10] A copy of EcoHealth Alliance's Objections and Responses to the Requests is attached hereto as Exhibit 3.

resumption of the Project, which will not involve WIV in any capacity (*see* NIH Grants Policy Sections 4 and 4.1.24), and EcoHealth Alliance has hereby provided, to the best of its ability, the information and materials requested by NIH in the Suspension. Accordingly, the Suspension should be withdrawn and all funding in the HHS Payment Management System should be released immediately.

Please note that this letter is not intended to provide an exhaustive list of all possible grounds for vacating the Suspension and may not reflect all arguments and claims that EcoHealth Alliance will assert in the event that it is required to file a first-level appeal or other action or proceeding concerning any future adverse determination by NIAID affecting the Grant or the Project. All of EcoHealth Alliance's rights and remedies to seek review of any adverse determination are expressly reserved.

Should you wish to present evidence in an effort to refute any of the factual assertions made in this letter, and/or to engage in good faith negotiations regarding appropriate terms and conditions for the resumption of funding for grant 2R01 AI 110964-6, we are prepared to review such evidence and to participate in such negotiations.

We await your response to this letter.

Very truly yours,

(b) (6)

Andrew W. Krinsky

cc: (*by email*)

Dr. Erik Stemmy (b) (6)
Ms. Emily Linde (b) (6)

Exhibit 1

Tarter Krinsky & Drogin LLP
1350 Broadway
New York, NY 10018
P 212.216.8000
F 212.216.8001
www.tarterkrinsky.com

Andrew N. Krinsky, *Partner*
212-216-8080, *Direct Dial*
akrinsky@tarterkrinsky.com

May 22, 2020

Via Email, Certified Mail, & FedEx
(b) (6)

Michael S. Lauer, MD
NIH Deputy Director for Extramural Research
National Institutes of Health
National Institute of Allergy and Infectious Diseases
1 Center Drive, Building 1, Room 144
Bethesda, Maryland 20892

Re: Termination of NIH Grant 2R01 AI 110964-6

Dear Dr. Lauer:

This firm represents EcoHealth Alliance, Inc. ("EcoHealth Alliance") with regard to the post-award decision by the National Institute of Allergy and Infectious Diseases ("NIAID"), an Institute within the National Institute of Health ("NIH"), under the Department of Health and Human Services ("HHS"), to terminate the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI 110964, on April 24, 2020 (the "Termination").

This letter, pursuant to NIH Grants Policy Statement Section 8.7 and 42 CFR 50, Subpart D, constitutes EcoHealth Alliance's first-level appeal of the Termination, which was "for convenience." As set forth in more detail below, the Termination is not authorized under the NIH Grants Policy Statement, arbitrary and capricious and an indefensible attack on public health and welfare given that it undermines a pivotal 10-year research project involving the origins, spread and threat of emerging bat coronaviruses during the peak of an unprecedented worldwide coronavirus pandemic. Accordingly, EcoHealth Alliance hereby demands that grant 2R01 AI 110964-6 be reinstated immediately.

BACKGROUND

A. EcoHealth Alliance

EcoHealth Alliance is a prominent New York-based nonprofit institution dedicated to protecting the health of people, animals, and the environment from emerging zoonotic diseases. For more than a decade, EcoHealth Alliance has been conducting cutting edge scientific research to identify hundreds of new coronaviruses ("CoVs") in bats and to study the capacity of these viruses to infect human cells. The purpose of this research is to identify high risk populations so international actors can leverage their resources to address potential pandemics. In cooperation with a global network of over seventy partners, including academic institutions, intergovernmental

and governmental agencies, infectious disease surveillance laboratories, and other international and national organizations in over thirty countries, EcoHealth Alliance's work has led to numerous scientific papers published in high impact journals. These publications have been critical in raising awareness of the threat that CoVs pose to global health, the global economy, and U.S. National Security.

EcoHealth Alliance has a long history of successful cooperation with NIH including multiple Research Project Grant R01 awards. In particular, Peter Daszak, EcoHealth Alliance's President and Chief Scientist, has been the Principal Investigator on five multidisciplinary R01s. All of these projects used modeling, epidemiology, laboratory, and field science to test hypotheses on the emergence of wildlife-origin viral zoonoses, including SARS-CoV, the Nipah and Hendra viruses, Avian influenza, and other bat-origin viruses. EcoHealth Alliance, a 501(c)(3) organization, is unique in that it goes one step further by leveraging its research goals to create an alliance of international collaborators that can advocate for real-world changes to protect high risk populations.

Notably, in collaboration with virologists in China, EcoHealth Alliance isolated and characterized SARSr-CoVs from bats that use the same human host cell receptor (ACE2) as SARS-CoV. This work provided critical reagents and resources that have advanced scientific understanding of virus-host binding and contributed to vaccine development. For example, the genetic sequences of the bat viruses that EcoHealth Alliance discovered under its NIH research funding, which were published online (Genbank & GISAID), have been used to test the effectiveness of the drug Remdesivir against not only SARS-CoV, but also MERS, and other potentially zoonotic or pre-pandemic bat CoVs. Significantly, this type of testing can be performed without the need for viral cultures or shipping viruses internationally.

B. NIH Awards And Extends EcoHealth Alliance Research Grant R01 AI 110964

In 2014, NIH issued EcoHealth Alliance a five-year research award for the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI 110964 (the "Project"). EcoHealth Alliance received additional awards for the Project each year between 2015 and 2018. Between 2015 and 2019, the Project resulted in the publication of more than twenty papers.

In 2019, EcoHealth Alliance submitted a renewal application to NIH through NIAID to extend the Project period for an additional five years. Upon filing of its renewal application, the Project was ranked as an "extremely high priority" (in the top 3%) by NIAID during its external review process. In light of its success and the importance of EcoHealth Alliance's work, on July 24, 2019, NIH reauthorized grant R01 AI 110964 and increased EcoHealth Alliance's funding. EcoHealth Alliance was issued a notice of award in the amount of $733,750.00 (the "2019 Award"). The notice of award also extended the Project period for an additional five years to 2024. A copy of the notice of award is attached hereto as Exhibit A.

C. EcoHealth Alliance Agrees Not To Fund The Wuhan Institute Of Virology

During the pendency of the Project, in December of 2019, China reported a cluster of cases of pneumonia in Wuhan, Hubei Province. It was later determined that the cause of this pneumonia

was a novel CoV, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing coronavirus disease (COVID-19). Thereafter, SARS-CoV-2 spread to nearly every country throughout the world. In response, EcoHealth Alliance has prioritized its efforts in conducting research that will be integral to developing an effective strategy to combat SARS-CoV-2.

On April 19, 2020, Michael S. Lauer, MD, NIH Deputy Director for Extramural Research, sent a letter to EcoHealth Alliance on behalf of NIH regarding a laboratory in China, the Wuhan Institute of Virology ("WIV"). WIV was a prior sub-recipient of a small portion of the R01 AI 110964 grant funds. The letter stated that, given allegations that COVID-19 "was precipitated by the release from WIV of the coronavirus responsible for COVID-19", NIH was pursuing suspension of WIV from participating in Federal programs. However, Mr. Lauer assured EcoHealth Alliance that "[t]his suspension of the sub-recipient does not affect the remainder of [EcoHealth Alliance's] grant assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension." A copy of the letter is attached hereto as Exhibit B.

On April 21, 2020, Dr. Daszak of EcoHealth Alliance responded by email to Dr. Lauer stating that he could "categorically state that no funds from [sic] 2R01 AI 110964-6 have been sent to Wuhan Institute of Virology, nor has any contract been signed." Dr. Daszak further represented that EcoHealth Alliance would comply with all NIAID requirements. Dr. Lauer acknowledged (1) that no monies from grant 2R01 AI 110964-6 had gone to WIV and no contract between EcoHealth Alliance and WIV had been signed and (2) EcoHealth Alliance's agreement that it would not provide any funds to WIV until and unless directed otherwise by NIH. A copy of the email correspondence between NIH and EcoHealth Alliance is attached hereto as Exhibit C.

D. NIH Abruptly Terminates Research Grant 2R01 AI 110964-6 "For Convenience"

Notwithstanding NIH's representation that suspension of WIV would not affect the remainder of EcoHealth Alliance's 2019 Award, on April 24, 2020, NIH notified EcoHealth Alliance by letter that, effective immediately, the 2019 Award had been terminated by NIAID. The stated grounds for the Termination were: (1) convenience; (2) NIH's discretion not to award a grant, or to award a grant at a particular funding level; and (3) NIH's belief that the Project outcomes did not align with the program goals and agency priorities. A copy of the Termination is attached hereto as Exhibit D.

ARGUMENT

A. NIH Research Grants Are Not Subject To Termination For Convenience

"Termination for convenience" refers to the exercise of the government's right to bring to an end the performance of all or part of the work provided for under a contract prior to the expiration of the contract "when it is in the Government's interest" to do so. Federal agencies typically incorporate clauses in their procurement contracts which give them the right to terminate for convenience. Here, there is no clause in the terms and conditions applicable to the 2019 Award, or in the NIH Grants Policy Statement, that permits NIAID or NIH to issue a post-award decision to terminate a NIH research grant award "for convenience."

Moreover, the unprecedented assertion by NIH that active research grants can be terminated "for convenience" during the subject budget period renders Section 8.5.2 of the NIH Grants Policy Statement meaningless. *See, e.g., Li v. Eddy*, 324 F.3d 1109, 1110 (9th Cir. 2003) (rejecting suggested statutory interpretation on the grounds that the interpretation ran squarely against the canon of construction that courts interpret statutes so as not to render any section meaningless). Section 8.5.2 of the NIH Grants Policy Statement governs, *inter alia*, modification or termination of an award for misconduct. If NIH grants were terminable for convenience, NIH could always choose to terminate for convenience to avoid (1) the "for cause" restriction on grant terminations and (2) the labor intensive task of enforcing compliance through disallowing costs, withholding further awards, or wholly suspending the grant, pending corrective action.

B. NIH's Discretion Not To Award A Grant, Or To Award a Grant At A Particular Funding Level, Does Not Authorize A Post-Award Decision To Terminate

NIH's discretion regarding the "decision not to award a grant, or to award a grant at a particular funding level" does not give NIH the authority to issue a post-award decision terminating a duly awarded grant during the budget period. This purported discretion, which is based on language in the last paragraph of NIH Grants Policy Statement Section 2.4.4, entitled *Disposition of Applications*, concerns NIH's authority to reject incomplete or otherwise undesirable grant applications in the first instance only. The provisions of Section 2, generally, have no bearing on post-award decisions affecting duly approved grants for which specified funds have already been allocated. As the 2019 Grant in the amount of $733,750.00 was awarded to EcoHealth Alliance on July 24, 2019, NIH's authority to deny initial grant applications does not allow NIH to terminate the 2019 Grant.

C. The Research Goals Of EcoHealth Alliance And NIAID Are Virtually Identical

NIH's contention that the Project's outcomes do not align with the agency's priorities is demonstrably false. First, the Project was ranked as "extremely high priority" on external review by NIAID less than nine months ago, before the discovery of SARS-CoV-2. Since this discovery, NIH has promulgated new grants seeking applicants to conduct research on the same issues covered by the Project and the 2019 Award.

In addition, there is substantial overlap between the four strategic research priorities on page 1 of NIAID's Strategic Plan for COVID-19 Research, published April 22, 2020, and the three Specific Aims of the Project. Both NIAID and EcoHealth Alliance seek to: (1) improve fundamental knowledge of SARS-Cov-2; (2) develop methods to assess the rate of infection and disease incidence; (3) contribute to the development of an effective vaccine; and (4) increase public health preparedness. Copies of the Project's Specific Aims and the NIAID Strategic Plan's four strategic research priorities for COVID-19 research are attached hereto as Exhibit E.

D. There Is No Rational Basis To Terminate The 2019 Award For Cause

The grounds and procedures for suspension and termination of awards are specified in NIH Grants Policy Statement Section 8.5.2 and 45 CFR Parts 75.371 through 75.373. Notably, Section

8.5.2 provides, *inter alia*, that NIH will generally suspend (rather than immediately terminate) a grant and allow the recipient an opportunity to take appropriate corrective action before NIH makes a termination decision. Through this lens, 45 CFR 75.372 provides that NIH may terminate a Federal award, in whole or in part, if: (1) the non-Federal entity fails to comply with the terms and conditions of the award; (2) for cause; (3) by the HHS awarding agency or pass-through entity with the consent of the non-Federal entity; or (4) by the non-Federal entity upon written notice to the HHS awarding agency setting forth the reasons for such termination, and other information. None of the foregoing predicate conditions exist here.

As of the date of the Termination, EcoHealth Alliance had not received any notice from NIH, NIAID, or HHS that it either failed to comply with any of the terms or conditions of the 2019 Award, or committed any misconduct in connection with the award. To the contrary, in email correspondence following EcoHealth Alliance's representation that it had not and would not give any funds from the 2019 Award to WIV, Aleksei Chmura, EcoHealth Alliance's Chief of Staff, memorialized the mutual agreement between NIH and EcoHealth Alliance that EcoHealth Alliance was in compliance with all requests. (Ex. C, p. 1). To be clear, EcoHealth Alliance clearly and unequivocally stated that it had not and will not distribute any funds from the 2019 Award to WIV.

In sum, there is no statutory, regulatory, or contractual basis for NIAID's termination of the Project, *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant 2R01 AI 110964-6. However, please note that this letter is not intended to provide an exhaustive list of all possible grounds for reversal of the Termination and may not reflect all arguments and claims that EcoHealth Alliance will assert in the event that a formal second-level appeal of the Termination is required.

Should you wish to present evidence in an effort to refute any of the factual assertions made in this letter and/or to engage in good faith negotiations regarding appropriate terms and conditions for the resumption of funding for grant 2R01 AI 110964-6, we are prepared to review such evidence and to participate in such negotiations.

We await your response to this letter.

Very truly yours,

(b) (6)

Andrew W. Krinsky

cc: (*by email*)

Dr. Erik Stemmy (b) (6)
Ms. Emily Linde (b) (6)

Exhibit A

RESEARCH
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 07/24/2019

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 2R01AI110964-06
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Dr. Daszak, Peter
PD/PI
460 West 34th Street
Suite 1701
New York, NY 100012320

Award e-mailed to: (b) (6)

Period Of Performance:
Budget Period: 07/24/2019 – 06/30/2020
Project Period: 06/01/2014 – 06/30/2024

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $733,750 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to ECOHEALTH ALLIANCE, INC. 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 R01AI110964. 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,

Tseday G Girma
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 2R01AI110964-06

[redacted]

[redacted]

Approved Budget	$733,750
Total Amount of Federal Funds Obligated (Federal Share)	$733,750
TOTAL FEDERAL AWARD AMOUNT	$733,750
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$733,750

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
6	$733,750	$733,750
7	$709,750	$709,750
8	$709,750	$709,750
9	$709,750	$709,750
10	$709,750	$709,750

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Allergy and Infectious Diseases Research
CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964B
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019	2020	2021	2022	2023
AI	8472364	$733,750	$709,750	$709,750	$709,750	$709,750

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C B / **OC**: 414B / **Released**: (b) (6) 07/18/2019
Award Processed: 07/24/2019 12:03:26 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2R01AI110964-06

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 – 2R01AI110964-06

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).

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) R01AI110964. 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/.

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 – 2R01AI110964-06

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.

[redacted]

****

The Research Performance Progress Report (RPPR), Section G.9 (Foreign component), includes reporting requirements for all research performed outside of the United States. Research conducted at the following site(s) must be reported in your RPPR:

[redacted]

****

This award reflects current Federal policies regarding Facilities & Administrative (F&A) Costs for foreign grantees including foreign sub-awardees, and domestic awards with foreign sub-awardees. Please see: Chapter 16 Grants to Foreign Organizations, International Organizations, and Domestic Grants with Foreign Components, Section 16.6 "Allowable and Unallowable Cost" of the NIH Grants Policy.

****

This award may include collaborations with and/or between foreign organizations. Please be advised that short term travel visa expenses are an allowable expense on this grant, if justified as critical and necessary for the conduct of the project.

****

The budget period anniversary start date for future year(s) will be **July** 1.

****

Dissemination of study data will be in accord with the Recipient's accepted genomic data sharing plan as stated in the page(s) **203** of the application. Failure to adhere to the sharing plan as mutually agreed upon by the Recipient and the NIAID may result in Enforcement Actions as described in the NIH Grants Policy Statement.

****

This award is subject to the Clinical Terms of Award referenced in the NIH Guide for Grants and Contracts, July 8, 2002, NOT AI-02-032. These terms and conditions are hereby incorporated by reference, and can be accessed via the following World Wide Web address: https://www.niaid.nih.gov/grants-contracts/niaid-clinical-terms-award All submissions required by the NIAID Clinical Terms of Award must be forwarded electronically or by mail to the responsible NIAID Program Official identified on this Notice of Award.

****

Awardees who conduct research involving Select Agents (see 42 CFR 73 for the Select Agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens at http://www.selectagents.gov/Regulations.html) must complete registration with CDC (or APHIS, depending on the agent) before using NIH funds. No funds can be used for research involving Select Agents if the final registration certificate is denied.

Prior to conducting a restricted experiment with a Select Agent or Toxin, awardees must notify the NIAID and must request and receive approval from CDC or APHIS.

****

Select Agents:
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:

- A list of the new and/or additional Agent(s) that will be studied;
- A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
- 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

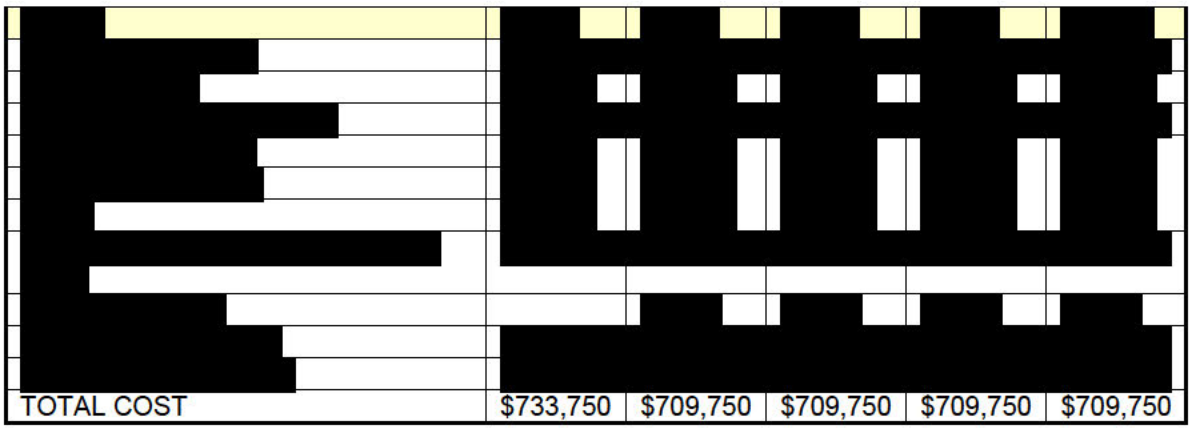
The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals 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: Tseday G Girma
Email: (b) (6) **Phone**: (b) (6) **Fax**: 301-493-0597

Program Official: Erik J. Stemmy
Email: (b) (6) **Phone**: (b) (6)

SPREADSHEET SUMMARY
GRANT NUMBER: 2R01AI110964-06

INSTITUTION: ECOHEALTH ALLIANCE, INC.



TOTAL COST	$733,750	$709,750	$709,750	$709,750	$709,750

Facilities and Administrative Costs	Year 6	Year 7	Year 8	Year 9	Year 10
F&A Cost Rate 1	32%	32%	32%	32%	32%
F&A Cost Base 1	$438,711	$363,711	$363,711	$363,711	$363,711
F&A Costs 1	$140,388	$116,388	$116,388	$116,388	$116,388

Exhibit B

Date: April 19, 2020

From: Michael S Lauer, MD
NIH Deputy Director for Extramural Research

Lauer, Michael (NIH/OD) [E] Digitally signed by Lauer, Michael (NIH/OD) [E] Date: 2020.04.19 10:47:40 -04'00'

To: Kevin Olival, PhD
Vice-President for Research
EcoHealth Alliance
(b) (6)

Naomi Schrag, JD
Vice-President for Research Compliance, Training, and Policy
Columbia University
(b) (6)

Subject: Project Number 2R01AI110964-06

Dear Dr. Olival and Ms. Schrag:

EcoHealth Alliance, Inc. is the recipient, as grantee, of an NIH grant entitled "Understanding the Risk of Bat Coronavirus Emergence." It is our understanding that one of the sub-recipients of the grant funds is the Wuhan Institute of Virology ("WIV"). It is our understanding that WIV studies the interaction between corona viruses and bats. The scientific community believes that the coronavirus causing COVID-19 jumped from bats to humans likely in Wuhan where the COVID-19 pandemic began. There are now allegations that the current crisis was precipitated by the release from WIV of the coronavirus responsible for COVID-19. Given these concerns, we are pursuing suspension of WIV from participation in Federal programs.

While we review these allegations during the period of suspension, you are instructed to cease providing any funds from the above noted grant to the WIV. This temporary action is authorized by 45 C.F.R. § 75.371(d) ("Initiate suspension or debarment proceedings as authorized under 2 C.F.R. part 180"). The incorporated OMB provision provides that the funding agency may, through suspension, immediately and temporarily exclude from Federal programs persons who are not presently responsible where "immediate action is necessary to protect the public interest." 2 C.F.R. § 180.700(c). It is in the public interest that NIH ensure that a sub-recipient has taken all appropriate precautions to prevent the release of pathogens that it is studying. This suspension of the sub-recipient does not affect the remainder of your grant assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension.

Exhibit C

1 Michael Lauer email 20 April 2020

From: Lauer, Michael (NIH/OD) [E] (b) (6)
Sent: Sunday, April 19, 2020 11:00 AM
To: (b) (6); Naomi Schrag (b) (6)
Cc: Black, Jodi (NIH/OD) [E] (b) (6)
Subject: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Importance: High

Dear Dr. Olival and Ms. Schrag

Please see attached.

Many thanks, Mike

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: (b) (6)
Email: (b) (6)

2 Kevin Olival email on 20 April 2020

From: Kevin Olival [redacted]
Subject: Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 20, 2020 at 4:12:28 PM EDT
To: "Lauer, Michael (NIH/OD) [E]" [redacted]
Cc: Naomi Schrag [redacted], "Black, Jodi (NIH/OD) [E]" [redacted]

Dear Mike,

I received the attached letter, however please note:

1. I am not the PI on this award. You should contact Dr. Peter Daszak [redacted] who is the PI and leading this project for EcoHealth Alliance.
2. Columbia University is not involved in this NIH project, and it is not clear to me why Naomi and Columbia University were included.

Thank you,
Kevin

Kevin J. Olival, PhD
Vice President for Research

EcoHealth Alliance
460 West 34th Street, Suite 1701
New York, NY 10001

[redacted] (direct)
[redacted] (mobile)
1.212.380.4465 (fax)
www.ecohealthalliance.org

3 Michael Lauer email on 20 April 2020

Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

Lauer, Michael (NIH/OD) [E] (b) (6)

Mon 4/20/2020 4:31 PM

To: Kevin Olival (b) (6) Peter Daszak (b) (6)

Cc: Naomi Schrag (b) (6); Black, Jodi (NIH/OD) [E] (b) (6); Lauer, Michael (NIH/OD) [E] (b) (6)

Importance: High

2 attachments

Screen Shot 2020-04-20 at 4.23.38 PM.png; EcoHealth Alliance re AI grant 4 19 20.pdf;

Thank you Kevin

- We need to work with a senior responsible business official – usually PI's and senior business officials are different people.
- When I looked you up on the web, I see the Columbia logo (see attached screenshot). Specifically, it appears to be Columbia University > Ecology, Evolution, and Environmental Biology > EcoHealth Alliance (labeled as an "Affiliation/Department"). Thus the web profile makes it look to me as if EcoHealth Alliance is linked to Columbia University.
- In any case, I'm looping in Dr. Daszak.
- We need to know all sites in China that have been in any way linked to this award (Type 1 and Type 2). We have data in NIH, but we want to make absolutely sure that we're of the same understanding.

We greatly appreciate your prompt attention to this matter.

Best, Mike

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: (b) (6)
Email: (b) (6)

Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

4 Michael Lauer email on 20 April 2020

Lauer, Michael (NIH/OD) [E] (b) (6)

Mon 4/20/2020 6:34 PM

To:Naomi Schrag (b) (6); Kevin Olival (b) (6) Peter Daszak (b) (6);

Cc:Black, Jodi (NIH/OD) [E] (b) (6); Lauer, Michael (NIH/OD) [E] (b) (6);

1 attachment

Screen Shot 2020-04-20 at 4.23.38 PM.png;

Thanks Naomi – not the impression an observer would get looking at the website (see screen shot), but we understand about the grant.

If they "are entirely separate entities" then why does Columbia identify EcoHealth Alliance as an "Affiliation/Department" on its website.

Maybe with the label "Affiliation/Department" you would have a clearly visible disclaimer that says, "EcoHealth Alliance is not affiliated with nor a department of Columbia"? – although even that is internally contradictory.

Best, Mike

From: Naomi Schrag (b) (6)
Date: Monday, April 20, 2020 at 5:19 PM
To: "Lauer, Michael (NIH/OD) [E]" (b) (6), Kevin Olival (b) (6), (b) (6)
Cc: Naomi Schrag (b) (6), "Black, Jodi (NIH/OD) [E]" (b) (6).
Subject: RE: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

Dear Dr. Lauer,
Columbia and EcoHealth Alliance are entirely separate entities. Some individuals affiliated with EcoHealth Alliance do have adjunct appointments in Columbia's Ecology, Evolution, and Environmental Biology ("E3B") department, but we are not aware of any Columbia involvement with the referenced grant, and have found no agreement or record in our grants system to the contrary.

We would be happy to answer any additional questions. Thank you.
Sincerely,
Naomi Schrag

Naomi J. Schrag

Vice President for Research Compliance, Training and Policy
Office of Research Compliance and Training
475 Riverside Drive, Suite 840
New York, New York 10115
(b) (6)
www.researchcompliance.columbia.edu

RE: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

5 Peter Daszak email on 21 April 2020

Peter Daszak

Tue 4/21/2020 1:32 AM

To:Lauer, Michael (NIH/OD) [E] (b) (6); Naomi Schrag (b) (6); Kevin Olival (b) (6);

Cc:Black, Jodi (NIH/OD) [E] (b) (6);

Dear Michael Lauer & Jodi Black – I now have your email and will deal with it directly with you and your staff. Naomi is correct that there is no involvement of Columbia University in this grant. I'm sure NIH has records to confirm that.

From this moment on, I will not cc any staff at Columbia as part of this discussion, and I hope you will also honor that. Respecfully, the discussion of whether or not EHA is an affiliate of CU is entirely irrelevant to the request that you contacted us about, and should remain a private matter between EcoHealth Alliance and Columbia University.

I'll look over your email and respond tomorrow.

Cheers,

Peter

Peter Daszak
President

EcoHealth Alliance
460 West 34th Street
New York, NY 10001
USA

Tel.: (b) (6)
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

RE: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06

6 Peter Daszak email on 21 April 2020

Peter Daszak

Tue 4/21/2020 7:03 PM

To:Lauer, Michael (NIH/OD) [E] (b) (6);

Cc:Black, Jodi (NIH/OD) [E] (b) (6); Aleksei Chmura (b) (6);
Stemmy, Erik (NIH/NIAID) [E] (b) (6); (b) (6);

Importance: High

1 attachment

EcoHealth Alliance re AI grant 4 19 20.pdf;

Dear Michael – Confirming receipt of your email. I'm also cc'ing the following people so they're aware of this request:

1. Our AOR – Dr. Aleksei Chmura, who has access to all our records
2. My Program Officer for this award, Dr. Erik Stemmy & the Division Director (DMID), Dr. Emily Erberding, so they are informed and aware of the request and our response.

That said we need some time to go through the request for information and will provide this as quickly as we can.

However, **I can categorically state that no funds form 2R01AI110964-06 have been sent to Wuhan Institute of Virology, nor has any contract been signed.** Furthermore, we will comply with NIAID requirements, of course.
Concerning the request for information on all of the sites linked to this award in China, you should be aware that these are documented in our progress reports over the course of the grant. As you can understand we are under enormous pressure to generate data related to the current pandemic, and we do not want to divert staff to this effort. We are hoping the previously filed reports will satisfy this request.

We are well aware of the political concerns over the origins of this outbreak. Our collaboration with Wuhan Institute of Virology has been scientific and we have been consistently impressed with the scientific capabilities of that laboratory and its research staff. Our joint work has led to a series of critical papers published in high impact journals that served to raise awareness of the future threat coronaviruses pose for global health and therefore US national security. Scientific insights with epidemiological significance have been jointly published and our relationship has always been open and transparent and with one concern only, scientific validity. We are concerned that current actions may jeopardize 15 years of fruitful collaboration with colleagues in Wuhan, who are working at the leading edge to design vaccines and drugs that could help us fight this new threat in future years. It is quite remarkable that of the 5 vaccine candidates listed by WHO that are already in human trials, 3 have been developed in China. That said, we of course will

do all we can to make sure any further questions from NIH or any Federal agency are addressed to our fullest knowledge.

Yours sincerely,

Peter Daszak
President

EcoHealth Alliance
460 West 34th Street
New York, NY 10001
USA

Tel.: (b) (6)
Website: www.ecohealthalliance.org
Twitter: @PeterDaszak

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation

7 Michael Lauer email on 21 April 2020

From: **Lauer, Michael (NIH/OD) [E]** (b) (6)
Subject: Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 21, 2020 at 19:28
To: Peter Daszak (b) (6)
Cc: Black, Jodi (NIH/OD) [E] (b) (6), Aleksei Chmura (b) (6), Stemmy, Erik (NIH/NIAID) [E] (b) (6), Erbelding, Emily (NIH/NIAID) [E] (b) (6), Lauer, Michael (NIH/OD) [E] (b) (6)

ML

Many thanks Peter for your response.

We note that:

- No monies have gone to WIV on the Type 2 award and no contract has been signed.
- You agree that you will not provide any funds to WIV until and unless directed otherwise by NIH.
- All foreign sites for the Type 1 and Type 2 awards have been documented in the progress reports submitted to NIH.

We appreciate your working with us.

Best, Mike

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: (b) (6)
Email: (b) (6)

8 Aleksei Chmura email on 21 April 2020

From: **Aleksei Chmura** (b) (6)
Subject: Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 23, 2020 at 13:50
To: Lauer, Michael (NIH/OD) [E] (b) (6)
Cc: Peter Daszak (b) (6), Black, Jodi (NIH/OD) [E] (b) (6), Erik Stemmy (b) (6), Erbelding, Emily (NIH/NIAID) [E] (b) (6)

Dear Mike,

I read that we are in agreement and in compliance with all requests. Please let us know if anything further is required. We will continue in our usual close communication with our Program Officer Erik Stemmy.

Sincerely,

-Aleksei

Aleksei Chmura
Chief of Staff &
Authorized Organizational Representative

EcoHealth Alliance
460 West 34th Street, Suite 1701
New York, NY 10001

(b) (6) (office)
(b) (6) (mobile)
www.ecohealthalliance.org

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

From: **Lauer, Michael (NIH/OD) [E]** (b) (6)
Subject: Re: Please read and acknowledge receipt -- Acticns needed regarding 2R01AI110964-06
Date: April 23, 2020 at 13:59
To: Aleksei Chmura (b) (6)
Cc: Peter Daszak (b) (6), Black, Jodi (NIH/OD) [E] (b) (6), Stemmy, Erik (NIH/NIAID) [E] (b) (6), Erbelding, Emily (NIH/NIAID) [E] (b) (6), Lauer, Michael (NIH/OD) [E] (b) (6), Compliance Review (b) (6)

ML

Many thanks Aleksei.

9 Michael Lauer email on 21 April 2020

Best, Mike

From: **Lauer, Michael (NIH/OD) [E]** (b) (6)
Subject: PLEASE READ -- Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 24, 2020 at 16:47
To: Aleksei Chmura (b) (6), Peter Daszak (b) (6)
Cc: Black, Jodi (NIH/OD) [E] (b) (6), Stemmy, Erik (NIH/NIAID) [E] (b) (6), Erbelding, Emily (NIH/NIAID) [E] (b) (6), Linde, Emily (NIH/NIAID) [E] (b) (6), Lauer, Michael (NIH/OD) [E] (b) (6), Bulls, Michelle G. (NIH/OD) [E] (b) (6)

ML

Dear Dr. Chmura and Dr. Daszak

Please see attached.

10 Michael Lauer email on 24 April 2020

Sincerely,
Michael S Lauer, MD

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
1 Center Drive, Building 1, Room 144
Bethesda, MD 20892
Phone: (b) (6)
Email: (b) (6)

From: **Aleksei Chmura** (b) (6)
Subject: Re: PLEASE READ -- Re: Please read and acknowledge receipt -- Actions needed regarding 2R01AI110964-06
Date: April 27, 2020 at 23:57
To: Lauer, Michael (NIH/OD) [E] (b) (6)
Cc: Peter Daszak (b) (6), Black, Jodi (NIH/OD) [E] (b) (6), Erik Stemmy (b) (6), Emily Erbelding (b) (6), Linde, Emily (NIH/NIAID) [E] (b) (6), Bulls, Michelle G. (NIH/OD) [E] (b) (6), Alison Andre (b) (6)

Dear Michael,

Could Peter and I have a quick chat with you sometime tomorrow (Tuesday) about your email, below?

Sincerely,

11 Aleksei Chmura email on 27 April 2020

-Aleksei

Aleksei Chmura, PhD
Chief of Staff

EcoHealth Alliance
460 West 34th Street, Suite 1701
New York, NY 10001

(b) (6) (office)
(b) (6) (mobile)
www.ecohealthalliance.org

EcoHealth Alliance develops science-based solutions to prevent pandemics and promote conservation.

Exhibit D

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

24 April 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: Termination of NIH Grant R01 AI 110964

Dear Drs. Chmura and Daszak:

I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS) has elected to terminate the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI110964, for convenience. This grant project was issued under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284). This grant was funded as a discretionary grant as outlined in the NIH Grants Policy Statement, which states that the decision not to award a grant, or to award a grant at a particular funding level, is at the discretion of the agency, in accordance with NIH's dual review system.

At this time, NIH does not believe that the current project outcomes align with the program goals and agency priorities. NIAID has determined there are no animal and human ethical considerations, as this project is not a clinical trial, but rather an observational study.

As a result of this termination, a total of $369,819.56 will be remitted to NIAID and additional drawdowns will not be supported. The remaining funds have been restricted in the HHS Payment Management System, effective immediately.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

Lauer, Michael (NIH/OD) [E] Digitally signed by Lauer, Michael (NIH/OD) [E]
Date: 2020.04.24 16:41:16 -04'00'

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy
Ms. Emily Linde

Exhibit E

SPECIFIC AIMS

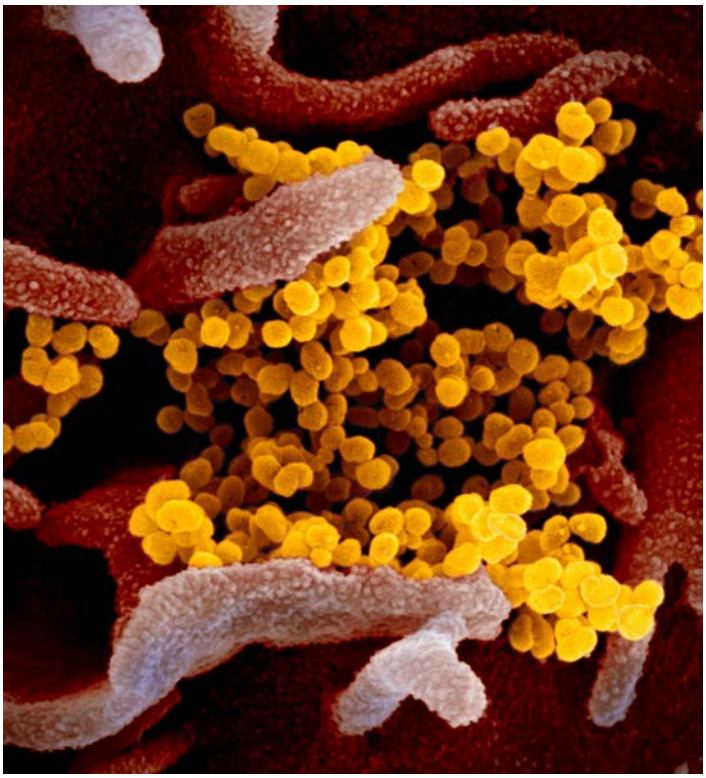
Zoonotic coronaviruses are a significant threat to global health, as demonstrated with the emergence of Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) in 2002, and the continuing spread of Middle East Respiratory Syndrome (MERS-CoV). The wildlife reservoirs of SARS-CoV were identified by our group as bat species, and since then we have sequenced dozens of novel SARS-related CoV (SARSr-CoV) strains. Our previous R01 work demonstrates that bats in southern China harbor an extraordinary diversity of SARSr-CoVs, some of which are able to use human ACE2 to enter into human cells, can infect humanized mouse models to cause SARS-like illness, and evade available therapies or vaccines. We found that the bat hosts of SARSr-CoVs appear to no longer be traded in wildlife markets, and that people living close to bat habitats are the primary risk groups for spillover. At one of these sites, we found diverse SARSr-CoVs containing every genetic element of the wild-type SARS-CoV genome, and serological evidence of human exposure among people living nearby. Thus, there is significant potential for future spillover of SARSr-CoVs, and of public health impacts. *Yet salient questions remain: Are there specific bat communities and sites that harbor CoV strains with higher risk for bat-to-human spillover? Which human behaviors drive risk of bat SARSr-CoV exposure that could lead to infection? Does human exposure to these viruses cause SARS-like or other illness? Can we characterize viral strain diversity, bat traits and human behaviors to assess risk of potential future CoV spillover?* **The proposed work in this renewal R01 builds on these findings** to address these issues by conducting: **1)** focused sampling of bats in southern China to **identify viral strains with high predicted risk of spillover**; **2)** community-based, and clinic-based syndromic, sampling of people to **identify spillover, and assess behavioral risk factors and evidence of illness**; and **3)** conduct *in vitro* and *in vivo* viral characterization and analyze epidemiological data **to identify hotspots of future CoV spillover risk**. This work will follow 3 specific aims:

Aim 1: Characterize the diversity and distribution of high spillover-risk SARSr-CoVs in bats in southern China. We will conduct targeted bat sampling at sites where we predict that undiscovered high risk SARSr-CoV strains exist. Bat sampling will be targeted geographically and by host species to test predictions about evolutionary diversity of SARSr-CoV. We will analyze RdRp and S protein sequences to test their capacity for spillover to people in Aim 3.

Aim 2: Community- and clinic-based surveillance to capture SARSr-CoV spillover, routes of exposure and potential public health consequences. We will conduct focused, targeted human surveys and sampling to identify key risk factors for SARSr-CoV spillover and evidence of illness. To maximize our opportunity of capturing human exposure to bat CoVs, we will conduct community-based surveillance in regions with high SARSr-CoV prevalence and diversity, and individuals having contact with bats. We will assess bat-CoV seropositive status against a small number of questions about human-wildlife contact and exposure. We will conduct clinic-based syndromic surveillance close to these sites to identify patients presenting with influenza-like illness and severe acute respiratory illness, assess their exposure to bats via a questionnaire, and test samples for PCR- and serological evidence of SARSr-CoV infection. We will conduct follow-up sampling to capture patients who had not yet seroconverted at the time of clinic visit.

Aim 3: *In vitro* and *in vivo* characterization of SARSr-CoV spillover risk, coupled with spatial and phylogenetic analyses to identify the regions and viruses of public health concern. We will characterize the propensity of novel SARSr-CoVs to infect people *in vitro* using primary human airway epithelial cells and *in vivo* using the transgenic hACE2 mouse model. We will use mAb and vaccine treatments to test our hypothesis that SARSr-CoVs with 10-25% divergence in S protein sequences from SARS-CoV are likely able to infect human cells, and to evade mAb therapeutics and vaccines. We will then map the geographic distribution of their bat hosts and other ecological risk factors to identify the key 'hotspots' of risk for future spillover**.**

Overall, our SARSr-CoV program serves as a model platform to integrate virologic, molecular and ecologic factors contributing to CoV emergence while informing high impact strategies to intervene and prevent future pandemics. This includes providing critical reagents, therapeutic interventions and recombinant viruses for future SARSr-CoV pandemic and public health preparedness.



This scanning electron microscope image shows SARS-CoV-2 (yellow), the virus that causes COVID-19, isolated from a patient in the United States, emerging from the surface of cells (pink) cultured in the lab. Credit: NIAID-RML

NIAID STRATEGIC PLAN FOR COVID-19 RESEARCH

FY2020 – FY2024

April 22, 2020

National Institute of Allergy and Infectious Diseases

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

Table of Contents

Executive Summary

The National Institute of Allergy and Infectious Diseases (NIAID) at the United States (U.S.) National Institutes of Health (NIH) is committed to safeguarding the health of Americans and people around the world by accelerating research efforts to prevent, diagnose, and treat COVID-19 and characterize the causative agent of this disease, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This *NIAID Strategic Plan for COVID-19 Research* builds on current trans-NIAID efforts to better understand SARS-CoV-2 pathogenesis, transmission, and mechanisms of protective immunity by expanding resources and activities that support rapid development of biomedical tools to more effectively combat this disease and pandemic. Given the urgency of the public health response, studies that inform efforts to control virus spread and mitigate morbidity and mortality, including therapeutic and vaccine development, are the priority. In addition, it is essential to develop rapid, accurate, point-of-care diagnostics—a critical asset to mitigating the spread of COVID-19.

Box 1
NIAID Strategic Plan for COVID-19 Research Mission

Conduct and support research on SARS-CoV-2 and COVID-19 to accelerate the development of safe and effective medical countermeasures that decrease disease incidence, mitigate morbidity and prevent mortality.

The *NIAID Strategic Plan for COVID-19 Research* aligns with the priorities set by U.S. Government–wide task forces for the development of medical countermeasures. NIAID actively participates in COVID-19 task forces to identify opportunities, ensure open communication, encourage resource sharing, and avoid duplication of effort. The plan is structured around four strategic research priorities:

1. **Improve fundamental knowledge of SARS-CoV-2 and COVID-19,** including studies to characterize the virus and how it is transmitted and understand the natural history, epidemiology, host immunity, disease immunopathogenesis, and the genetic, immunologic, and clinical associations with more severe disease outcomes. This includes accelerating the development of small and large animal models that replicate human disease.

2. **Support the development of diagnostics and assays**, including point-of-care molecular and antigen-based diagnostics for identifying and isolating COVID-19 cases and serologic assays to better understand disease prevalence in the population. Diagnostics also will be essential for evaluating the effectiveness of candidate countermeasures.

3. **Characterize and test therapeutics,** including identifying and evaluating repurposed drugs and novel broad-spectrum antivirals, virus-targeted antibody-based therapies (including plasma-derived intravenous immunoglobulin (IVIG) and monoclonal antibodies), and host-directed strategies to combat COVID-19.

4. **Develop safe and effective vaccines against SARS-CoV-2,** including support of clinical trial testing.

To accelerate research, NIAID will leverage current resources and global collaborations, including existing research programs and clinical trials networks. NIAID's research response to COVID-19 will build on experience with diseases caused by other zoonotic coronaviruses (CoVs), including severe acute

respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). NIAID will pursue public-private partnerships to facilitate the translation of research outcomes into life-saving public health interventions. Working with pharmaceutical companies, NIAID has already initiated Phase 1 clinical trials for candidate COVID-19 vaccines and therapeutics. A concerted effort will be made to include minority populations, as well as at-risk and vulnerable populations, in all aspects of NIAID-sponsored research to address health disparities between diverse groups. Characterization of the fundamental virology of SARS-CoV-2 and the immunological response to infection will inform future studies and facilitate the development of effective medical countermeasures. With collaboration from all agencies within the U.S. government and other key U.S. and global partners, NIAID will rapidly disseminate these results so that the information can be translated into clinical practice and public health interventions to combat the pandemic. As such, NIAID has already implemented open sharing of scientific data through publicly available websites and will continue to promote the prompt disclosure of SARS-CoV-2 and COVID-19 research data by the scientific community.

Research Plan

Priority 1: Improve fundamental knowledge of SARS-CoV-2 and COVID-19

Developing effective medical and public health countermeasures against a newly emergent virus like SARS-CoV-2 will require a better understanding of the complex molecular and immune mechanisms underlying infection and disease. Studies that delineate the viral lifecycle and host immune responses to infection can lead to the identification of novel targets for intervention against SARS-CoV-2 infection and COVID-19. Early studies suggest that the clinical manifestations of COVID-19 can vary significantly, and disease severity can range from mild to critical. Thus, a detailed understanding of the clinical course of disease, as well as the clinical, virologic, immunological, and genetic predictors of disease severity, are needed. Gaps also exist in our understanding of the dynamics of disease transmission in different populations over time, including the role of pediatric and elderly populations in viral spread, and the potential seasonality of viral circulation.

Objective 1.1: Characterize fundamental SARS-CoV-2 virology and immunological host response to infection

- **Support the development and distribution of reagents and viral isolates to researchers.** NIAID will continue to support both intramural and extramural researchers by developing reagents and assays for virus characterization and immunological analyses. NIAID will continue to accelerate SARS-CoV-2 research by sourcing viral isolates and clinical specimens for the research community and placing them in repositories to help advance research and countermeasure development. In addition, NIAID will place other critical reagents needed for assay development (e.g., pseudovirions and antigens) in publicly available repositories for distribution.

- **Characterize virus biology and immunological responses to disease.** A comprehensive understanding of the

Box 2 Priority 1: Improve fundamental knowledge of SARS-CoV-2 and COVID-19
Objective 1.1: Characterize fundamental SARS-CoV-2 virology and immunological host response to infection *Objective 1.2: Evaluate disease dynamics through natural history, transmission, and surveillance studies* *Objective 1.3: Develop animal models that recapitulate human disease*

biological processes involved in SARS-CoV-2 infection and the pathogenesis of COVID-19 are paramount to developing new medical countermeasures to fight the spread of disease. Building on prior research related to MERS and SARS coronaviruses, early studies confirmed several critical features of SARS-CoV-2 infection, including the primary host receptor, angiotensin converting enzyme 2 (ACE-2), and the structure of the virus receptor-binding domain. Studies that delineate the viral lifecycle and host immune responses to infection can lead to the identification of novel targets for intervention against SARS-CoV-2 infection and COVID-19. Understanding the function of essential viral proteins will be necessary for improving diagnostic and immunological assays, *in vitro* and *in vivo* models, and other resources needed to advance safe and effective medical countermeasure development. In addition, evaluating the dynamics of host-pathogen interactions at the molecular and cellular levels will be critical to advancing our understanding of viral pathogenesis and immune responses that contribute to SARS-CoV-2 infection.

- **Determine viral evolution and molecular epidemiology.** With a newly emergent virus like SARS-CoV-2, studies to characterize genetic diversity, including those that assess the potential for the virus to evolve and escape host immunity, are pivotal for understanding disease progression and transmission dynamics and may have implications for countermeasure development. Viral genomic analysis matched with patient clinical data will be important to identify biomarkers of virulence and establish paradigms of sequence diversity. In addition, evaluating viral sequence associations with disease outcomes, immune status, and viral replication will provide crucial data to accelerate the development of effective medical countermeasures.

- **Develop low-containment assays to study virus neutralization.** Studies using non-infectious pseudovirions can be conducted in labs without BSL-3 capacity, making them an important tool to enhance understanding of SARS-CoV-2 infection. This capability would enable researchers without high-containment infrastructure to study the dynamics of virus neutralization *in vitro*.

- **Research into optimal public health prevention and mitigation modalities**. Clinical trials including family members of a COVID-19 positive individual can be devised to evaluate transmission, prevention, and other mitigation measures within the household.

Objective 1.2: Evaluate disease dynamics through natural history, transmission, and surveillance studies

- **Characterize disease incidence through surveillance studies.** Clinical manifestations of COVID-19 can vary greatly, ranging from asymptomatic or mildly symptomatic to the development of pneumonia, acute respiratory distress syndrome, and even death.[1] The variation in clinical presentation of COVID-19, combined with the challenges in diagnostic capacity, have made accurate initial assessments of disease incidence a formidable challenge. However, rapid point-of-care and point-of-need molecular tests, which became available in March 2020, will enable hospitals and other healthcare facilities to make informed decisions regarding patient isolation and care. Studies that leverage existing high-throughput diagnostic capacity along with these rapid tests will advance our understanding of disease incidence across the nation and will be a critical component of strategies to implement effective medical countermeasures. Combining these studies with broad serosurveillance studies across existing surveillance networks, including blood bank studies, would

[1] Wu Z and McGoogan JM. *JAMA* 2020 Feb 24. Epub. PMID 32091533.

provide a more complete picture of the scope of disease and the dynamics of infection. Detailed knowledge of host genetics and the human responses to infection across the lifespan will not only provide insights into new approaches for diagnosis, treatment, and prevention, but also may elucidate why individuals respond to SARS-CoV-2 in different ways. Reports to date suggest that COVID-19 resolves in most cases,[2] implying that the immune system can keep the infection from progressing to severe disease in many individuals. However, additional research is needed to better understand why some people progress to severe disease, which will lend critical insights to medical countermeasure development.

- **Assess the dynamics of disease transmission.** Our current understanding of COVID-19 transmission is limited. While recent studies have suggested timeframes for virus survival in aerosols and on surfaces,[3] the contributions of different routes of transmission and the dynamics of animal-to-human and human-to-human transmission remain unclear. The diverse clinical presentations of COVID-19, including a high prevalence of asymptomatic cases, add further complexity to understanding transmission dynamics. Providing a clearer picture of the natural history of viral shedding is a priority, both in acute cases and in asymptomatic infection. Given the challenges of accurately diagnosing asymptomatic individuals because they do not present for treatment, determining the role they play in transmission would provide valuable insights. Elucidating the role of pediatric cases in the spread of SARS-CoV-2 is particularly important. Although pediatric COVID-19 cases are generally asymptomatic or have less severe clinical manifestations than those of adults, the role that children play in spreading the virus is unknown. Additionally, studies to identify potential animal reservoirs and better understand transmission from animals to humans are a research priority, as these reservoirs may lead to future virus introductions and re-emergence of disease in humans. Virus transmission depends on a complex interplay of host, viral, and environmental factors that contribute to disease incidence and spread. Identifying the factors that maintain the disease transmission cycle is critical to developing effective medical countermeasures and public health interventions that will prevent future pandemics.

- **Determine disease progression through natural history studies.** Delineating the natural history of COVID-19 will inform immunopathogenesis, viral tropisms and length of shedding, immune phenotypes, and both protective immunity and host susceptibility. Disease assessment using longitudinal cohort studies, including among high-risk populations such as healthcare workers and the elderly, are important to better understand disease pathogenesis and immune responses to infection. Biomarkers identified from these studies may provide valuable insights into predictors of disease severity.

Objective 1.3: Develop animal models that recapitulate human disease

- **Develop small and large animal models that replicate SARS-CoV-2 pathogenesis.** Developing animal models that recapitulate human disease is a vital early step toward understanding disease pathogenesis and testing the efficacy of medical countermeasures. Small animal models enable rapid, scalable analyses that are particularly valuable for screening countermeasure candidates for efficacy and addressing issues concerning vaccine-induced immune enhancement. Among the small animal models being tested, transgenic mice expressing the human ACE-2 receptor are a promising candidate. In parallel, development and characterization of large animal models, including non-human primates (NHPs) that mimic human COVID-19, are a pivotal step to advance promising

[2] ibid.

[3] van Doremalen *N et al. N Engl J Med* 2020 Mar 17. Epub. PMID 32182409.

countermeasure candidates. Previous experience with related coronavirus diseases such as MERS and SARS suggests that replicating human disease, particularly its more severe manifestations, in an animal model may be challenging. Fundamental research assessing animal models ranging from mice to NHPs is already underway. NIAID will continue to support the development of small and large animal model candidates to better understand this emerging infection and investigate optimal ways to treat and prevent COVID-19. NIAID also will ensure that validated animal models are made available to the scientific community for evaluating priority countermeasures.

Priority 2: Support the development of diagnostics and assays

Availability of rapid, accurate Food and Drug Administration (FDA)-cleared or authorized diagnostics will increase testing capacity and are critical for identifying and rapidly isolating cases, tracking spread of the virus, managing patient care, and supporting clinical trials. Molecular tests specifically designed to detect SARS-Cov-2 RNA in clinical samples are able to detect low levels of pathogen in clinical samples and offer robust specificity in differentiating SARS-CoV-2 from other related viruses. Continuing to improve the speed and accuracy of molecular and antigen-based diagnostics and making them available at point- of-care will be paramount to accelerating the ability to mitigate disease spread in the current outbreak and any future outbreaks. The development of serologic assays would further bolster surveillance efforts, including the ability to identify individuals who may have resolved prior infection with SARS-CoV-2.

Objective 2.1: Accelerate the development and evaluation of diagnostic platforms

- **Support the development, characterization and availability of reagents for diagnostic validation.** NIAID will support this effort through the development and testing of reagents for diagnostic validation that will be made available through NIAID-sponsored repositories.

Box 3 **Priority 2: Support the development of diagnostics and assays**
Objective 2.1: Accelerate the development and evaluation of diagnostic platforms *Objective 2.2: Develop assays to increase understanding of infection and disease incidence*

- **Support the development of new rapid diagnostics.** NIAID will provide funding to support the development of new rapid diagnostics, including molecular tests and novel antigen detection tests with improved sensitivity, if deemed feasible based on natural history studies.

- **Support the evaluation of promising diagnostics.** In some cases, stakeholders that develop potential diagnostic tests do not have the infrastructure needed to rigorously validate those tests against clinical samples. NIAID will support the testing of promising diagnostics and provide the capacity for evaluating them with live virus samples using our biocontainment laboratories.

Objective 2.2: Develop assays to increase understanding of infection and disease incidence

- **Develop and validate SARS-CoV-2 serological assays.** Serological tests, which detect host antibodies to infectious agents, do not detect the presence of a pathogen directly but can be used as a surrogate marker of infection. Developing more effective serologic tests would help provide information on the extent of asymptomatic infections and cumulative disease incidence, for example through serosurveillance studies. NIAID, with the Centers for Disease Control and

Prevention and the FDA, is developing tests that identify antibodies to SARS-CoV-2 proteins to determine seroprevalence rates and potentially help distinguish antibody responses in individuals receiving vaccines. NIAID will support the development and validation of additional serological assays for serosurveillance studies and as tools for testing the efficacy of promising vaccine or therapeutic candidates.

Priority 3: Characterize and test therapeutics

Currently, there are no FDA-approved or licensed therapeutics specific for coronaviruses. While traditional development pathways for therapeutics can take years, the urgency of the current outbreak underscores the need for rapid development and testing of promising therapeutics. Possible avenues for developing therapeutics include the evaluation of broad-spectrum antiviral agents (antivirals) that have shown promise for other coronaviruses and the identification of novel monoclonal antibodies (mAbs). For broad-spectrum antivirals, Phase 2/2b testing of the RNA polymerase inhibitor developed by Gilead, remdesivir, is already underway. Additional studies will be critical to identify promising therapeutic candidates and to advance them through clinical trial testing. To optimize findings during the pandemic, multiple clinical trials will be conducted in parallel among various populations, including both inpatient and outpatient studies.

Objective 3.1: Identify promising candidates with activity against SARS-CoV-2

- **Screen protease inhibitor and nucleotide analogue class agents and other small molecules with documented activity against other coronaviruses SARS-CoV-2**. Screening drugs that are already licensed by the FDA for other indications and might be efficacious against SARS-CoV-2 infection may provide a route to identifying a therapeutic for use in the current pandemic. Broad-spectrum antivirals that are already FDA approved or in clinical development for other indications—including those previously targeting SARS-CoV-1 and MERS CoV—can be evaluated for their potential activity against SARS-CoV-2 infections. Approved therapeutics for other infectious diseases also are being evaluated as possible treatments for COVID-19. By leveraging their existing efficacy, safety, and manufacturability data, the time to development and production can be reduced. NIAID also will continue working with partners to screen compound libraries for potential activity against SARS-CoV-2. For these studies, priority will be given to compounds based on *in vitro* screening data and the existence of human safety data.

- **Identify viral targets for therapeutic development**. Advances in structural biology technology enable researchers to map key viral structures at an unprecedented level. The Structural Genomics Centers for Infectious Diseases (SGCID) apply state-of-the-art, high-throughput technologies and methodologies, including computational modeling, x-ray crystallography, nuclear magnetic resonance imaging, and cryogenic electron microscopy, to experimentally characterize the three dimensional atomic structure of proteins that play an important biological role in human pathogens and infectious diseases. NIAID will continue to support use of this powerful technology to identify viral targets of SARS-CoV-2 for therapeutics or vaccines.

Box 4
Priority 3: Characterize and test therapeutics

Objective 3.1: Identify promising candidates with activity against SARS-CoV-2
Objective 3.2: Conduct treatment studies to advance high-priority therapeutic candidates

- **Identify novel mAbs for use as therapy or prophylaxis.** Data from early studies indicate that well-characterized convalescent plasma may provide a treatment benefit in COVID-19.[4] Therefore, IVIG derived from convalescent plasma may also hold promise for treatment. Moreover, peripheral blood mononuclear cells and plasma are being used to identify novel neutralizing antibodies. Through collaborations with structural biologists, binding properties can be quickly assessed. Paired with assessment of neutralization activity, the most promising mAbs will be identified for further characterization in animal models and human trials.

Objective 3.2: Conduct treatment studies to advance high-priority therapeutic candidates

- **Characterize and evaluate host-directed strategies for treatment of disease.** Experience with other coronaviruses indicates that infection of the respiratory tract is rapid and damage is primarily mediated by the host inflammatory response.[5] These conditions may make it difficult to modify COVID-19 with pathogen-directed therapeutics. Instead, host-directed strategies that target the immune response may exert a beneficial therapeutic effect. Host-directed strategies, including immune-modulating agents, will be investigated as potential therapeutic candidates.

- **Conduct clinical trials to demonstrate safety and efficacy of lead therapeutic candidates.** Many potential therapeutic candidates have been identified and are being tested in clinical trials.
  - In March 2020, NIAID launched a multicenter, adaptive, randomized controlled clinical trial to evaluate the safety and efficacy of the investigational antiviral drug remdesivir (GS-5734) for the treatment of COVID-19 in hospitalized adults with laboratory-confirmed SARS-CoV-2 infection and evidence of lung involvement. The trial builds on recent studies by NIAID scientists showing that remdesivir can improve the disease course in rhesus macaques when administered promptly after viral challenge with the MERS CoV.[6] The trial is also adaptive, allowing for additional arms should other therapeutics warrant assessment for efficacy.
  - NIAID is finalizing the protocol for the Big Effect Trial (BET), in which putative therapeutics that have existing human data and are readily available will be tested in patients hospitalized with lower respiratory tract disease. Each potential intervention will be given to approximately 75 patients and evaluated for mitigating disease symptoms. Candidate therapeutics that meet the criteria in this initial study will be further evaluated in larger clinical trials for which the infrastructure is already in place.
  - As mentioned above, identification of novel mAbs for therapy or prophylaxis is another strategic priority. These mAbs should be safe, highly effective, amenable to fast manufacturing, and easy to administer. They will be tested in clinical trials to develop immunotherapies for the prevention and early treatment of COVID-19, potentially in high-risk populations including healthcare workers.

- **Conduct outpatient studies for mild COVID-19 cases**. In cases of mild COVID-19 that do not require hospitalization, outpatient studies could be extremely valuable for testing promising, orally administered FDA-approved drugs that have existing safety data. The antiviral activity of hydroxychloroquine and azithromycin against SARS-CoV-2 has been the focus of many early

[4] Roback JD and Guarner J. *JAMA* 2020 Mar 27. Epub. 32219429.

[5] Newton AH et al. *Semin Immunopathol*. 2016;38(4):471-82. PMID 26965109.

[6] de Wit E et al. *Proc Natl Acad Sci USA* 2020;117(12):6771-6. PMID 32054787.

therapeutic studies.[7,8,9] Testing of these and other candidates, including protease inhibitors and other molecules, in outpatient studies may provide critical efficacy data and could identify an existing drug or drug combination that is safe and effective against COVID-19.

- **Conduct outpatient studies in high-risk populations.** High-risk populations, including health care workers, the elderly or individuals with chronic conditions, are a critical target for the development of therapeutics. Conducting studies in patients with mild cases of COVID-19 among these high-risk groups would be of interest for identifying the benefits of early treatment strategies to mitigate the impact of infection. Therapeutic candidates that have once a day dosing could also be considered for pre-exposure prophylaxis (PrEP) in some of these populations.

Priority 4: Develop safe and effective vaccines against SARS-CoV-2

Developing a safe and effective SARS-CoV-2 vaccine is a priority for preventing future outbreaks of the virus. As vaccine candidates for MERS-CoV, SARS-CoV-1 and other coronaviruses have previously been developed, NIAID investigators and the scientific community are well poised to use similar approaches in the current pandemic. NIAID will leverage its broad intramural and extramural infrastructure to advance vaccine candidates through Phase 1 safety and dosing clinical trials, with considerations for Phase 2/2b clinical trials for the most promising candidates.

Objective 4.1: Advance promising vaccine candidates through clinical trial testing

- **Conduct a Phase 1 clinical trial of (mRNA) platform candidate mRNA-1273.** Given the urgency of the response effort to develop a safe and effective vaccine, NIAID is prioritizing promising vaccine candidates that can be rapidly produced and tested. NIAID, in collaboration with the biotechnology company Moderna, is conducting a Phase 1 clinical trial of a vaccine candidate that uses a messenger RNA (mRNA) vaccine platform expressing a NIAID-designed recombinant spike protein of SARS-CoV-2. The trial is being conducted at NIAID-funded clinical research sites, with the first enrolled individual receiving the vaccine on March 16, 2020.

- **Prepare for a pivotal Phase 2/2b clinical trial of candidate mRNA-1273. Preparing for the likelihood of a seasonal recurrence of SARS-CoV-2 is imperative to the public health response.** Given the theoretical risk of vaccine-enhanced respiratory disease, large Phase 2 trials are unlikely to launch until this possibility is evaluated in animal models. Planning for those animal studies is underway, and, assuming favorable results, a Phase 2/2b study could be launched later in 2020. This represents a historically fast timeline for the development and testing of a vaccine candidate. Additionally, these studies will provide information on correlates of immunity that will help accelerate the advancement of other vaccine candidates. If the mRNA-1273 vaccine candidate shows protection against SARS-CoV-2 infection in a Phase 2/2b trial, NIAID will work with government partners to ensure that the vaccine is manufactured in sufficient quantities to allow prompt distribution to those at highest risk of acquiring disease.

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[7] Gautret P et al. *Int J Antimicrob Agents*. 2020 Mar 20:105949. Epub. PMID 32205204.

[8] Molina JM et al. 2020 Med Mal Infect. 2020 Mar 30. pii:S0399-077X(20)30085-8. Epub. PMID 32240719.

[9] Chen Z et al. medRxiv 2020:2020.03.22.20040758.
https://www.medrxiv.org/content/10.1101/2020.03.22.20040758v2

Box 5.
Priority 4: Develop safe and effective vaccines against SARS-CoV-2

Objective 4.1: Advance promising vaccine candidates through clinical trial testing
Objective 4.2: Advance vaccine development through assay and reagent development
Objective 4.3: Advance vaccine development through adjuvant characterization and development

- **Investigate additional candidates through NIAID vaccine programs.** Although promising candidates may show efficacy in preclinical studies, many do not translate into effective vaccines in clinical trials. Therefore, it is crucial to support multiple promising preclinical candidates in the research and development pipeline. To that end, NIAID is advancing multiple additional SARS-CoV-2 vaccine candidates through its Rocky Mountain Laboratories (RML), including approaches that have shown promise against coronaviruses that cause SARS and MERS. Building on previous research to develop a MERS-CoV vaccine, scientists at RML are collaborating with Oxford University investigators to develop a SARS-CoV-2 vaccine that uses a chimpanzee adenovirus vector. RML investigators also are partnering with the biopharmaceutical company CureVac on an mRNA vaccine candidate and collaborating with the University of Washington on a universal coronavirus vaccine development. By leveraging its extensive expertise and research infrastructure, NIAID will continue working with partners and collaborators to advance promising SARS-CoV-2 vaccine candidates.

- **Leverage existing vaccine approaches to target SARS-CoV-2.** NIAID is pursuing multiple strategies to develop a COVID-19 vaccine. Building on past research on emerging pathogens, especially MERS-CoV and SARS-CoV-1 (the virus that causes SARS), NIAID is using previously developed vaccine platforms to rapidly assess the potential of SARS-CoV-2 vaccine candidates. This approach has already resulted in several promising strategies that may be leveraged for SARS-CoV-2, including vaccination using recombinant spike protein, chimpanzee adenovirus vaccine vector, virus-like particles, and live attenuated virus. In addition, NIAID is funding the development of novel vaccine candidates that will be efficacious across the lifespan, including in the elderly.

Objective 4.2: Advance vaccine development through assay and reagent development

- **Develop critical reagents to support vaccine development.** Appropriate tools are needed to identify the most promising vaccine candidates and advance the development of lead candidates as rapidly as possible. To accelerate the vaccine pipeline, NIAID is generating master and working SARS-CoV-2 virus stocks and other reagents critical for developing SARS-CoV-2 immune assays, developing quantitative tests for characterizing SARS-CoV2 assay material, developing a quantitative SARS-CoV-2-specific ELISA, developing virus-specific neutralization assays, and developing quantitative assays for assessing SARS-CoV-2 viral load.

Objective 4.3: Advance vaccine development through adjuvant characterization and development

- **Provide adjuvants to support vaccine development.** Adjuvants are vaccine components that improve vaccine efficacy by inducing long-lived protective immunity. Selection of appropriate adjuvants is crucial for developing safe and effective vaccines. NIAID is working with multiple collaborators to provide adjuvants to the research community for use in SARS-CoV-2 vaccine candidates. These adjuvants are at various stages of development and include compounds that

specifically improve vaccine efficacy in elderly individuals or modulate host immunity toward protective responses while limiting or preventing harmful inflammatory responses.

Conclusion

The sudden emergence and rapid global spread of the novel coronavirus SARS-CoV-2 has created a daunting public health challenge. To address this challenge, NIAID is focusing its considerable expertise and emerging infectious disease resources to facilitate the development of medical countermeasures including diagnostics, therapeutics, and vaccines. The resulting discoveries will not only help mitigate the current pandemic, but also inform prevention, diagnosis, and treatment of future emerging infectious diseases.

A comprehensive strategy requires a coordinated effort among governmental, academic, private, and community-based organizations. The *NIAID Strategic Plan for COVID-19 Research* defines the areas of COVID-19 research within the NIAID mission and outlines the institute's research priorities and goals. This strategic plan builds on many other national efforts and represents a commitment from multiple U.S. government agencies to improve coordination of COVID-19 research and discovery efforts and the development of medical countermeasures.

Exhibit 2

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

8 July 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

In follow-up to my previous letter of April 24, 2020, I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS), has withdrawn its termination of grant R01AI110964, which supports the project *Understanding the Risk of Bat Coronavirus Emergence*. Accordingly, the grant is reinstated.

However, as you are aware, the NIH has received reports that the Wuhan Institute of Virology (WIV), a subrecipient of EcoHealth Alliance under R01AI110964, has been conducting research at its facilities in China that pose serious bio-safety concerns and, as a result, create health and welfare threats to the public in China and other countries, including the United States. Grant award R01AI110964 is subject to biosafety requirements set forth in the NIH Grants Policy Statement (e.g., NIH GPS, Section 4.1.24 "Public Health Security") and the Notice of Award (e.g., requiring that "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]."). Moreover, NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients. 45 C.F.R. § 75.101.

As the grantee, EcoHealth Alliance was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). We have concerns that WIV has not satisfied safety requirements under the award, and that EcoHealth Alliance has not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance.

Moreover, as we have informed you through prior Notices of Award, this award is subject to the Transparency Act subaward and executive compensation reporting requirement of 2 C.F.R. Part

170. To date you have not reported any subawards in the Federal Subaward Reporting System.

Therefore, effective the date of this letter, July 8, 2020, NIH is suspending all activities related to R01AI110964, until such time as these concerns have been addressed to NIH's satisfaction. This suspension is taken in accordance with 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable in accordance with 42 C.F.R. § 50.404 and the NIH GPS Section 8.7, Grant Appeals Procedures. However, EcoHealth Alliance has the opportunity to provide information and documentation demonstrating that WIV and EcoHealth Alliance have satisfied the above-mentioned requirements.

Specifically, to address the NIH's concerns, EcoHealth must provide the NIH with the following information and materials, which must be complete and accurate:

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.
3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.
4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.
5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.
6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.
7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

During this period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further asses compliance by EcoHealth Alliance and WIV, including compliance with other terms and conditions of award that may be implicated. Additionally, during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the

recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. Once the original award is reinstated, NIH will take additional steps to restrict all funding in the HHS Payment Management System in the amount of $369,819. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 CFR Part 75, including, but not limited to, terminating the grant award. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

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Sincerely,

Michael S. Lauer -S

Digitally signed by Michael S. Lauer -S
Date: 2020.07.08 21:43:41 -04'00'

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy
Ms. Emily Linde

Exhibit 3

ECOHEALTH ALLIANCE'S OBJECTIONS AND RESPONSES TO NIH'S ADDITIONAL CONDITIONS ON GRANT 2R01 AI 110964-6

EcoHealth Alliance, Inc. ("EcoHealth Alliance"), by and through its attorneys, Tarter Krinsky & Drogin LLP, hereby responds and objects to the additional conditions (the Requests") imposed on grant 2R01 AI 110964-6 on July 8, 2020, by the National Institute of Allergy and Infectious Diseases ("NIAID"), an Institute within the National Institutes of Health ("NIH"), under the Department of Health and Human Services ("HHS"), as follows:

GENERAL OBJECTIONS[1]

1. EcoHealth Alliance objects to the Requests to the extent they purport to impose obligations beyond those authorized by the NIH Grants Policy Statement and the applicable statutes and regulations.

2. EcoHealth Alliance objects to the Requests to the extent they seek information and documents that are neither relevant to the Project nor reasonably likely to affect the safety or efficacy of EcoHealth Alliance's continued research funded by grant 2R01 AI 110964-6.

3. EcoHealth Alliance objects to the Requests to the extent they seek the production of documents that are not in EcoHealth Alliance's possession, custody, or control.

4. EcoHealth Alliance objects to the Requests to the extent they are vague, ambiguous, or otherwise unclear as to the precise categories of documents and information sought.

5. EcoHealth Alliance objects to the Requests to the extent that they are overbroad, unduly burdensome, or unreasonably cumulative and duplicative.

6. EcoHealth Alliance objects to the Requests to the extent they seek documents and information concerning personal information relating to individuals not affiliated with the Project or Grant on the ground that such requests may invade the rights of privacy of such individuals.

[1] Any capitalized terms not otherwise defined herein shall have the same meaning ascribed to them in EcoHealth Alliance's letter to NIAID, dated August 12, 2020.

7. EcoHealth Alliance objects to the Requests to the extent they seek documents and information regarding transactions or occurrences that took place on or before July 1, 2019, on the ground that such requests are overbroad, and that such documents and information are not relevant to EcoHealth Alliance's continued research funded by grant 2R01 AI 110964-6.

8. EcoHealth Alliance's Responses and Objections to the Requests (including each Request therein) shall not be interpreted as implying that: (i) responsive documents or information exist, (ii) EcoHealth Alliance acknowledges the proprietary of any Request; or (iii) that any Request propounded by NIH is either factually correct or legally binding upon EcoHealth Alliance.

9. EcoHealth Alliance specifically reserves its right to amend, modify, or supplement the objections and responses provided herein.

10. These general objections ("General Objections") are hereby incorporated by reference into each and every of EcoHealth Alliance's responses to the Requests, below.

RESPONSES AND OBJECTIONS TO THE REQUESTS

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.

Response to Request No. 1:

EcoHealth Alliance objects to the Request to the extent it seeks documents and information that are not in EcoHealth Alliance's possession, custody, or control. EcoHealth Alliance further objects to the Request to the extent it seeks information that is not relevant to the Project, which was granted prior to the discovery of SARS-CoV-2. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that it has no knowledge or information regarding the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.

2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.

Response to Request No. 2:

See General Objections. EcoHealth Alliance objects to the Request to the extent it purports to seek information or documents that are not in EcoHealth Alliance's possession, custody, or control. EcoHealth Alliance further objects to the Request to the extent it seeks information that is not relevant to the Project. EcoHealth Alliance further objects to the extent the Request seeks documents and information concerning personal information relating to individuals who are not affiliated with the Project. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that it lacks knowledge or information regarding the alleged "disappearance of Huang Yanling" or the contention that her "lab web presence has been deleted."

3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.

Response to Request No. 3:

See General Objections. EcoHealth Alliance objects to the Request to the extent it purports to seek information or documents that are not in EcoHealth Alliance's possession, custody, or control. EcoHealth Alliance further objects to the Request to the extent it seeks information that is not relevant to the Project. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that, upon information and belief, it is not in possession, custody, or control of "WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns."

4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.

Response to Request No. 4:

See General Objections. EcoHealth Alliance objects to the Request in that it is vague, ambiguous, or otherwise unclear as to the precise categories of documents and information that are being sought and because the term "out-of-ordinary" is undefined. EcoHealth Alliance further objects to the Request to the extent it purports to seek documents or information that are not in EcoHealth Alliance's possession, custody, or control. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that it lacks knowledge or information regarding "diminished cell-phone traffic in October 2019" and/or "roadblocks surrounding [WIV] from October 14-19, 2019."

5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.

Response to Request No. 5:

See General Objections. EcoHealth Alliance objects to the Request to the extent it purports to seek information or documents that are not in EcoHealth Alliance's possession, custody, or control. EcoHealth Alliance further objects to the Request to the extent it seeks information that is not relevant to the Project. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that it lacks knowledge or information regarding the contention that "WIV failed to note that the RatG13 virus…was [] isolated from an abandoned mine where three men died in 2012" and why this was not followed up.

6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.

Response to Request No. 6:

See General Objections. EcoHealth Alliance objects to the Request to the extent it seeks to impose obligations on EcoHealth Alliance that are not authorized by the NIH Grants Policy Statement or any applicable statute or regulation. EcoHealth Alliance further objects to the Request to the extent it seeks to impose obligations that are wholly unrelated to the Project or EcoHealth Alliance's ongoing research funding by the Grant. Subject to and notwithstanding the foregoing and without prejudice thereto, EcoHealth Alliance responds that, on April 19, 2020, Michael S. Lauer, MD, NIH Deputy Director for Extramural Research, sent a letter to EcoHealth Alliance on behalf of NIH that stated that EcoHealth Alliance was not allowed to collaborate with WIV regarding the Project and that it should not remit any Grant funds to WIV. On April 21, 2020, Peter Daszak of EcoHealth Alliance sent an email to Dr. Lauer that confirmed (i) no funds from the Grant had been sent to WIV, (ii) no contract had been signed between EcoHealth Alliance regarding research funded under the Grant, and (iii) EcoHealth Alliance would not provide any funds to WIV. As a result, at this time, EcoHealth Alliance is not collaborating with WIV, is not

in possession, custody, or control of WIV, and has no authority to grant NIAID and the U.S. National Academy of Sciences access the facility to conduct an inspection.

7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System.

Response to Request No. 7:

See General Objections. Subject to and notwithstanding the General Objections and without prejudice thereto, EcoHealth Alliance responds that, upon information and belief, as of the date of these responses, all of EcoHealth Alliance's subawards are fully reported in the Federal Subaward Reporting System.

Dated: New York, New York
August 13, 2020

TARTER KRINSKY & DROGIN LLP
Attorneys for EcoHealth Alliance

By: [redacted]
Andrew N. Krinsky
1350 Broadway, 11th Floor
New York, New York 10018
Tel: [redacted]

TO: Dr. Michael S. Lauer [redacted]
Dr. Erik Stemmy [redacted]
Ms. Emily Linde [redacted]

From:	Lauer, Michael (NIH/OD) [E]
To:	Fine, Amanda (NIH/OD) [E]
Cc:	Burklow, John (NIH/OD) [E]; Myles, Renate (NIH/OD) [E]; Wojtowicz, Emma (NIH/OD) [E]; OER Press Group; Lauer, Michael (NIH/OD) [E]; Black, Jodi (NIH/OD) [E]
Subject:	Re: follow up on NIH grant, EcoHealth Alliance
Date:	Monday, August 17, 2020 8:52:46 PM
Attachments:	image001.jpg Daszak 7 8 20.pdf

Hi Amanda – yes, agree, [redacted (b) (5)]. The letter speaks for itself.

Many thanks, Mike

From: "Fine, Amanda (NIH/OD) [E]" [redacted (b) (6)]
Date: Monday, August 17, 2020 at 6:08 PM
To: "Lauer, Michael (NIH/OD) [E]" [redacted (b) (6)]
Cc: "Burklow, John (NIH/OD) [E]" [redacted (b) (6)], "Myles, Renate (NIH/OD) [E]" [redacted (b) (6)], "Wojtowicz, Emma (NIH/OD) [E]" [redacted (b) (6)], OER Press Group [redacted (b) (6)]
Subject: FW: follow up on NIH grant, EcoHealth Alliance

Hi Mike-

See below from WSJ about EcoHealth. Looks like she has a copy of the letter. [redacted (b) (5)] Just checking that is accurate and wanted to get your input on how you think it is most appropriate to respond.

Thanks in advance!
Amanda

From: McKay, Betsy <betsy.mckay@wsj.com>
Sent: Monday, August 17, 2020 4:02 PM
To: Fine, Amanda (NIH/OD) [E] [redacted (b) (6)]; Routh, Jennifer (NIH/NIAID) [E] [redacted (b) (6)]; Myles, Renate (NIH/OD) [E] [redacted (b) (6)]
Subject: follow up on NIH grant, EcoHealth Alliance

Hi Amanda et. al,

We were emailing late last week about NIH's reinstatement of a grant to EcoHealth Alliance for bat coronavirus research. The grant had been terminated in April. Looking into that further, I have some follow-up questions. The grant was reinstated, then immediately suspended until EcoHealth Alliance supplies information and material addressing seven areas of concern.

Six of these areas of concern appear to be outside the scope of the

grant, such as providing a sample of the SARS-CoV-2 virus used to sequence the virus in January, an explanation of the disappearance of a WIV scientist, and arranging for WIV to submit to an outside inspection to address whether WIV staff had SARS-CoV-2 in their possession before December 2019.

My questions are:

1. Why is EcoHealth Alliance being asked to provide these materials and information?

2. How does the requirement that EcoHealth Alliance provide this information fit into the scope of its grant?

3. Who specifically (which agency or person) has ordered EcoHealth Alliance to supply this information?

4. Any further comment on why these requirements are being placed on this grant recipient at this time?

Thanks very much.

Best,
Betsy

--

Betsy McKay
SENIOR WRITER

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M: +1 404 229 0472
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T: @betswrites

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

8 July 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

In follow-up to my previous letter of April 24, 2020, I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS), has withdrawn its termination of grant R01AI110964, which supports the project *Understanding the Risk of Bat Coronavirus Emergence*. Accordingly, the grant is reinstated.

However, as you are aware, the NIH has received reports that the Wuhan Institute of Virology (WIV), a subrecipient of EcoHealth Alliance under R01AI110964, has been conducting research at its facilities in China that pose serious bio-safety concerns and, as a result, create health and welfare threats to the public in China and other countries, including the United States. Grant award R01AI110964 is subject to biosafety requirements set forth in the NIH Grants Policy Statement (e.g., NIH GPS, Section 4.1.24 "Public Health Security") and the Notice of Award (e.g., requiring that "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]."). Moreover, NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients. 45 C.F.R. § 75.101.

As the grantee, EcoHealth Alliance was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). We have concerns that WIV has not satisfied safety requirements under the award, and that EcoHealth Alliance has not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance.

Moreover, as we have informed you through prior Notices of Award, this award is subject to the Transparency Act subaward and executive compensation reporting requirement of 2 C.F.R. Part

170. To date you have not reported any subawards in the Federal Subaward Reporting System.

Therefore, effective the date of this letter, July 8, 2020, NIH is suspending all activities related to R01AI110964, until such time as these concerns have been addressed to NIH's satisfaction. This suspension is taken in accordance with 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable in accordance with 42 C.F.R. § 50.404 and the NIH GPS Section 8.7, Grant Appeals Procedures. However, EcoHealth Alliance has the opportunity to provide information and documentation demonstrating that WIV and EcoHealth Alliance have satisfied the above-mentioned requirements.

Specifically, to address the NIH's concerns, EcoHealth must provide the NIH with the following information and materials, which must be complete and accurate:

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.
3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.
4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.
5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.
6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.
7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

During this period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further asses compliance by EcoHealth Alliance and WIV, including compliance with other terms and conditions of award that may be implicated. Additionally, during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the

recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. Once the original award is reinstated, NIH will take additional steps to restrict all funding in the HHS Payment Management System in the amount of $369,819. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 CFR Part 75, including, but not limited to, terminating the grant award. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

.

Sincerely,

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy
Ms. Emily Linde

From: Lauer, Michael (NIH/OD) [E]
To: Fine, Amanda (NIH/OD) [E]
Cc: Burklow, John (NIH/OD) [E]; Myles, Renate (NIH/OD) [E]; Wojtowicz, Emma (NIH/OD) [E]; Lauer, Michael (NIH/OD) [E]
Subject: Re: FOR AWARENESS: follow up on NIH grant, EcoHealth Alliance
Date: Tuesday, August 18, 2020 9:37:56 PM
Attachments: image001.jpg
Daszak 7 8 20.pdf
A Proposed Origin for SARS-CoV-2 and the COVID-19 Pandemic - Independent Science News Food, Health and Agriculture Bioscience News.pdf
China Masters Thesis Analysis-of-Six-Patients-With-Unknown-Viruses.pdf

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Thanks Amanda – one item from the letter that is not mentioned is WIV's failure to follow-up on RATG13, a coronavirus very similar to SARS-CoV-2 that killed 3 men who went into an abandoned mineshaft. FYI see attached (second attachment bottom page 19 and top page 20) and see here.

Best, Mike

From: "Fine, Amanda (NIH/OD) [E]" (b) (6)
Date: Tuesday, August 18, 2020 at 7:26 PM
To: "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: "Burklow, John (NIH/OD) [E]" (b) (6), "Myles, Renate (NIH/OD) [E]" (b) (6), "Wojtowicz, Emma (NIH/OD) [E]" (b) (6)
Subject: FOR AWARENESS: follow up on NIH grant, EcoHealth Alliance

Hi Mike-

Just want to share the below from Betsy at WSJ for your awareness. Let me know if there is anything additional you think we should provide to her.

Thanks,
Amanda

From: McKay, Betsy <betsy.mckay@wsj.com>
Sent: Tuesday, August 18, 2020 5:49 PM
To: Fine, Amanda (NIH/OD) [E] (b) (6)
Cc: Routh, Jennifer (NIH/NIAID) [E] (b) (6); Myles, Renate (NIH/OD) [E] (b) (6); Wojtowicz, Emma (NIH/OD) [E] (b) (6)
Subject: Re: follow up on NIH grant, EcoHealth Alliance

Hi Amanda,
Just wanted to circle back and let you know what we are planning to mention from the letter to EcoHealth Alliance signed by Dr. Lauer.
We are citing the following from the July 8, 2020 letter:

- That NIH received reports of "serious biosafety concerns" at the Wuhan

Institute of Virology.
- That NIH has concerns that WIV "has not satisfied safety requirements" under the grant, and that EcoHealth Alliance "has not satisfied its obligations to monitor" WIV's compliance.
- The letter listed seven conditions that EcoHealth Alliance must fulfill in order for the suspension of the grant to be lifted. They include:
- provide to NIH a sample of the new coronavirus that the Wuhan Institute of Virology used to determine its genetic sequence.
- EcoHealth Alliance must arrange for an inspection of the Wuhan Institute of Virology by an outside team to examine the facility's lab and records "with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019."
- EcoHealth Alliance must "explain the apparent disappearance" of a scientist who worked in the Wuhan lab.
- EcoHealth Alliance must explain purported restrictions at the Wuhan institute, including "diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019."

- EcoHealth Alliance must provide NIH with the Wuhan institute's response to safety concerns about it described in a 2018 cable sent to the U.S. State Department.

We're also briefly citing the April 24 termination letter from NIH to EcoHealth Alliance, saying the five-year, $3.7 million grant was terminated because NIH did not believe that work aligned with "program goals and agency priorities."

Many thanks again for your help, and if you have any comment on any of the above, please let me know.

Best,

Betsy

On Tue, Aug 18, 2020 at 3:17 PM Fine, Amanda (NIH/OD) [E] (b) (6) wrote:

Hi Betsy-

So sorry for the delay in getting back to you. It's been a little nutty this week with some folks out. Dr. Lauer has declined the interview. In answer to your questions about the letter, attributable to NIH generally: NIH does not discuss internal deliberations on specific grants.

Thanks and hope you're staying well,
Amanda

From: McKay, Betsy <betsy.mckay@wsj.com>
Sent: Tuesday, August 18, 2020 10:40 AM
To: Fine, Amanda (NIH/OD) [E] (b) (6)
Cc: Routh, Jennifer (NIH/NIAID) [E] (b) (6); Myles, Renate (NIH/OD) [E] (b) (6); Wojtowicz, Emma (NIH/OD) [E] (b) (6)
Subject: Re: follow up on NIH grant, EcoHealth Alliance

Amanda - one more question to add.
Some scientists say the termination of the grant to EcoHealth Alliance, and now the reinstatement with these conditions, damages NIH's credibility. I would like to ask for NIH's comment on that view.
Thanks!

Betsy

On Mon, Aug 17, 2020 at 8:49 PM Fine, Amanda (NIH/OD) [E] (b) (6) wrote:

Ok thanks!

From: McKay, Betsy <betsy.mckay@wsj.com>
Sent: Monday, August 17, 2020 8:46 PM
To: Fine, Amanda (NIH/OD) [E] (b) (6)
Cc: Routh, Jennifer (NIH/NIAID) [E] (b) (6); Myles, Renate (NIH/OD) [E] (b) (6); Wojtowicz, Emma (NIH/OD) [E] (b) (6)
Subject: Re: follow up on NIH grant, EcoHealth Alliance

Yes, thanks, sorry I should have specified - Tuesday noon.

Best,
Betsy

On Mon, Aug 17, 2020 at 8:10 PM Fine, Amanda (NIH/OD) [E] (b) (6) wrote:

> Ok thanks! Are you working on deadline and if so when is your hard stop?
>
> Thanks!
> Amanda
>
> **From:** McKay, Betsy <betsy.mckay@wsj.com>
> **Sent:** Monday, August 17, 2020 6:32 PM
> **To:** Fine, Amanda (NIH/OD) [E] (b) (6)
> **Cc:** Routh, Jennifer (NIH/NIAID) [E] (b) (6); Myles, Renate (NIH/OD) [E] (b) (6); Wojtowicz, Emma (NIH/OD) [E] (b) (6)
> **Subject:** Re: follow up on NIH grant, EcoHealth Alliance
>
> Thank you very much Amanda.
> More on this: the criteria are laid out in a letter from Dr. Michael Lauer. So I would like to ask to speak with him about the reinstatement/suspension/criteria.
> (not necessary tonight)
>
> Best,
> Betsy
>
> On Mon, Aug 17, 2020 at 6:05 PM Fine, Amanda (NIH/OD) [E] (b) (6) wrote:
>
> > Hi Betsy-
> >
> > Thanks for reaching out. We're looking into your questions.
> >
> > Will get back to you,
> > Amanda
> >
> > **From:** McKay, Betsy <betsy.mckay@wsj.com>
> > **Sent:** Monday, August 17, 2020 4:02 PM
> > **To:** Fine, Amanda (NIH/OD) [E] (b) (6); Routh, Jennifer (NIH/NIAID) [E] (b) (6); Myles, Renate (NIH/OD) [E] (b) (6)
> > **Subject:** follow up on NIH grant, EcoHealth Alliance
> >
> > Hi Amanda et. al,
> > We were emailing late last week about NIH's reinstatement of a grant to EcoHealth Alliance for bat coronavirus research. The grant had been terminated in April. Looking into that further, I have some follow-up questions. The grant was reinstated, then immediately suspended until EcoHealth Alliance supplies

information and material addressing seven areas of concern.

Six of these areas of concern appear to be outside the scope of the grant, such as providing a sample of the SARS-CoV-2 virus used to sequence the virus in January, an explanation of the disappearance of a WIV scientist, and arranging for WIV to submit to an outside inspection to address whether WIV staff had SARS-CoV-2 in their possession before December 2019.

My questions are:

1. Why is EcoHealth Alliance being asked to provide these materials and information?

2. How does the requirement that EcoHealth Alliance provide this information fit into the scope of its grant?

3. Who specifically (which agency or person) has ordered EcoHealth Alliance to supply this information?

4. Any further comment on why these requirements are being placed on this grant recipient at this time?

Thanks very much.

Best,
Betsy

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

8 July 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

In follow-up to my previous letter of April 24, 2020, I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS), has withdrawn its termination of grant R01AI110964, which supports the project *Understanding the Risk of Bat Coronavirus Emergence*. Accordingly, the grant is reinstated.

However, as you are aware, the NIH has received reports that the Wuhan Institute of Virology (WIV), a subrecipient of EcoHealth Alliance under R01AI110964, has been conducting research at its facilities in China that pose serious bio-safety concerns and, as a result, create health and welfare threats to the public in China and other countries, including the United States. Grant award R01AI110964 is subject to biosafety requirements set forth in the NIH Grants Policy Statement (e.g., NIH GPS, Section 4.1.24 "Public Health Security") and the Notice of Award (e.g., requiring that "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]."). Moreover, NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients. 45 C.F.R. § 75.101.

As the grantee, EcoHealth Alliance was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). We have concerns that WIV has not satisfied safety requirements under the award, and that EcoHealth Alliance has not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance.

Moreover, as we have informed you through prior Notices of Award, this award is subject to the Transparency Act subaward and executive compensation reporting requirement of 2 C.F.R. Part

170. To date you have not reported any subawards in the Federal Subaward Reporting System.

Therefore, effective the date of this letter, July 8, 2020, NIH is suspending all activities related to R01AI110964, until such time as these concerns have been addressed to NIH's satisfaction. This suspension is taken in accordance with 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable in accordance with 42 C.F.R. § 50.404 and the NIH GPS Section 8.7, Grant Appeals Procedures. However, EcoHealth Alliance has the opportunity to provide information and documentation demonstrating that WIV and EcoHealth Alliance have satisfied the above-mentioned requirements.

Specifically, to address the NIH's concerns, EcoHealth must provide the NIH with the following information and materials, which must be complete and accurate:

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.
3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.
4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.
5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.
6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.
7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

During this period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further asses compliance by EcoHealth Alliance and WIV, including compliance with other terms and conditions of award that may be implicated. Additionally, during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the

recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. Once the original award is reinstated, NIH will take additional steps to restrict all funding in the HHS Payment Management System in the amount of $369,819. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 CFR Part 75, including, but not limited to, terminating the grant award. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

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Sincerely,

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy
Ms. Emily Linde

A Proposed Origin for SARS-CoV-2 and the COVID-19 Pandemic

by Jonathan Latham

by Jonathan Latham, PhD and Allison Wilson, PhD

In all the discussions of the origin of the COVID-19 pandemic, enormous scientific attention has been paid to the molecular character of the SARS-CoV-2 virus, including its novel genome sequence in comparison with its near relatives. In stark contrast, virtually no attention has been paid to the physical provenance of those nearest genetic relatives, its presumptive ancestors, which are two viral sequences named BtCoV/4991 and RaTG13.

This neglect is surprising because their provenance is more than interesting. BtCoV/4991 and RaTG13 were collected from a mineshaft in Yunnan province, China, in 2012/2013 by researchers from the lab of Zheng-li Shi at the Wuhan Institute of Virology (WIV). Very shortly before, in the spring of 2012, six miners working in the mine had contracted a mysterious illness and three of them had died (Wu et al., 2014). The specifics of this mystery disease have been virtually forgotten; however, they are described in a Chinese Master's thesis written in 2013 by a doctor who supervised their treatment.

We arranged to have this Master's thesis translated into English. The evidence it contains has led us to reconsider everything we thought we knew about the origins of the COVID-19 pandemic. It has also led us to theorise a plausible route by which an apparently isolated disease outbreak in a mine in 2012 led to a global pandemic in 2019.

The origin of SARS-CoV-2 that we propose below is based on the case histories of these miners and their hospital treatment. This simple theory

accounts for all the key features of the novel SARS-CoV-2 virus, including ones that have puzzled virologists since the outbreak began.

The theory can account for the origin of the polybasic furin cleavage site, which is a region of the viral spike protein that makes it susceptible to cleavage by the host enzyme furin and which greatly enhances viral spread in the body. This furin site is novel to SARS-CoV-2 compared to its near relatives (Coutard, et al., 2020). The theory also explains the exceptional affinity of the virus spike protein for human receptors, which has also surprised virologists (Letko et al., 2020; Piplani et al, 2020; Wrapp et al., 2020; Walls et al., 2020). The theory further explains why the virus has barely evolved since the pandemic began, which is also a deeply puzzling aspect of a virus supposedly new to humans (Zhan et al., 2020; van Dorp et al., 2020; Chaw et al., 2020). Lastly, the theory neatly explains why SARS-CoV-2 targets the lungs, which is unusual for a coronavirus (Huang et al., 2020).

We do not propose a specifically genetically engineered or biowarfare origin for the virus but the theory does propose an essential causative role in the pandemic for scientific research carried out by the laboratory of Zheng-li Shi at the WIV; thus also explaining Wuhan as the location of the epicentre.

Why has the provenance of RaTG13 and BtCoV/4991 been ignored?

The apparent origin of the COVID-19 pandemic is the city of Wuhan in Hubei province, China. Wuhan is also home to the world's leading research centre for bat coronaviruses. There are two virology labs in the city, both have either collected bat coronaviruses or researched them in the recent past. The Shi lab, which collected BtCoV/4991 and RaTG13, recently received grants to evaluate *by experiment* the potential for pandemic pathogenicity of the novel bat coronaviruses they collected from the wild.

To add to these suggestive data points, there is a long history of accidents,

disease outbreaks, and even pandemics resulting from lab accidents with viruses (Furmanski, 2014; Weiss et al., 2015). For these and other reasons, summarised in our article *The Case is Building that COVID-19 Had a Lab Origin*, we (a virologist and a geneticist) and others have concluded that a lab outbreak is a credible thesis. Certainly, a lab origin has at least as much circumstantial evidence to support it as does any natural zoonotic origin theory (Piplani et al., 2020; Segreto and Deigin, 2020; Zhan et al., 2020).

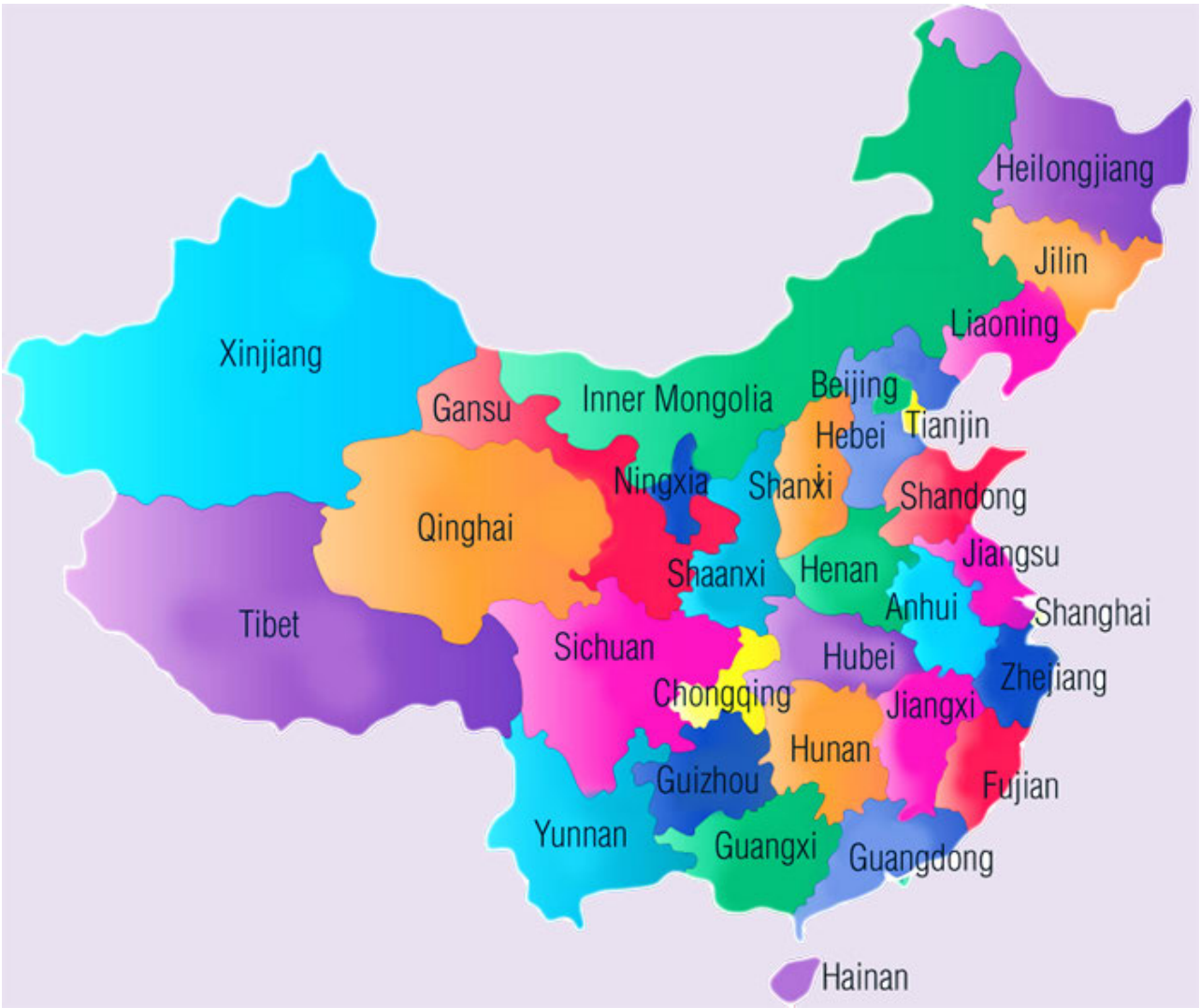
The media, normally so enamoured of controversy, has largely declined even to debate the possibility of a laboratory escape. Many news sites have simply labelled it a conspiracy theory.

The principal reason for media dismissals of the lab origin possibility is a review paper in *Nature Medicine* (Andersen et al., 2020). Although by Jun 29 2020 this review had almost 700 citations it also has major scientific shortcomings. These flaws are worth understanding in their own right but they are also useful background for understanding the implications of the Master's thesis.

Andersen et al., a critique

The question of the origin of the COVID-19 pandemic is, in outline, simple. There are two incontrovertible facts. One, the disease is caused by a human viral pathogen, SARS-CoV-2, first identified in Wuhan in December 2019 and whose RNA genome sequence is known. Second, all of its nearest known relatives come from bats. Beyond any reasonable doubt SARS-CoV-2 evolved from an ancestral bat virus. The task the *Nature Medicine* authors set for themselves was to establish the relative merits of each of the various possible routes (lab vs natural) by which a bat coronavirus might have jumped to humans and in the same process have acquired an unusual furin site and a spike protein having very high affinity for the human ACE2 receptor.

When Andersen et al. outline a natural zoonotic pathway they speculate extensively about how the leap might have occurred. In particular they elaborate on a proposed residence in intermediate animals, likely pangolins. For example, "The presence in pangolins of an RBD [Receptor Binding Domain] very similar to that of SARS-CoV-2 means that we can infer that this was probably in the virus that jumped to humans. This leaves the insertion of [a] polybasic cleavage site to occur during human-to-human transmission." This viral evolution occurred in "Malayan pangolins illegally imported into Guangdong province". Even with these speculations there are major gaps in this theory. For example, why is the virus so well adapted to humans? Why Wuhan, which is 1,000 Km from Guangdong? (See map).



ch na prov nce gu de

The authors provide no such speculations in favour of the lab accident thesis, only speculation *against* it:

"Finally, the generation of the *predicted* O-linked glycans is also *unlikely* to have occurred due to cell-culture passage, as such features suggest the involvement of an immune system." (italics added).

[Passaging is the deliberate placing of live viruses into cells or organisms to which they are NOT adapted for the purpose of making them adapted, i.e. speeding up their evolution.]

It is also noteworthy that the Andersen authors set a higher hurdle for the lab thesis than the zoonotic thesis. In their account, the lab thesis is required to explain *all* of the evolution of SARS-CoV-2 from its presumed bat viral ancestor, whereas under their telling of the zoonotic thesis the key step of the addition of the furin site is allowed to happen in humans and is thus effectively unexplained.

A further imbalance is that key information needed to judge the merits of a lab origin theory is missing from their account. As we detailed in our previous article, in their search for SARS-like viruses with zoonotic spillover potential, researchers at the WIV have passaged live bat viruses in monkey and human cells (Wang et al., 2019). They have also performed many recombinant experiments with diverse bat coronaviruses (Ge et al., 2013; Menachery et al., 2015; Hu et al., 2017). Such experiments have generated international concern over the possible creation of potential pandemic viruses (Lipsitch, 2018). As we showed too, the Shi lab had also won a grant to extend that work to whole live animals. They planned "virus infection experiments across a range of cell cultures from different species and humanized mice" with recombinant bat coronaviruses. Yet Andersen et al did not discuss this

research at all, except to say:

"Basic research involving passage of bat SARS-CoV-like coronaviruses in cell culture and/or animal models has been ongoing for many years in biosafety level 2 laboratories across the world"

This statement is fundamentally misleading about the kind of research performed at the Shi lab.

A further important oversight by the Andersen authors concerns the history of lab outbreaks of viral pathogens. They write: "there are documented instances of laboratory escapes of SARS-CoV". This is a rather matter-of-fact allusion to the fact that since 2003 there have been six documented outbreaks of SARS from labs, not all in China, with some leading to fatalities (Furmanski, 2014).

Andersen et al might have also have noted that two major human pandemics are widely accepted to have been caused by lab outbreaks of viral pathogens, H1N1 in 1977 and Venezuelan Equine Encephalitis (summarised in Furmanski, 2014). Andersen could even have noted that literally hundreds of lab accidents with viruses have resulted in near-misses or very localised outbreaks (summarised by Lynn Klotz and Sam Husseini and also Weiss et al., 2015).

Also unmentioned were instances where a lab outbreak of an experimental or engineered virus has been plausibly theorised but remains uninvestigated. For example, the most coherent explanation for the H1N1 variant 'swine flu' pandemic of 2009/10 that resulted in a death toll estimated by some as high as 200,000 (Duggal et al., 2016; Simonsen et al. 2013), is that a vaccine was improperly inactivated by its maker (Gibbs et al., 2009). If so, H1N1 emerged from a lab not once but twice.

Given that human and livestock viral outbreaks have frequently come from laboratories and that many scientists have warned of probable lab escapes

(Lipsitch and Galvani, 2014), and that the WIV itself has a questionable biosafety record, the Andersen paper is not an even-handed treatment of the possible origins of the COVID-19 virus.

Yet its text expresses some strong opinions: "Our analyses clearly show that SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus....It is improbable that SARS-CoV-2 emerged through laboratory manipulation of a related SARS-CoV-like coronavirus.....the genetic data irrefutably show that SARS-CoV-2 is not derived from any previously used backbone....the evidence shows that SARS-CoV2 is not a purposefully manipulated virus....we do not believe that any type of laboratory-based scenario is possible." (Andersen et al., 2020).

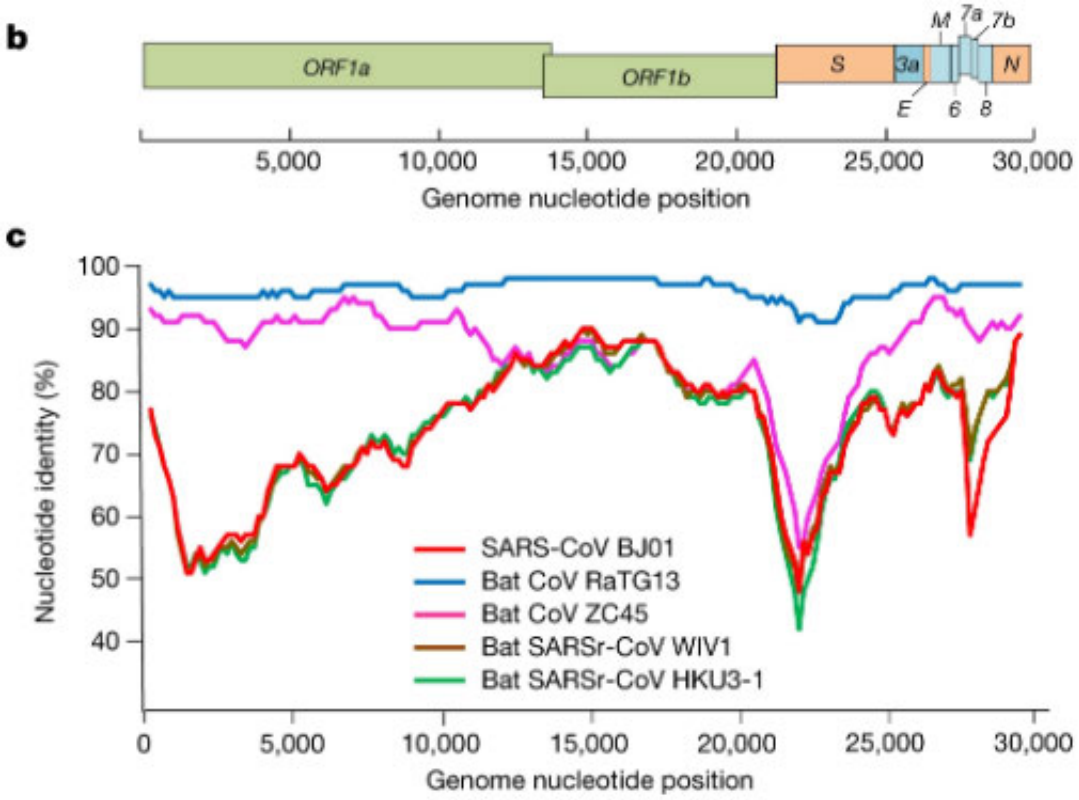
It is hard not to conclude that what their paper mostly shows is that Drs. Andersen, Rambaut, Lipkin, Holmes and Garry much prefer the natural zoonotic transfer thesis. Their rhetoric is forthright but the evidence does not support that confidence.

Indeed, since the publication of Andersen et al., important new evidence has emerged that undermines their zoonotic origin theory. On May 26th the Chinese CDC ruled out the Huanan "wet" market in Wuhan as the source of the outbreak. Additionally, new research on pangolins, the favoured intermediate mammal host, suggests they are not a natural reservoir of coronaviruses (Lee et al., 2020; Chan and Zhan, 2020). Furthermore, SARS-CoV-2 was found not to replicate in bat kidney or lung cells (*Rhinolophus sinicus*), implying that SARS-CoV-2 is not a recently-adapted spill over Chu et al., 2020).

The Mojiang mine and the Master's thesis

In our own search to resolve the COVID-19 origin question we chose to focus on the provenance of the coronavirus genome sequences BtCoV/4991 and

RaTG13, since these are the most closely related sequences to SARS-CoV-2 (98.7% and 96.2% identical respectively). See FIG 1. (reproduced from P. Zhou et al., 2020).



S m ar ty of SARS-CoV-2 to RaTG13 (b ue ne) and other coronav ruses (red, green, p nk) (mage from Zhou et a ., 2020). The h gher the ne the more s m ar the v rus.

For comparison, the next closest virus to SARS-CoV-2 is RmYN02 (not shown in Fig 1.) (H. Zhou et al., 2020). RmYN02 has an overall similarity to SARS-CoV-2 of 93.2%, making its evolutionary distance from SARS-CoV-2 almost twice as great.

BtCoV/4991 was first described in 2016. It is a 370 nucleotide virus fragment collected from the Mojiang mine in 2013 by the lab of Zeng-li Shi at the WIV (Ge et al., 2016). BtCoV/4991 is 100% identical in sequence to one segment of RaTG13. RaTG13 is a complete viral genome sequence (almost 30,000 nucleotides) that was only published in 2020, after the pandemic began (P. Zhou et al., 2020).

Despite the confusion created by their different names, in a letter obtained by us Zheng-li Shi confirmed to a virology database that BtCoV/4991 and RaTG13 are both from the same bat faecal sample and the same mine. They are thus sequences from the same virus. In the discussion below we will refer primarily to RaTG13 and specify BtCoV/4991 only as necessary.

These specifics are important because it is these samples and their provenance that we believe are ultimately key to unravelling the mystery of the origins of COVID-19.

The story begins in April 2012 when six workers in that same Mojiang mine fell ill from a mystery illness while removing bat faeces. Three of the six subsequently died.

In a March 2020 interview with Scientific American Zeng-li Shi dismissed the significance of these deaths, claiming the miners died of fungal infections. Indeed, no miners or deaths are mentioned in the paper published by the Shi lab documenting the collection of RaTG13 (Ge et al., 2016).

But Shi's assessment does not tally with any other contemporaneous accounts of the miners and their illness (Rahalkar and Bahulikar, 2020). As these authors have pointed out, *Science* magazine wrote up part of the incident in 2014 as A New Killer Virus in China?. *Science* was citing a different team of virologists who found a paramyxovirus in rats from the mine. These virologists told *Science* they found "no direct relationship between human infection" and their virus. This expedition was later published as the discovery of a new virus called MojV after Mojiang, the locality of the mine (Wu et al., 2014).

What this episode suggests though is that these researchers were looking for a potentially lethal virus and not a lethal fungus. Also searching the Mojiang mine for a virus at around the same time was Canping Huang, the author of a PhD thesis carried out under the supervision of George Gao, the head of the

Chinese CDC.

All of this begs the question of why the Shi lab, which has no interest in fungi but a great interest in SARS-like bat coronaviruses, also searched the Mojiang mine for bat viruses on four separate occasions between August 2012 and July 2013, even though the mine is a 1,000 Km from Wuhan (Ge et al., 2016). These collecting trips began while some of the miners were still hospitalised.

Fortunately, a detailed account of the miner's diagnoses and treatments exists. It is found in a Master's thesis written in Chinese in May 2013. Its suggestive English title is "*The Analysis of 6 Patients with Severe Pneumonia Caused by Unknown viruses*".

The original English version of the abstract implicates a SARS-like coronavirus as the probable causative agent and that the mine "had a lot of bats and bats' feces".

The findings of the Master's thesis

To learn more, especially about the reasonableness of this diagnosis, we arranged to have the whole Master's thesis translated into English and are here making the translation available. To read it in full see the embedded document below (or download it here).

The six ill miners were admitted to the No. 1. School of Clinical Medicine, Kunming Medical University, in short succession in late April and early May 2012. Kunming is the capital of Yunnan province and 250 Km from Mojiang.

Of the descriptions of the miners and their treatments, which include radiographs and numerous CAT scans, several features stand out:

1) From their admission to the hospital their doctors informed the "medical office" of a potential "outburst of disease" i.e. a potential epidemic outbreak. Thus, the miners were treated for infections and not as if they had inhaled noxious gases or other toxins.

2) The symptoms (on admission) of the six miners were: a) dry cough, b) sputum, c) high fevers, especially shortly before death d) difficulty breathing, e) myalgia (sore limbs). Some patients had hiccoughs and headaches. (See Table 1).

The syndromes of the six patients

表格 1 Table 1 6 位患者入院主诉及伴随症状

症状 / 患者		咳嗽 Coughi	咳痰 Coughi	发热 ≥39℃ Fever	呼吸困难 Difficulty	四肢酸痛 Soreness	血性痰 Bloody	头痛 Headac	胸痛 Chest
Patient Zhou	周 XX	+	+	+	+	+	-	+	+
Patient Lu	吕 XX	+	+	+	+	+	+	-	-
Patient Guo	郭 XX	+	+	+	+	+	+	+	-
Patient Liu	刘 XX	+	+	+	+	+	+	-	+
Patient Wu	吴 XX	+	+	+	+	+	-	+	-
Patient Li	李 XX	+	+	+	-	-	-	-	-

The Syndromes of the s x Moj ang M ne pat ents

3) Clinical work established that patients 1-4 had low blood oxygen "for sure it was ARDS" (Acute Respiratory Distress Syndrome) and immune damage considered indicative of viral infection. Additionally, a tendency for thrombosis was noted in patients 2 and 4. Symptom severity and mortality were age-related (though from a sample of 6 this must be considered anecdotal).

4) Potential common and rare causes of their symptoms were tested for and mostly eliminated. For patients 3 and 4 these included tests for HIV, Cytomegalovirus, Epstein-Barr Virus (EBV), Japanese encephalitis,

haemorrhagic fever, Dengue, Hepatitis B, SARS, and influenza. Of these, only patient 2 tested positive for Hepatitis and EBV.

5) Treatment of the six patients included ventilation (patients 2-4), steroids (all patients), antivirals (all except patient 5), and blood thinners (patients 2 and 4). Antibiotics and antifungal medications were administered to counter what were considered secondary (but significant) co-infections.

6) A small number of remote meetings were held with researchers at other universities. One was with Zhong Nanshan at Sun Yat-Sen University, Guangdong. Zhong is the Chinese hero of the SARS epidemic, a virologist, and arguably the most famous scientist in China.

7) Samples from the miners were later sent to the WIV in Wuhan and to Zhong Nanshan, further confirming that viral disease was strongly suspected. Some miners did test positive for coronavirus (the thesis is unclear on how many).

8) The source of infection was concluded to be *Rhinolophus sinicus*, a horseshoe bat and the ultimate conclusion of the thesis reads "the unknown virus lead to severe pneumonia could be: The SARS-like-CoV from the Chinese rufous horseshoe bat." Thus the miners had a coronavirus but it apparently was not SARS itself.

The significance of the Master's thesis

These findings of the thesis are significant in several ways.

First, in the light of the current coronavirus pandemic it is evident the miners' symptoms very closely resemble those of COVID-19 (Huang et al, 2020; Tay et al., 2020; M. Zhou et al., 2020). Anyone presenting with them today would immediately be assumed to have COVID-19. Likewise, many of the treatments given to the miners have become standard for COVID-19 (Tay et al., 2020).

Second, the remote meeting with Zhong Nanshan is significant. It implies that the illnesses of the six miners were of high concern and, second, that a SARS-like coronavirus was considered a likely cause.

Third, the abstract, the conclusions, and the general inferences to be made from the Master's thesis contradict Zheng-li Shi's assertion that the miners died from a fungal infection. Fungal infection as a potential primary cause was raised but largely discarded.

Fourth, if a SARS-like coronavirus was the source of their illness the implication is that it could *directly* infect human cells. This would be unusual for a bat coronavirus (Ge et al., 2013). People do sometimes get ill from bat faeces but the standard explanation is histoplasmosis, a fungal infection and not a virus (McKinsey and McKinsey, 2011; Pan et al., 2013).

Fifth, the sampling by the Shi lab found that bat coronaviruses were unusually abundant in the mine (Ge at al., 2016). Among their findings were two betacoronaviruses, one of which was RaTG13 (then known as BtCoV/4991). In the coronavirus world betacoronaviruses are special in that both SARS and MERS, the most deadly of all coronaviruses, are both betacoronaviruses. Thus they are considered to have special pandemic potential, as the concluding sentence of the Shi lab publication which found RaTG13 implied: "special attention should particularly be paid to these lineages of coronaviruses" (Ge at al., 2016). In fact, the Shi and other labs have for years been predicting that bat betacoronaviruses like RaTG13 would go pandemic; so to find RaTG13 where the miners fell ill was a scenario in perfect alignment with their expectations.

The Mojiang miners passaging proposal

How does the Master's thesis inform the search for a plausible origin of the pandemic?

In our previous article we briefly discussed how the pandemic might have been caused either by a virus collection accident, or through viral passaging, or through genetic engineering and a subsequent lab escape. The genetic engineering possibility deserves attention and is extensively assessed in an important preprint (Segreto and Deigin, 2020).

We do not definitively rule out these possibilities. Indeed it now seems that the Shi lab at the WIV did not forget about RaTG13 but were sequencing its genome in 2017 and 2018. However, we believe that the Master's thesis indicates a much simpler explanation.

We suggest, first, that inside the miners RaTG13 (or a very similar virus) evolved into SARS-CoV-2, an unusually pathogenic coronavirus highly adapted to humans. Second, that the Shi lab used medical samples taken from the miners and sent to them by Kunming University Hospital for their research. It was this human-adapted virus, now known as SARS-CoV-2, that escaped from the WIV in 2019.

We refer to this COVID-19 origin hypothesis as the Mojiang Miners Passage (MMP) hypothesis.

Passaging is a standard virological technique for adapting viruses to new species, tissues, or cell types. It is normally done by deliberately infecting a new host species or a new host cell type with a high dose of virus. This initial viral infection would ordinarily die out because the host's immune system vanquishes the ill-adapted virus. But, in passaging, before it does die out a sample is extracted and transferred to a new identical tissue, where viral infection restarts. Done iteratively, this technique (called "serial passaging" or just "passaging") intensively selects for viruses adapted to the new host or cell type (Herfst et al., 2012).

At first glance RaTG13 is unlikely to have evolved into SARS-CoV-2 since

RaTG13 is approximately 1,200 nucleotides (3.8%) different from SARS-CoV-2. Although RaTG13 is the most closely related virus to SARS-CoV-2, this sequence difference still represents a considerable gap. In a media statement evolutionary virologist Edward Holmes has suggested this gap represents 20-50 years of evolution and others have suggested similar figures.

We agree that ordinary rates of evolution would not allow RaTG13 to evolve into SARS-CoV-2 but we also believe that conditions inside the lungs of the miners were far from ordinary. Five major factors specific to the hospitalised miners favoured a very high rate of evolution inside them.

i) When viruses infect new species they typically undergo a period of very rapid evolution because the selection pressure on the invading pathogen is high. The phenomenon of rapid evolution in new hosts is well attested among corona- and other viruses (Makino et al., 1986; Baric et al., 1997; Dudas and Rambaut 2016; Forni et al., 2017).

ii) Judging by their clinical symptoms such as the CT scans, all the miner's infections were primarily of the lungs. This localisation likely occurred initially because the miners were exerting themselves and therefore inhaling the disturbed bat guano deeply. As miners, they may already have had damaged lung tissues (patient 3 had suspected pneumoconiosis) and/or particulate matter was present that irritated the tissues and may have facilitated initial viral entry.

In contrast, standard coronavirus infections are confined to the throat and upper respiratory tract. They do not normally reach the lungs (Perlman and Netland, 2009). Lungs are far larger tissues by weight (kilos vs grammes) than the upper respiratory tract. There was therefore likely a much larger quantity of virus inside the miners than would be the case in an ordinary coronavirus infection.

Comparing a typical coronavirus respiratory tract infection with the extent of infected lungs in the miners from a purely mathematical point of view indicates the potential scale of this quantitative difference. The human aerodigestive tract is approximately 20cm in length and 5cm in circumference, i.e. approximately 100 cm^2 in surface area. The surface area of a human lung ranges from 260,000-680,000 cm^2 (Hasleton, 1972). The amount of potentially infected tissue in an average lung is therefore approximately 4500-fold greater than that available to a normal coronavirus infection. The amount of virus present in the infected miners, sufficient to hospitalise all of them and kill half of them, was thus proportionately very large.

Evolutionary change is in large part a function of the population size. The lungs of the miners, we suggest, supported a very high viral load leading to proportionately rapid viral evolution.

Furthermore, according to the Master's thesis, the immune systems of the miners were compromised and remained so even for those discharged. This weakness on the part of the miners may also have encouraged evolution of the virus.

iii) The length of infection experienced by the miners (especially patients 2, 3 and 4) far exceeded that of an ordinary coronavirus infection. From first becoming too sick to work in the mine, patient 2 survived 57 days until he died. Patient 3 survived 120 days after stopping work. Patient 4 survived 117 days and then was discharged as cured. Each had been exposed in the mine for 14 days prior to the onset of severe symptoms; thus each presumably had nascent infections for some time before calling in sick (See Table 2 of the thesis).

In contrast, in ordinary coronavirus infections the viral infection is cleared within about ten to fourteen days after being acquired (Tay et al., 2020). Thus,

unlike most sufferers from coronavirus infection, the hospitalised miners had very long-term bouts of disease characterised by a continuous high load of virus. In the cases of patients 3 and 4 their illnesses lasted over 4 months.

iv) Coronaviruses are well known to recombine at very high rates: 10% of all progeny in a cell can be recombinants (Makino et al., 1986; Banner and Lai, 1991; Dudas and Rambaut, 2016). In normal virus evolution the mutation rate and the selection pressure are the main foci of attention. But in the case of a coronavirus adapting to a new host where many mutations distributed all over the genome are required to fully adapt to the new host, the recombination rate is likely to be highly influential in determining the overall speed of adaptation by the virus population (Baric et al., 1997).

Inside the miners a large tissue was simultaneously infected by a population of poorly-adapted viruses, with each therefore under pressure to adapt. Even if the starting population of virus lacked any diversity, many individual viruses would have acquired mutations independently but only recombination would have allowed these mutations to unite in the same genome. To recombine, viruses must be present in the same cell. In such a situation the particularities of lung tissues become potentially important because the existence of airways (bronchial tubes, etc.) allows partially-adapted viruses from independent viral populations to travel to distal parts of the lung (or even the other lung) and encounter other such partially-adapted viruses and populations. This movement around the lungs would likely have resulted in what amounted to a passaging effect without the need for a researcher to infect new tissues. Indeed, in the Master's thesis the observation is several times made that areas of the lungs of a specific patient would appear to heal even while other parts of the lungs would become infected.

v) There were also a number of unusual things about the bat coronaviruses in the mine. They were abnormally abundant but also there were many different

kinds, often causing co-infections of the bats (Ge et al., 2016). Viral co-infections are often more infectious or more pathogenic (Latham and Wilson, 2007).

As the WIV researchers remarked about the bats in the mine:

"we observed a high rate of co-infection with two coronavirus species and interspecies infection with the same coronavirus species within or across bat families. These phenomena may be owing to the diversity and high density of bat populations in the same cave, facilitating coronavirus intra- and interspecies transmissions, which may result in recombination and acceleration of coronavirus evolution." (Ge et al., 2016).

The diversity of coronaviruses in the mine suggests that the miners were similarly exposed and that their illness may potentially have begun as co-infections.

Combining these observations, we propose that the miners' lungs offered an unprecedented opportunity for accelerated evolution of a highly bat-adapted coronavirus into a highly human-adapted coronavirus and that decades of ordinary coronavirus evolution could easily have been condensed into months. However, we acknowledge that these conditions were unique. They and their scale have no exact scientific precedent we can refer to and they would be hard to replicate in a lab; thus it is important to emphasize that our proposal is fully consistent with the underlying principles of viral evolution as understood today.

In support of the MMP theory we also know something about the samples taken from the miners. According to the Master's thesis, samples were taken from patients for "scientific research" and blood samples (at least) were sent to the WIV.

"In the later stage we worked with Dr. Zhong Nan Shan and did some sampling. The patient* tested positive for serum IgM by the WuHan Institute of Virology. It suggested the existence of virus infection" (p62 in the section "Comprehensive Analysis".)

(*The original does not specify the number of patients tested.)

The Master's thesis also states its regret that no samples for research were taken from patients 1 and 2, implying that samples were taken from all the others.

We further know that, on June 27th, 2012, the doctors performed an unexplained thymectomy on patient 4. The thymus is an immune organ that can potentially be removed without greatly harming the patient and it could have contained large quantities of virus. Beyond this the Master's thesis is unfortunately unclear on the specifics of what sampling was done, for what purpose, and where each particular sample went.

Given the interests of the Shi lab in zoonotic origins of human disease, once such a sample was sent to them, it would have been obvious and straightforward for them to investigate how a virus from bats had managed to infect these miners. Any viruses recoverable from the miners would likely have been viewed by them as a unique natural experiment in human passaging offering unprecedented and otherwise-impossible-to-obtain insights into how bat coronaviruses can adapt to humans.

The logical course of such research would be to sequence viral RNA extracted directly from unfrozen tissue or blood samples and/or to generate live infectious clones for which it would be useful (if not imperative) to amplify the virus by placing it in human cell culture. Either technique could have led to accidental infection of a lab researcher.

Our supposition as to why there was a time lag between sample collection (in 2012/2013) and the COVID-19 outbreak is that the researchers were awaiting BSL-4 lab construction and certification, which was underway in 2013 but delayed until 2018.

We propose that, when frozen samples derived from the miners were eventually opened in the Wuhan lab they were already highly adapted to humans to an extent possibly not anticipated by the researchers. One small mistake or mechanical breakdown could have led directly to the first human infection in late 2019.

Thus, one of the miners, most likely patient 3, or patient 4 (whose thymus was removed), was effectively patient zero of the COVID-19 epidemic. In this scenario, COVID-19 is not an engineered virus; but, equally, if it had not been taken to Wuhan and no further molecular research had been performed or planned for it then the virus would have died out from natural causes, rather than escaped to initiate the COVID-19 pandemic.

Evidence in favour of the MMP proposal

Our proposal is consistent with all the principal undisputed facts concerning SARS-CoV-2 and its origin. The MMP proposal has the additional benefit of reconciling many observations concerning SARS-CoV-2 that have proven difficult to reconcile with any natural zoonotic hypothesis.

For instance, using different approaches, numerous researchers have concluded that the SARS-CoV-2 spike protein has a very high affinity for the human ACE2 receptor (Walls et al., 2020; Piplani et al., 2020; Shang and Ye et al., 2020; Wrapp et al., 2020). Such exceptional affinities, ten to twenty times as great as that of the original SARS virus, do not arise at random, making it very hard to explain in any other way than for the virus to have been strongly selected in the presence of a human ACE2 receptor (Piplani et al., 2020).

In addition to this, a recent report found that the spike of RaTG13 binds the human ACE2 receptor (Shang and Ye et al., 2020). We proposed above that the virus in the mine directly infected humans lung cells. The main determinant of cell infection and species specificity of coronaviruses is initial receptor binding (Perlman and Netland, 2009). Thus RaTG13, unlike most bat coronaviruses, probably can enter and infect human cells, providing biological plausibility to the idea that the miners became infected with a coronavirus resembling RaTG13.

Moreover, the receptor binding domain (RBD) of SARS-CoV-2, which is the region of the spike that physically contacts the human ACE2 receptor, has recently been crystallised to reveal its spatial structure (Shang and Ye et al., 2020). These authors found close structural similarities between the spikes of SARS-CoV-2 and RaTG13 in how they bound the human ACE2 receptor:

"Second, as with SARS-CoV-2, bat RaTG13 RBM [a region of the RBD] contains a similar four-residue motif in the ACE2 binding ridge, *supporting the notion that SARS-CoV-2 may have evolved from RaTG13 or a RaTG13-related bat coronavirus* (Extended Data Table 3 and Extended Data Fig. 7). Third, the L486F, Y493Q and D501N residue changes from RaTG13 to SARS CoV-2 enhance ACE2 recognition and may have facilitated the bat-to-human transmission of SARS-CoV-2 (Extended Data Table 3 and Extended Data Fig. 7). A lysine-to-asparagine mutation at the 479 position in the SARS-CoV RBD (corresponding to the 493 position in the SARS-CoV-2 RBD) enabled SARS-CoV to infect humans. Fourth, Leu455 contributes favourably to ACE2 recognition, and it is conserved between RaTG13 and SARS CoV-2; its presence in the SARS CoV-2 RBM may be important for the bat-to-human transmission of SARS-CoV-2" (Shang and Ye et al., 2020). (*italics added*)

The significance of this molecular similarity is very great. Coronaviruses have evolved a diverse set of molecular solutions to solve the problem of binding

ACE2 (Perlman and Netland, 2009; Forni et al., 2017). The fact that RaTG13 and SARS CoV-2 share the same solution makes RaTG13 a highly likely direct ancestor of Sars-CoV-2.

A further widely noted feature of SARS-CoV-2 is its furin site (Coutard et al., 2020). This site is absent from RaTG13 and other closely related coronaviruses. The most closely related virus with such a site is the highly lethal MERS (which broke out in 2012). Possession of a furin site enables SARS-CoV-2 (like MERS) to infect lungs and many other body tissues (such as the gastrointestinal tract and neurons), explaining much of its lethality (Hoffman et al., 2020; Lamers et al., 2020). However, no convincing explanation for how SARS-CoV-2 acquired this site has yet been offered. Our suggestion is that it arose due to the high selection pressure which existed in the miner's lungs and which in general worked to ensure that the virus became highly adapted to the lungs. This explanation, which encompasses how SARS-CoV-2 came to target lung tissues in general, is an important aspect of our proposal.

The implication is therefore that the furin site was not acquired by recombination with another coronavirus and simply represents convergent evolution (as suggested by Andersen et al., 2020).

An intriguing alternative possibility is that SARS-CoV-2 acquired its furin site directly from the miner's lungs. Humans possess an epithelial sodium channel protein called ENaC-a whose furin cleavage site is identical over eight amino acids to SARS-CoV-2 (Anand et al., 2020). ENaC-a protein is present in the same airway epithelial and lung tissues infected by SARS-CoV-2. It is known from plants that positive-stranded RNA viruses recombine readily with host mRNAs (Greene and Allison, 1994; Greene and Allison, 1996; Lommel and Xiong, 1991; Borja et al., 2007). The same evidence base is not available for positive-stranded animal RNA viruses, (though see Gorbalenya, 1992) but if

plant viruses are a guide then acquisition of its furin site via recombination with the mRNA which encodes ENaC-a by SARS-CoV-2 is a strong possibility.

A further feature of SARS-CoV-2 has been the very limited adaptive evolution of its genome since the pandemic began (Zhan et al., 2020; van Dorp et al., 2020; Starr et al., 2020). It is a well-established principle that viruses that jump species undergo accelerated evolutionary change in their new host (e.g. Baric et al., 1997). Thus, SARS and MERS (both coronaviruses) underwent rapid and readily detectable adaptation to their new human hosts (Forni et al., 2017; Dudas and Rambaut, 2016). Such an adaptation period has not been observed for SARS-CoV-2 even though it has now infected many more individuals than SARS or MERS did. This has even led to suggestions that the SARS-CoV-2 virus had a period of cryptic circulation in humans infections that predated the pandemic (Chaw et al., 2020). The sole mutation consistently observed to accumulate across multiple studies is a D614G substitution in the spike protein (e.g. Korber et al., 2020). The numerically largest analysis of SARS-CoV-2 genomes, however, found no evidence at all for adaptive evolution, even for D614G (van Dorp et al., 2020).

The general observation is therefore that Sars-CoV-2 has remained functionally unchanged or virtually so (except for inconsequential genetic changes) since the pandemic began. This is a very important observation. It implies that SARS-CoV-2 is highly adapted across its whole set of component proteins and not just at the spike (Zhan et al., 2020). That is to say, its evolutionary leap to humans was completed before the 2019 pandemic began.

It is hard to imagine an explanation for this high adaptiveness other than some kind of passaging in a human body (Zhan et al., 2020). Not even passaging in human cells could have achieved such an outcome.

Two examples illustrate this point. In a follow up to Shang and Ye et al., (2020),

a similar group of Minnesota researchers identified a distinct strategy by which the spike (S) protein (which contains the receptor bind domain; RBD) of SARS-CoV-2 evades the human immune system (Shang and Wan et al., 2020). This strategy involves more effective hiding of its RBD, but it implies again that the spike and the RBD evolved in tandem and in the presence of the human immune system (i.e. in a human body and not in tissue culture).

The Andersen authors, in their critique of a possible engineered origin for SARS-CoV-2, also stress the need for passaging in whole humans:

"Finally, the generation of the predicted O-linked glycans is also unlikely to have occurred during cell-culture passage, as such features suggest the involvement of an immune system" (Andersen et al., 2020).

The final point that we would like to make is that the principal zoonotic origin thesis is the one proposed by Andersen et al. Apart from being poorly supported this thesis is very complex. It requires two species jumps, at least two recombination events between quite distantly related coronaviruses and the physical transfer of a pangolin (having a coronavirus infection) from outside China (Andersen et al., 2020). Even then it provides no logical explanation of the adaptedness of SARS-CoV-2 across its whole genome or why the virus emerged in Wuhan.

By contrast, our MMP proposal requires only the one species jump, which is documented in the Master's thesis. Although we do not rule out a possible role for mixed infections in the lungs of the miners, nor the possibility of recombination between closely related variants in those lungs, nor the potential acquisition of the furin site from a host mRNA, only mutation was needed to derive SARS-CoV-2 from RaTG13. Hence our attention earlier to the figure from P. Zhou et al., 2020 showing that RaTG13 is the most closely related virus to SARS-CoV-2 *over its entire length*. This extended similarity is

perfectly consistent with a mutational origin of SARS-CoV-2 from RaTG13.

In short, the MMP theory is a plausible and parsimonious explanation of all the key features of the COVID-19 pandemic and its origin. It accounts for the propensity of SARS-CoV-2 infections to target the lungs; the apparent preadapted nature of the virus; and its transmission from bats in Yunnan to humans in Wuhan.

Further questions

The hypothesis that SARS-CoV-2 evolved in the Mojiang miner's lungs potentially resolves many scientific questions about the origin of the pandemic. But it raises others having to do with why this information has not come to light hitherto. The most obvious of these concern the actions of the Shi lab at the WIV.

Why did the Shi lab not acknowledge the miners' deaths in any paper describing samples taken from the mine (Ge et al., 2016 and P. Zhou et al., 2020)? Why in the title of the Ge at al. 2016 paper did the Shi lab call it an "abandoned" mine? When they published the sequence of RaTG13 in Feb. 2020, why did the Shi lab provide a new name (RaTG13) for BtCoV/4991 when they had by then cited BtCoV/4991 twice in publications and once in a genome sequence database and when their sequences were from the same sample and 100% identical (P. Zhou et al., 2020)? If it was just a name change, why no acknowledgement of this in their 2020 paper describing RaTG13 (Bengston, 2020)? These strange and unscientific actions have obscured the origins of the closest viral relatives of SARS-CoV-2, viruses that are suspected to have caused a COVID-like illness in 2012 and which may be key to understanding not just the origin of the COVID-19 pandemic but the future behaviour of SARS-CoV-2.

These are not the only questionable actions associated with the provenance of

samples from the mine. There were five scientific publications that very early in the pandemic reported whole genome sequences for SARS-CoV-2 (Chan et al., 2020; Chen et al., 2020; Wu et al., 2020; P. Zhou et al., 2020; Zhu et al., 2020). Despite three of them having experienced viral evolutionary biologists as authors (George Gao, Zheng-li Shi and Edward Holmes) only one of these (Chen et al., 2020) succeeded in identifying the most closely related viral sequence by far: BtCoV/4991 a viral sequence in the possession of the Shi lab at the WIV that differed from SARS-CoV-2 by just 5 nucleotides.

As we noted in our earlier article, the most important of the questions surrounding the origins of SARS-CoV-2 could potentially be resolved by a simple examination of the complete lab notebooks and biosafety records of relevant researchers at the WIV. Now that a credible and testable lab escape hypothesis exists this task becomes potentially much easier. This moment thus represents an opportune one to renew that call for an independent and transparent investigation of the WIV.

In requesting an investigation we are aware that no scientific institution anywhere has made a comparable request. We believe that this failure undermines public trust in a "scientific response" to the pandemic. Instead, the scientific establishment has labeled the lab escape theory a "rumor", an "unverified theory" and a "conspiracy" when its proper name is a hypothesis. By taking this stance the scientific establishment has given the unambiguous message that scientists who take the possibility of a lab origin seriously are jeopardising their careers. Thus, while countless scientific publications on the pandemic assert in their introductions that a zoonotic origin for SARS-CoV-2 is a matter of fact or near-certainty (and Andersen et al has 860 citations as of July 14th), there is still not one published scientific paper asserting that a lab escape is even a credible hypothesis that deserves investigation.

Anyone who doubts this pressure should read the interview with Birger

Sørensen in Norway's Minerva magazine in which Sørensen discusses the "reluctance" of journals to publish his assessment that the existence of a virus that is "exceptionally well adjusted to infect humans" is "suspicious" and "cannot have evolved naturally". The source of this reluctance, says Sørensen, is not rationality or scientific evidence. It results from conflicts of interest. This mirrors our experience. To find genuinely critical analysis of COVID-19 origin theories one has to go to Twitter, blog posts, and preprint servers. The malaise runs deep when even scientists start to complain that they don't trust science.

We nevertheless hope that journalists will investigate some of the conflicts of interest that are keeping scientists and institutions from properly investigating the lab escape hypothesis.

References

Anand, P., Puranik, A., Aravamudan, M., Venkatakrishnan, A. J., & Soundararajan, V. (2020). SARS-CoV-2 strategically mimics proteolytic activation of human ENaC. *Elife*, *9*, e58603.

Andersen, K. G., Rambaut, A., Lipkin, W. I., Holmes, E. C., & Garry, R. F. (2020). The proximal origin of SARS-CoV-2. *Nature medicine*, *26*(4), 450-452.

Banner, L. R., & Mc Lai, M. (1991). Random nature of coronavirus RNA recombination in the absence of selection pressure. *Virology*, *185*(1), 441-445.

Baric, R. S., Yount, B., Hensley, L., Peel, S. A., & Chen, W. A. N. (1997). Episodic evolution mediates interspecies transfer of a murine coronavirus. *Journal of virology*, *71*(3), 1946-1955.

Becker, Y. (2000). Evolution of viruses by acquisition of cellular RNA or DNA nucleotide sequences and genes: an introduction. *Virus Genes*, *21*(1-2), 7-12.

Bengston, D. (2020). All journal articles evaluating the origin or epidemiology of SARS-CoV-2 that utilize the RaTG13 bat strain genomics are potentially flawed and should be retracted. *OSF Preprint*: https://osf.io/wy89d

Borja, M., Rubio, T., Scholthof, H. B., & Jackson, A. O. (1999). Restoration of wild-type virus by double recombination of tombusvirus mutants with a host transgene. *Molecular Plant-Microbe Interactions*, *12*(2), 153-162.

Chan, J. F. W., Kok, K. H., Zhu, Z., Chu, H., To, K. K. W., Yuan, S., & Yuen, K. Y. (2020). Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerging microbes & infections*, *9*(1), 221-236.

Chaw, S. M., Tai, J. H., Chen, S. L., Hsieh, C. H., Chang, S. Y., Yeh, S. H., ... & Wang, H. Y. (2020). The origin and underlying driving forces of the SARS-CoV-2 outbreak. *Journal of biomedical science*, *27*(1), 1-12.

Chen, L., Liu, W., Zhang, Q., Xu, K., Ye, G., Wu, W., ... & Mei, Y. (2020). RNA based mNGS approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 Wuhan outbreak. *Emerging microbes & infections*, *9*(1), 313-319.

Coutard, B., Valle, C., de Lamballerie, X., Canard, B., Seidah, N. G., & Decroly, E. (2020). The spike glycoprotein of the new coronavirus 2019-nCoV contains a furin-like cleavage site absent in CoV of the same clade. *Antiviral research*, *176*, 104742.

Dudas, G., & Rambaut, A. (2016). MERS-CoV recombination: implications about the reservoir and potential for adaptation. *Virus evolution*, *2*(1).

Duggal, A., Pinto, R., Rubenfeld, G., & Fowler, R. A. (2016). Global variability in reported mortality for critical illness during the 2009-10 influenza A (H1N1)

pandemic: a systematic review and meta-regression to guide reporting of outcomes during disease outbreaks. *PloS one*, *11*(5), e0155044.

Forni, D., Cagliani, R., Clerici, M., & Sironi, M. (2017). Molecular evolution of human coronavirus genomes. *Trends in microbiology*, *25*(1), 35-48.

Furmanski, M. (2014). Laboratory Escapes and "Self-fulfilling prophecy" Epidemics. Report: *Center for Arms Control and Nonproliferation*. PDF available at: https://armscontrolcenter.org/wp-content/uploads/2016/02/Escaped-Viruses-final-2-17-14-copy.pdf

Ge, X. Y., Li, J. L., Yang, X. L., Chmura, A. A., Zhu, G., Epstein, J. H., ... & Zhang, Y. J. (2013). Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature*, *503*(7477), 535-538.

Ge, X. Y., Wang, N., Zhang, W., Hu, B., Li, B., Zhang, Y. Z., ... & Wang, B. (2016). Coexistence of multiple coronaviruses in several bat colonies in an abandoned mineshaft. *Virologica Sinica*, *31*(1), 31-40.

Gibbs, A. J., Armstrong, J. S., & Downie, J. C. (2009). From where did the 2009'swine-origin'influenza A virus (H1N1) emerge?. *Virology journal*, *6*(1), 207.

Gorbalenya, A. E. (1992). Host-related sequences in RNA viral genomes. In *Seminars in Virology* (Vol. 3, pp. 359-359). HARCOURT BRACE JOVANOVICH.

Greene, A. E., & Allison, R. F. (1994). Recombination between viral RNA and transgenic plant transcripts. *Science*, *263*(5152), 1423-1425.

Greene, A. E., & Allison, R. F. (1996). Deletions in the 3′ untranslated region of cowpea chlorotic mottle virus transgene reduce recovery of recombinant viruses in transgenic plants. *Virology*, *225*(1), 231-234.

Hasleton, P. S. (1972). The internal surface area of the adult human lung. *Journal of anatomy*, *112*(Pt 3), 391.

Herfst, S., Schrauwen, E. J., Linster, M., Chutinimitkul, S., de Wit, E., Munster, V. J., ... & Rimmelzwaan, G. F. (2012). Airborne transmission of influenza A/H5N1 virus between ferrets. *science*, *336*(6088), 1534-1541.

Hoffmann, M., Kleine-Weber, H., & Pöhlmann, S. (2020). A multibasic cleavage site in the spike protein of SARS-CoV-2 is essential for infection of human lung cells. *Molecular Cell*.

Hu, B., Zeng, L. P., Yang, X. L., Ge, X. Y., Zhang, W., Li, B., ... & Luo, D. S. (2017). Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. *PLoS pathogens*, *13*(11), e1006698.

Huang, Canping (2016) Novel Virus Discovery in Bat and the Exploration of Receptor of Bat Coronavirus HKU9. PhD thesis (Original in Chinese). National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, June 2016. Accessed on July 15, 2020: https://eng.oversea.cnki.net/kcms/detail/detail.aspx?dbcode=CDFD&QueryID=4&CurRec=1&dbname=CDFDLAST2018&filename=1017118517.nh

Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... & Cheng, Z. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*, *395*(10223), 497-506.

Korber, B., Fischer, W., Gnanakaran, S. G., Yoon, H., Theiler, J., Abfalterer, W., ... & Partridge, D. G. (2020). Spike mutation pipeline reveals the emergence of a more transmissible form of SARS-CoV-2. *bioRxiv*.

Lamers, M. M., Beumer, J., van der Vaart, J., Knoops, K., Puschhof, J., Breugem, T. I., ... & van Donselaar, E. (2020). SARS-CoV-2 productively infects human gut enterocytes. *Science*.

Latham, J. R., & Wilson, A. K. (2008). Transcomplementation and synergism in plants: implications for viral transgenes?. *Molecular Plant Pathology*, *9*(1), 85-103.

Latinne, A., Hu, B., Olival, K. J., Zhu, G., Zhang, L., Li, H., ... & Li, B. (2020). Origin and cross-species transmission of bat coronaviruses in China. *bioRxiv*.

Lee, J., Hughes, T., Lee, M. H., Field, H., Rovie-Ryan, J. J., Sitam, F. T., ... & Lasimbang, H. (2020). No evidence of coronaviruses or other potentially zoonotic viruses in Sunda pangolins (Manis javanica) entering the wildlife trade via Malaysia. *bioRxiv*.

Letko, M., Marzi, A., & Munster, V. (2020). Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. *Nature microbiology*, *5*(4), 562-569.

Li, W., Shi, Z., Yu, M., Ren, W., Smith, C., Epstein, J. H., ... & Zhang, J. (2005). Bats are natural reservoirs of SARS-like coronaviruses. *Science*, *310*(5748), 676-679.

Lipsitch, M. (2018). Why Do Exceptionally Dangerous Gain-of-Function Experiments in Influenza?. In *Influenza Virus* (pp. 589-608). Humana Press, New York, NY.

Lipsitch, M., & Galvani, A. P. (2014). Ethical alternatives to experiments with novel potential pandemic pathogens. *PLoS Med*, *11*(5), e1001646.

Lommel, A., & Xiong, Z. (1991). Reconstitution of a functional red clover necrotic mosaic virus by recombinational rescue of the cell-to-cell movement

gene expressed in a transgenic plant. *Journal of Cellular Biochemistry A*, *15*, 151.

Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., ... & Bi, Y. (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The Lancet*, *395*(10224), 565-574.

Makino, S. H. I. N. J. I., Keck, J. G., Stohlman, S. A., & Lai, M. M. (1986). High-frequency RNA recombination of murine coronaviruses. *Journal of Virology*, *57*(3), 729-737.

McKinsey, D. S., & McKinsey, J. P. (2011, December). Pulmonary histoplasmosis. In *Seminars in respiratory and critical care medicine* (Vol. 32, No. 06, pp. 735-744). © Thieme Medical Publishers.

Menachery, V. D., Yount, B. L., Debbink, K., Agnihothram, S., Gralinski, L. E., Plante, J. A., ... & Randell, S. H. (2015). A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence. *Nature medicine*, *21*(12), 1508-1513.

Pan, B., Chen, M., Pan, W., & Liao, W. (2013). Histoplasmosis: a new endemic fungal infection in China? Review and analysis of cases. *Mycoses*, *56*(3), 212-221.

Perlman, S., & Netland, J. (2009). Coronaviruses post-SARS: update on replication and pathogenesis. *Nature reviews microbiology*, *7*(6), 439-450.

Piplani, S., Singh, P. K., Winkler, D. A., & Petrovsky, N. (2020). In silico comparison of spike protein-ACE2 binding affinities across species; significance for the possible origin of the SARS-CoV-2 virus. *arXiv preprint arXiv:2005.06199*.

Rahalkar, M.C.; Bahulikar, R.A. Understanding the Origin of 'BatCoVRaTG13', a

Virus Closest to SARS-CoV-2. *Preprints* **2020**, 2020050322 https://www.preprints.org/manuscript/202005.0322/v2

Segreto, R., & Deigin, Y. Is considering a genetic-manipulation origin for SARS-CoV-2 a conspiracy theory that must be censored?. https://www.researchgate.net/profile/Rossana_Segreto/publication/340924249_Is_considering_a_genetic-manipulation_origin_for_SARS-CoV-2_a_conspiracy_theory_that_must_be_censored/links/5ed7c17992851c9c5e74f7dc/Is-considering-a-genetic-manipulation-origin-f

Shang, J., Wan, Y., Luo, C., Ye, G., Geng, Q., Auerbach, A., & Li, F. (2020). Cell entry mechanisms of SARS-CoV-2. *Proceedings of the National Academy of Sciences*, *117*(21), 11727-11734.

Shang, J., Ye, G., Shi, K., Wan, Y., Luo, C., Aihara, H., ... & Li, F. (2020). Structural basis of receptor recognition by SARS-CoV-2. *Nature*, *581*(7807), 221-224.

Simonsen, L., Spreeuwenberg, P., Lustig, R., Taylor, R. J., Fleming, D. M., Kroneman, M., ... & Paget, W. J. (2013). Global mortality estimates for the 2009 Influenza Pandemic from the GLaMOR project: a modeling study. *PLoS Med*, *10*(11), e1001558.

Starr, T. N., Greaney, A. J., Hilton, S. K., Crawford, K. H., Navarro, M. J., Bowen, J. E., ... & Bloom, J. D. (2020). Deep mutational scanning of SARS-CoV-2 receptor binding domain reveals constraints on folding and ACE2 binding. *BioRxiv*.

Tay, M. Z., Poh, C. M., Rénia, L., MacAry, P. A., & Ng, L. F. (2020). The trinity of COVID-19: immunity, inflammation and intervention. *Nature Reviews Immunology*, 1-12.

van Dorp, L., Richard, D., Tan, C. C., Shaw, L. P., Acman, M., & Balloux, F. (2020). No evidence for increased transmissibility from recurrent mutations in SARS-CoV-2. *bioRxiv*. doi: https://doi.org/10.1101/2020.05.21.108506

https://www.biorxiv.org/content/10.1101/2020.05.21.108506v1.abstract

Wadman, M., Couzin-Frankel, J., Kaiser, J., & Matacic, C. (2020). A rampage through the body. Science, *368*(6489), 356-360.

Walls, A. C., Park, Y. J., Tortorici, M. A., Wall, A., McGuire, A. T., & Veesler, D. (2020). Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. *Cell*, *180*, 281-292.

Wang, N., Luo, C., Liu, H., Yang, X., Hu, B., Zhang, W., ... & Peng, C. (2019). Characterization of a new member of alphacoronavirus with unique genomic features in rhinolophus bats. *Viruses*, *11*(4), 379.

Weiss, S., Yitzhaki, S., & Shapira, S. C. (2015). Lessons to be Learned from Recent Biosafety Incidents in the United States. *The Israel Medical Association Journal: IMAJ*, *17*(5), 269-273.

Wrapp, D., Wang, N., Corbett, K. S., Goldsmith, J. A., Hsieh, C. L., Abiona, O., ... & McLellan, J. S. (2020). Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science*, *367*(6483), 1260-1263.

Wu, Z., Yang, L., Yang, F., Ren, X., Jiang, J., Dong, J., ... & Jin, Q. (2014). Novel henipa-like virus, Mojiang paramyxovirus, in rats, China, 2012. *Emerging infectious diseases*, *20*(6), 1064.

Wu, F., Zhao, S., Yu, B., Chen, Y. M., Wang, W., Song, Z. G., ... & Yuan, M. L. (2020). A new coronavirus associated with human respiratory disease in China. *Nature*, *579*(7798), 265-269.

Xu, Li (2013) The analysis of 6 patients with severe pneumonia caused by unknown viruses. MSc thesis (Original in Chinese). Emergency Department and EICU, The 1st Affiliated Hospital of Kunming Medical University, Kunming. Accessed on July, 15, 2020: http://eng.oversea.cnki.net/Kcms/detail/detail.aspx?filename=1013327523.nh&dbcode=CMFD&dbname=CMF D2014

Zhan, S. H., Deverman, B. E., & Chan, Y. A. (2020). SARS-CoV-2 is well adapted for humans. What does this mean for re-emergence?. *bioRxiv*. doi: https://doi.org/10.1101/2020.05.01.073262

Zhang, L., Jackson, C. B., Mou, H., Ojha, A., Rangarajan, E. S., Izard, T., ... & Choe, H. (2020). The D614G mutation in the SARS-CoV-2 spike protein reduces S1 shedding and increases infectivity. *bioRxiv*

Zhang, Y. Z., & Holmes, E. C. (2020). A genomic perspective on the origin and emergence of SARS-CoV-2. *Cell*.

Zhou, H., Chen, X., Hu, T., Li, J., Song, H., Liu, Y., ... & Shi, W. (2020). A novel bat coronavirus reveals natural insertions at the S1/S2 cleavage site of the Spike protein and a possible recombinant origin of HCoV-19. *bioRxiv*.

Zhou, P., Yang, X. L., Wang, X. G., Hu, B., Zhang, L., Zhang, W., ... & Chen, H. D. (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. *nature*, *579*(7798), 270-273.

Zhou, M., Zhang, X., & Qu, J. (2020). Coronavirus disease 2019 (COVID-19): a clinical update. *Frontiers of medicine*, 1-10.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., ... & Niu, P. (2020). A novel coronavirus from patients with pneumonia in China, 2019. *New England Journal of Medicine*.

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Master's Thesis

"The Analysis of Six Patients With Severe Pneumonia Caused By Unknown Viruses"

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硕 士 学 位 论 文

未知病毒引起重症肺炎6例分析

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二〇一三年五月

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Kun Ming Medical University

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英文缩略词表

英文缩略语	英文全称	中文全称
T	temperature	体温
PR	pulse rate	脉率
RR	respiration rate	呼吸频率
BP	blood pressure	血压
HR	heart rate	心率
CT	computed tomography	计算机断层扫描
CRP	C reactive protein	C 反应蛋白
PCT	procalcitonin	降钙素原
SAA	serum amyloid A protein	血清淀粉样蛋白 A
DD	D-dimer	D-二聚体
FDP	fibrin degradation product	纤维蛋白降解产物
$PaCO_2$	partial pressure of carbon dioxide	二氧化碳分压
PaO_2	partial pressure of oxygen	血氧分压
PH	hydrogen ion concentration	氢离子浓度指数
PF	oxygenation (PaO_2/FIO_2) index	氧合指数
RLS	reaction leuel scale	机体反应水平分级
BNP	brain natriuretic peptide	B 型尿钠肽
PCR	polymerase chain reaction	聚合酶链式反应
HIV	human immunodeficiency virus	人类免疫缺陷病毒
INR	international normalized ratio	国际标准化比值
ECG	electrocardiogram	心电图
DNA	deoxyribonucleic acid	脱氧核糖核酸

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RNA	ribonucleic acid	核糖核酸
ICTV	international committeeon taxonomy of viruses	国际病毒分类委员会
ARDS	acute respiratory distress syndrome	急性呼吸窘迫综合征
SARS	severe acute respiratory syndrome	严重急性呼吸综合征
SARS-CoV	SARS coronavirus	SARS 冠状病毒
SARS-like-CoV	SARS like coronavirus	SARS 样冠状病毒
ICU	intensive care unit	重症加强护理病房

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未知病毒引起重症肺炎 6 例分析

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摘要

2012 年 4 月、5 月，我院先后收住 6 例未知病毒引起相关重症肺炎患者。此 6 位患者均为同一矿洞工人，工作环境中接触大量蝙蝠及蝙蝠粪便。最终结局 3 位患者死亡，3 位患者存活。据中国科学院昆明动物研究所鉴定，此 6 位患者工作矿洞内蝙蝠正为中华菊头蝠，然而我国科学家在寻找 SARS 病原的过程中，在中华菊头蝠体内提取出了 SARS 样冠状病毒（SARS-like-CoV）。本文针对 6 例患者所感染未知病毒相关重症肺炎的诊治过程及可能引起的病因、病原学进行推断与分析。

关键词： 重症肺炎、蝙蝠、SARS 样冠状病毒

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The analysis of 6 patients with severe pneumonia caused by unknown viruses

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Abstract

There were 6 patients with severe pneumonia caused by unknown viruses sent to Dep. Emergency, the first affiliated hospital of Kunming medical university in April,May,2012.They were all workers at the same mine where had a lot of bats and bats' feces. After the treatment, 3 patients died and 3 patients survived.

According to the appraisal of the Kunming institute of zoology, Chinese academy of sciences, the type of the bat in mine where 6 patients worked is Rhinolophus sinicus, from which was extracted SARS-like-CoV when Scientists in China were in the process of looking for SARS pathogen. The article aims at making an inference and analysis on the diagnosis and treatment process and the may causes, etiology of 6 patients with severe pneumonia related to infection by the unknown viruses.

Keywords: severe pneumonia、bats、SARS-like-CoV

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Case 1

Patient Zhou, male, age 63, was admitted to the hospital on April 26, 2012. He had signs of fever, coughing, difficulty in breathing, chest pain, and hiccups for more than ten days. 24 days prior to the hospitalization, he was working in the mining well for half of a month. He worked 7 hours a day. After exposing to the mining well where there were many bats and bats' feces, he started to show signs of coughing and fever and had a 38 Celsius body temperature. He immediately went to the local hospital. His fever went on and off in the next five consecutive days. The actual treatment remained unknown. The highest body temperature was 40 Celsius and the lower is 37 Celsius. He also experienced headache, dizziness, ear congestion and dry cough. There was no pattern of his illness in daytime or night time, along with chest pain. Difficulty in breathing was getting worse. Occasionally, having hiccups. No sign of nausea, vomiting, or diarrhea. To pursue more treatment, the patient was admitted to my department. Since the onset of the disease, the patient had felt lethargic. He has insomnia and loss of appetite, but regular bowel movement and urination. Self-reported that he did not have a history of high blood pressure, diabetes and heart disease or other chronic diseases, nor did he have hepatitis, typhoid or any other contagious disease. He did not have surgical operation, trauma, and blood transfusion in the past. He was not allergic to any medication or food. His vaccination record remained unknown. Physical checkup: body temperature is 37.8 Celsius, pulse rate: 74 times/minute, respiratory rate: 20 times/ minute, blood pressure: 110/63 mmhg. The patient stays alert and could answer all the questions. No sign of malnutrition or obesity. He was sent to the room by stretcher. Skin and mucous membranes remained normal, and so were the pupils. They were 3mm in diameter. The pupils remained sensitive to light. The chest and respiratory movements were symmetrical. The breathing sounds were rough. Dry crackles were heard on both bases of the lung. His heart rate is 74 beats/minute, regular heart rate and no heart murmur from any of the heart valves. Softness of the abdomen, no pain when pressured, no rebound tenderness, or guarding. Normal bowel sound: 5 times/minute. No inflammation at the lower part of the legs. Regular body reflex. No pathological reflexes. The blood report from 04/25/2012: WBC12.10X10^9/L, N%89.3, Hemoglobin: 178g/L; Comprehensive Metabolic Panel was CRP 20.3 mg/L, blood ammonia: 43 umol/L; Normal result on the coagulation report. As the CT scan showed, there was extensive and patchy consolidated exudate bilaterally, elevated bronchovascular shadows and lung markings, some nodules in different sizes, parts were calcified. Mediastinal lymph node enlargement, partially calcified.

Initial Diagnosis: 1. Fever, coughing, dyspnea, hiccup 2. Hyponatremia; 3. Malfunctioning in liver and bladder

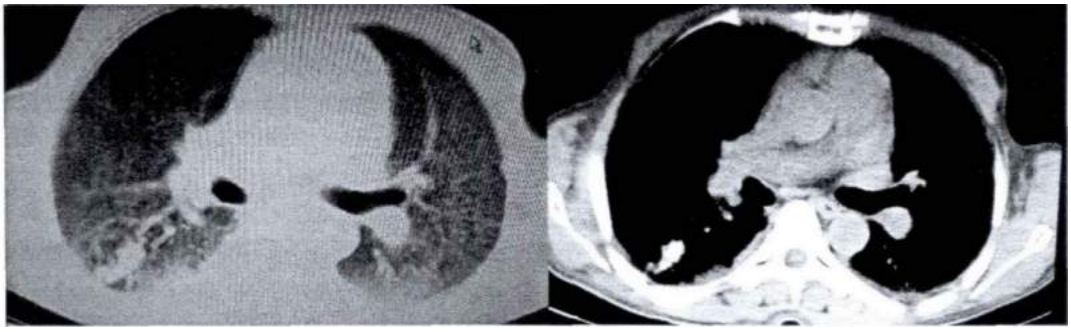
Method

The examination after hospitalization:

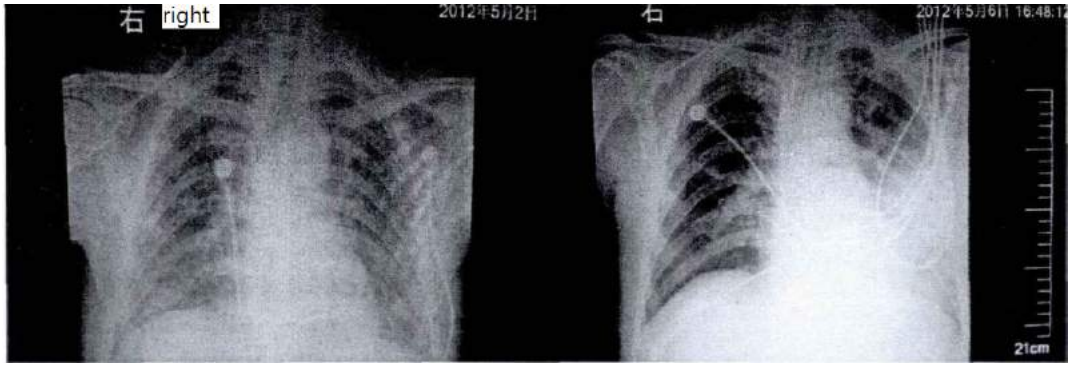
2012/4/25 Computed tomography report: extensive and patchy consolidated exudate over bilateral lung, increased Broncho vascular shadows and lung markings, some nodules in different sizes, parts were calcified. Mediastinal lymph node enlargement, partial were calcified.

2012/4/30 CT report: 1. No noticeable changes in the lung, little pleural effusion in both lungs..

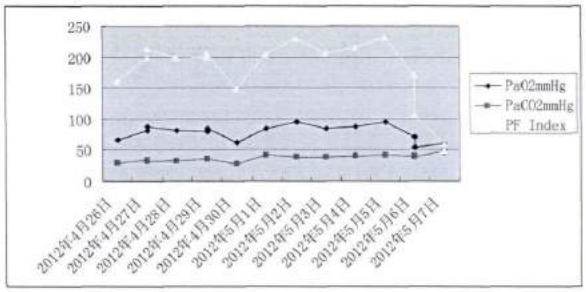
Pleural thickening posteriorly, and the rest was the same as the previous report. 2. As the scan showed, there was little ascites (see below).

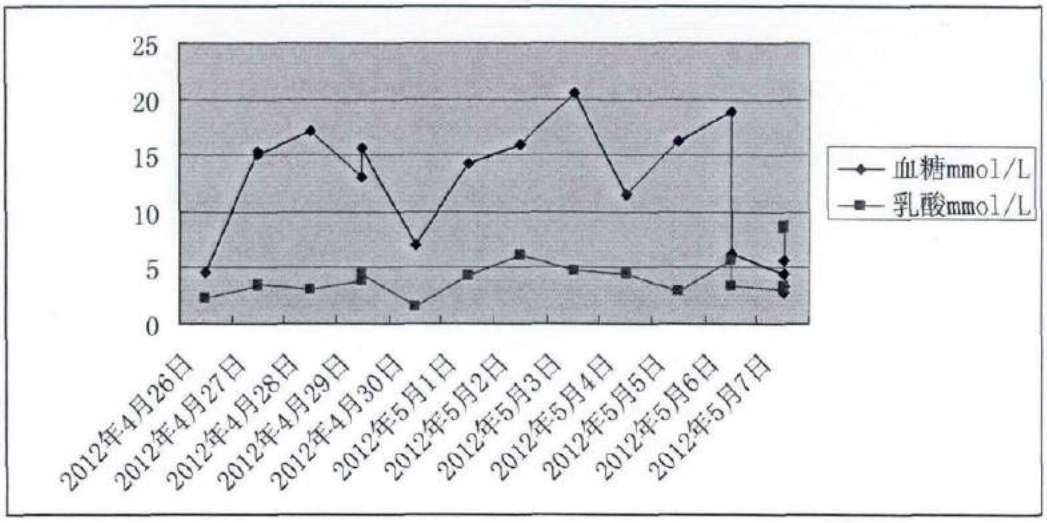


2012/5/2 bedside chest film: 1. Bilateral Lung markings worsening and getting blurry, and there were shadows of the clot. Nodular shadow was noted in 2nd intercostal space of right middle lobe, and a small opacity was over left hilar region. Requested a follow up examination after the clinical anti-inflammation treatment. 2. The outline of the heart is not too big 3. The diaphragm remains normal (see the left picture below).



2012/5/6 bedside chest film: 1. Bilateral Lung marking augmentation and getting blurry, and there were shadows of the clots. Increased laminar density in the middle and lower field of the left lung, the hilum of both lungs are blurred. Requested a follow up examination after the clinical anti-inflammation treatment. 2. Aorta is circuitous and the outline of the heart is normal. 3. Fluid in the left side of the pleural cavity and need to be evacuated. Please cooperate with the clinic (see the right picture on top). 2012/4/26 - 2012/5/7: Analysis on the arterial blood gas (see below):



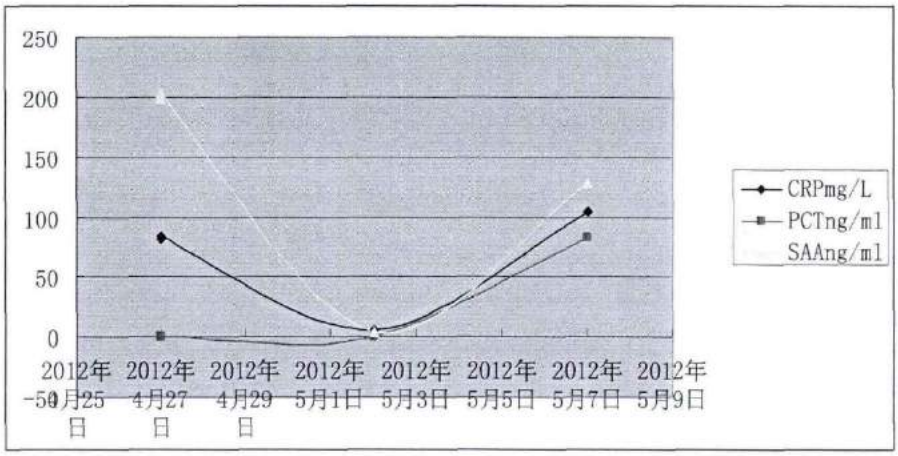


2012/4/27 tumor protein chip shows ferritin is 484.86 (Normal male < 322 microgram/ L), Human chorionic gonadotropin is 0.65 (normal< 3.0 microgram/ L), prostate Specific Antigen is 0.02 (normal< 0.1 microgram/L) carbohydrate antigen 125: 42.22 (normal < 35.0KU/L).

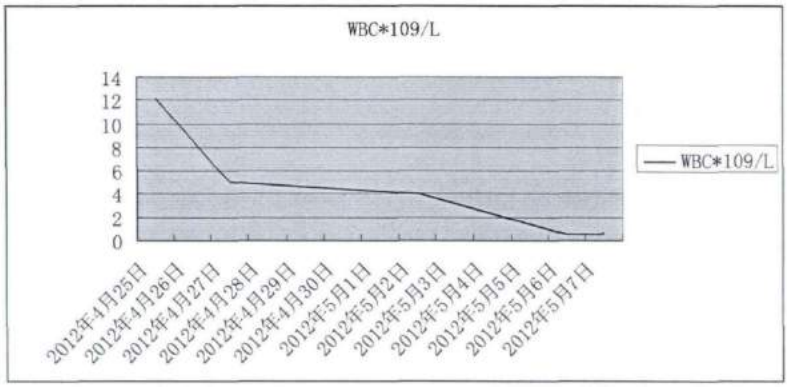
On 2012/4/27, the Widal test and WFR test both came back negative. Results for Herpes simplex virus, EB virus and CMV are all negative. Urine culture is negative and so is Ghb. The stool test is also normal. Autoantibody and anti-nuclear antibodies are both negative. 2012/4/24 report: compliment C3C4 has decreased; Glucose in Urine 4+, Ketone is negative. Thyroid test positive.

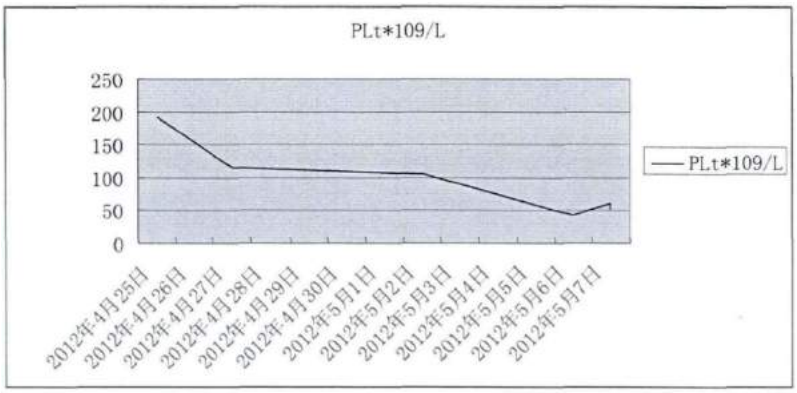
2012/4/27 - 2012/5/7: D-dimer reports 7.2 ug/ml (Apr, 27), D-dimer 3.6 ug/ml (May, 2), D-dimer 7.0 ug/ml (May, 6), D-dimer 5.0 ug/ml (May, 7).

2012/4/27 -2012/5/7 infected cell-specific protein (see below):



2012/4/25 - 2012/5/7 white blood cell and blood platelet (see below):





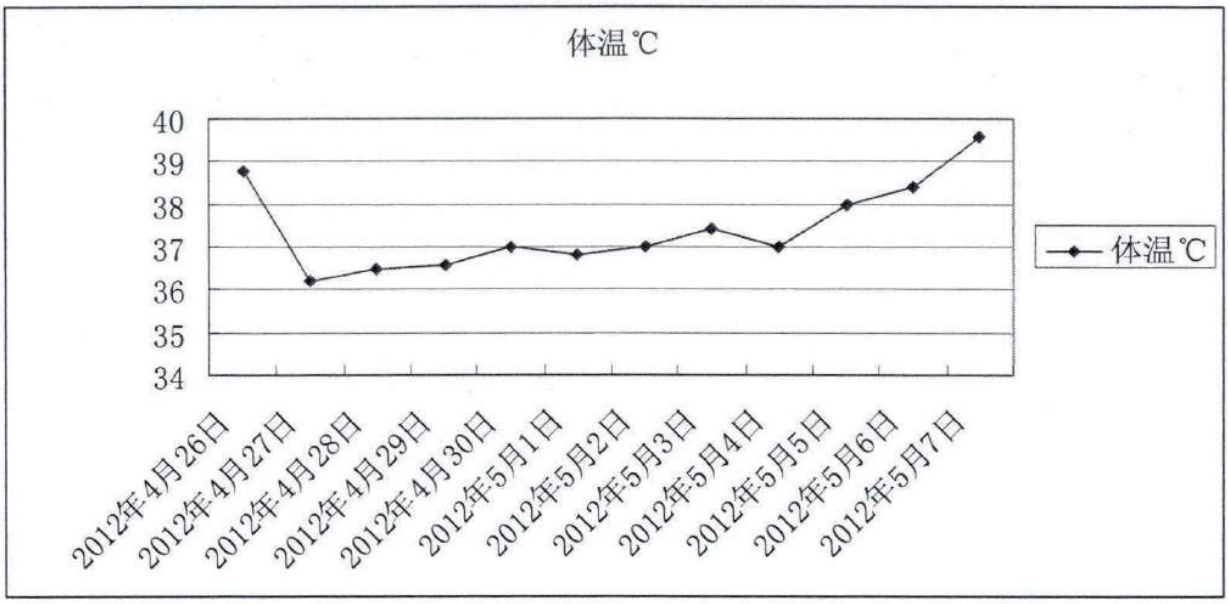
T, B, NK lymphocyte percentage and count (see below)

日期 Date	CD3 阳性 T 淋巴细胞绝对值 Positive Aboslute Value of Lymphocyte	T 抑制细胞 Suppressor Cell CD3+CD8+双阳细胞绝对值 double positve cell absoulute value	T 辅助细胞 supporting cell CD3+CD4+绝对值 abosolute Value	CD3CD4 CD8 均为阳性细胞绝对值 Positvie cell abosolute value	NK 细胞（CD16+CD56+双阳细胞） double positive cell	B 淋巴细胞（CD19+CD45+） Lymphocyte
4-27	384↓	262	109↓↓	5↓	215	56↓↓
5-7	63↓↓	27↓↓	32↓↓	0↓↓	13↓↓	106↓↓

2012/4/27 sputum culture and blood culture were both negative (three times).
2012/5/7 blood culture implies positive for Acinetobacter baumannii and negative for candidiasis
2012/5/7 sputum culture Acinetobacter baumannii, pan resistant
2012/5/6 ultrasound reports severe ascites

2012/5/7 Ascites. Result of tumor cell testing is negative. Gram positive in cultivation ascites regular test is negative. The Rivalta test is also negative.

Body temperature chart (see below):



Prescription after admission:

2012/4/26 – 2012/5/2 (J) Methylprednisolone 80mg, ivgtt, Q 12h.

21012/5/2 – 2012/5/7 (J) Methylprednisolone 40mg, ivgtt, Q 12h.

2012/5/7 – death (J) Methylprednisolone 80mg, ivgtt, Q 12h.

2012/4/26 – 2012/5/2 Meropenem 0.5gx2 shots, ivgtt, Q8h.

2012/5/7 – death Meropenem 0.5gx2 shots, ivgtt, Q8h.

2012/5/7 – death Vancomycin 0.5gx2 shots, ivgtt, Q12h.

2012/4/26 – death L - Voriconazole 0.1gx 2 shots (double the dosage on the first day), ivgtt, Q12h.

2012/4/26 – death Acyclovir 0.25g*2, ivgtt, Q8h.

Discussion

The patient worked from the mining site since 2012/4/2 for up to 14 days.

Patient admitted to the hospital: 2012/4/26. Patient discharged: 2012/5/7. Total days: 12 days.

Discharged Diagnosis: 1. Severe lung infection 2. Sepsis 3. Septic shock and infection in abdominal cavity 4. Asystole and stop breathing

Discharge reason: death

According to CT and Chest radiograph, the illness was progressively developed.

As the analysis on the arterial blood gas shows, during hospitalization, the patience had Type I respiratory failure. Oxygenation index was poor. According to the “ARDS Berlin Criteria” in 2012, for sure it was ARDS. Consequentially, one of the causes of death could be respiratory failure.

According to several researches from either abroad or domestically, glucose variability is associated with rate of prognosis or death. During the hospitalization, the patient was given intensive insulin treatment by our department. We tried to keep the blood sugar between 6-10 mmol/L. However, the patient’s glucose varies, poor prognosis.

The result for tumor protein chip came back positive, which means the patient had tumor related disease. As a result, the systems of the whole body was impacted.

After the patient was admitted to the hospital, WBC and PLt were constantly decreasing. Indicated by other virus infection related researches, WBC, PLt, T, B, NK Lymphocyte percentage and count of the patients are also decreasing. It shows that the immune system of the patient was impaired, had poor resistant to the disease and could easily be infected by hospital-acquired infection.

The day the patient died, the blood and mucus culture showed Acinetobacter baumannii, severe ascites. There was Gram-positive bacteria in ascites culture. On the same day, the PCT report was 83.30ng/ml. As a result, one of the causes of death is septic shock. (severe lung infection and abdominal cavity infection).

After admitted, the patient’s D-dimer was 7.2 ug/ml (Apr, 27), 3.6 ug/ml (May, 2), 7.0 ug/ml (May, 6) and 5.0 ug/ml (May, 7). The patient was bed ridden after admitted to the hospital and also had tumor. The oxygen level in the blood was significant low two days prior to his death. There was a possibility of pulmonary thromboembolism. However, the patient was severely ill, it was not recommended to have an intensified chest CT checkup. Therefore, acute pulmonary infection could be one of the causes of death. The family of the patient refused the autopsy procedure.

After the suspension of Meropenem on May 2, 2012, the patient was no longer treated with any antibiotics. His temperature went back up right after. Therefore, antibiotics play an important role in the treatment.

Cause of death analysis: the patient was the oldest out of the six patients and had some tumor related disease. His immune system was weak so had a poor body resistant to the disease. The disease was acute and fierce.

Case Two

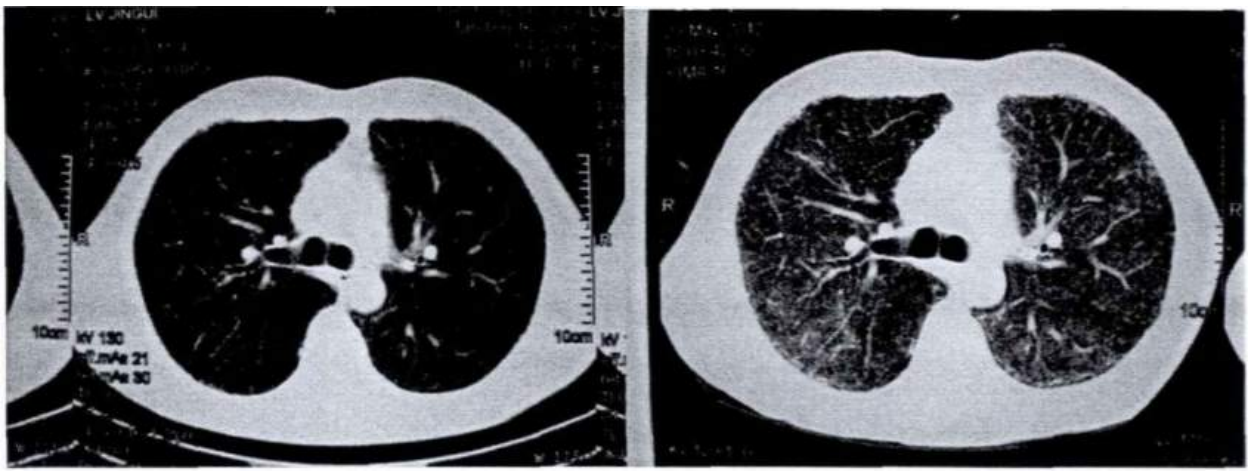
Patient Lu, Male, 42 years old, was admitted to the hospital on April 25, 2012. He had fever and been coughing for half of a month and for the past three days had difficulties in breathing. He worked in the mining hole before and was exposed to large amount of feces of bats. Half of month ago, he started to have fever. His body temperature was 38.5 Celsius at first. Occasionally, when he coughed, there was rusty colored mucus with blood clots. Felt bloated in the stomach, loss of appetite and hiccup. He initially went to the small clinic for transfusion but it was not helpful. Then, he was transferred to Yu Xi People's Hospital for treatment. During hospitalization, his body temperature was 40 Celsius and the fever did not follow any pattern. No sign of chills before the fever. Still coughed with rusty-colored mucus and blood clots. Difficulty in breathing for three days, especially after moving around. Chest tightness but no chest pain. No problem lying down. No sign of paroxysmal dyspnea at night. No abdominal pain. No visible hematuria. No history of high blood pressure, diabetes, coronary heart disease or stroke. He was born in Zhao Tong, Yun Nan and had been to Mo Jiang. He worked in the mining field prior to the illness and was exposed to large amount of bats' feces. Five of his colleagues had similar illness. He denied hepatitis, typhoid, tuberculosis or any other infectious disease. No history of blood transmission or allergy reaction. The vaccination report remained unknown. On examination: 36.6 Celsius, Pulse 110 times/ minute, Respiration rate 32 times/ minute, blood pressure 98/55mmHg, in poor condition. He was sent into the ward on a stretcher. Reaction level scale was rated 1. No deformation on the head and features. The pupils were big and round with 3 mm diameter. He was sensitive to the lights. Soft neck, no rigidity. Airway was in the center. The chest looked symmetric from the outside. Rough breath sounds bilaterally, and moist crackles were heard on both bases of the lung. The breathing sounds rough. Moist rales from the bottom of the lungs. Heart was in normal size. Heart rate 110 times/ minute, regular rhythm, no murmur, rubs or gallops. Abdomen soft, non-tender. Normal bowel sounds: 3 times/minute. Did not notice any rashes or eschar. No inflammation on the legs. Muscle strength and tension remained normal. Additional checkup: According to the CT from Yu Xi People's hospital on April 25, 2012: severe pneumonia over bilateral lung. The bottom of the left lung had limited pulmonary emphysema and bullae in the right lung; HBsAg (+), HbeAb (+), HbcAb (+). Our blood gas analysis shows pH 7.431, PaO_2 66.2mmHg, Oxygenation Index 162, lactic acid 1.7 mmol/L, Potassium in the blood 4.04mmol/L, Sodium in the blood 134.7 mmol/L.

Initial diagnosis after admission: 1. Severe pneumonia 2. Type I respiratory failure 3. Sepsis 4. Hepatitis B

Method (Some of the information was missing)

After admission, the complete examination:

Chest CT on 2012/4/30: 1. Increased lung markings, blurry and noticed multiple nodular shadows. Bilateral lung patchy exudate. 2. Mediastinal lymph node enlargement, regular heart shadow. Did not notice any abnormal in the artery. (see the left picture below)



2015/5/29 CT reports: Compared to the scan on 2015/5/23 about the treatment on bilateral lungs, marked interstitial opacities and exudation in both lungs. No significant increase of fibrosis. Scant pericardial effusion as before, same as the old scan (right picture above).

2012/5/7 CT reports: 1. increased of lung marking and more opacities same as before. Spotted multiple shadows of nodules spread across. The exudation seemed to recover a bit. 2. Inflammation of the mediastinal lymph node is the same as before. So are the heart and artery.

2012/5/14 CT reports: 1. increased lung marking and more opacities same as before. Spotted multiple shadows of nodules spread across. The exudation seemed to be the same. 2. The mediastinal lymph node is the same as before. So are the heart and artery.

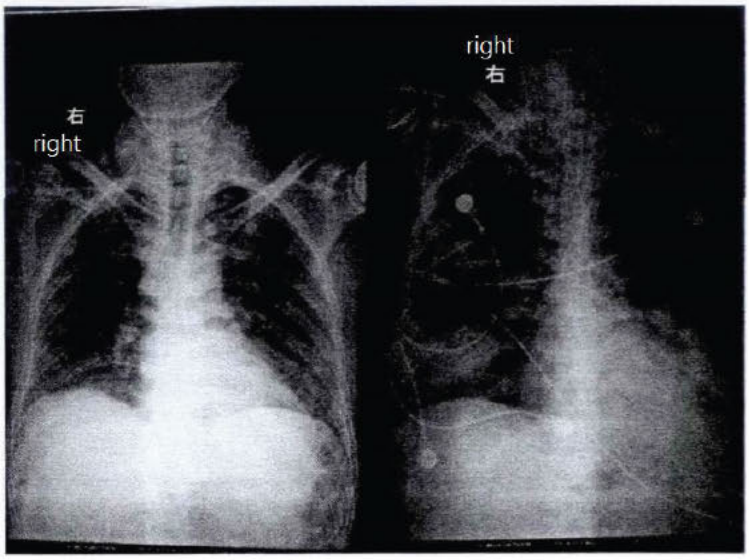
2012/5/18 CT reports: increased of lung marking and more opacities. Spotted multiple shadows of nodules in more density. The outline is blurry. Basically remain the same as before. Emphysema existed in lower left lobe. The structure of the hilar remain define and clear. The airway is clear. The mediastinal lymph node is the same as before. No sign of pleural effusions.

2012/5/23 CT reports: 1. marked interstitial opacities and exudation in both lungs. No significant increase of fibrosis 2. No cardiomegaly but the mediastinal lymph node was inflamed.

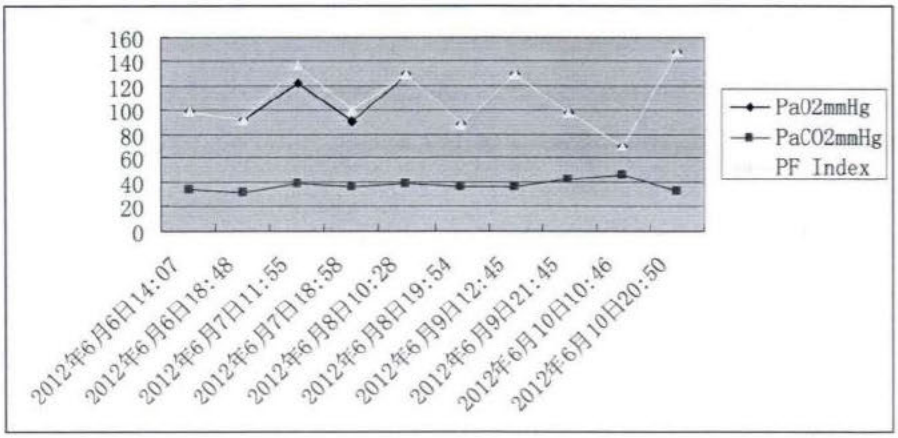
2012/6/2 bedside CT reports: 1. Noticed spread of flaky shadow and chestnut-shaped nodules in both lungs and it seemed progressed compared to before. The structure of the hilar appeared unclear. Need further confirmation. Please work with clinical for further diagnosis. 2. The outline of the heart is normal. 3. The diaphragm looked normal.

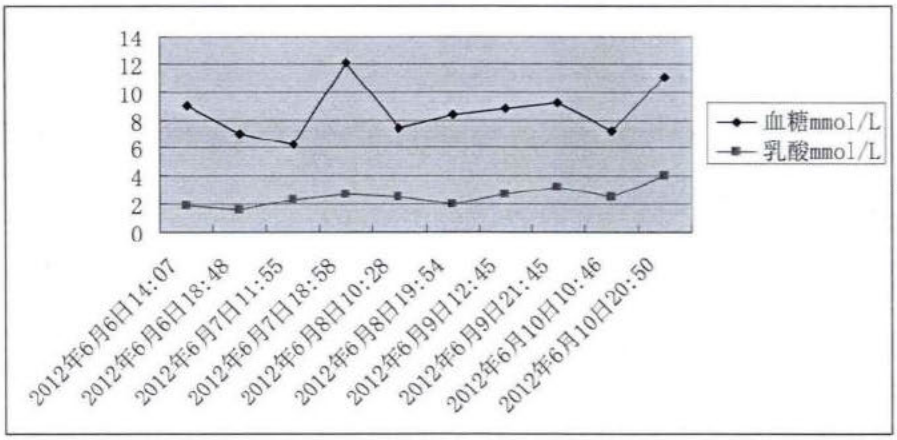
2012/6/5 bedside CT reports: 1. Noticed spread of flaky shadow and chestnut-shaped nodules in both lungs and it seemed progressed compared to before. 2. The outline of the heart looked poor. 3. The diaphragm looked normal. 4. Deep vein thrombosis at the right side of the first rib.

2012/5/16 – 2012/6/10 Chest film comparison (see below)



2012/6/6 – 2012/6/10 Analysis of the blood gas (see below)





Blood sugar
Lactic acid

Infection related protein (missing some data, did not make a table analysis):

2012/4/26 infection related protein report: C-Reactive protein 117.0 mg/L, SAA 398.00 ng/L.

2012/5/2 infection related protein report: C-Reaction protein 2.2 mg/L, PCT 0.04ng/ml, SAA 4.80ng/L.

2012/5/7 infection related protein report: C-Reaction protein 12.0 mg/L, PCT 0.04ng/ml, SAA 127.00 ng/L.

2012/5/18 infection related protein report: C-Reaction protein 66.3 mg/L, PCT 0.04ng/ml, SAA 230.00 ng/L.

2012/5/29 infection related protein report: C-Reaction protein 0.8 mg/L, PCT 0.04ng/ml, SAA 5.79 ng/L.

2012/5/30 infection related protein report: C-Reaction protein 23.7 mg/L, PCT 0.27ng/ml, SAA 190.00 ng/L.

2012/4/25 – 2012/5/2 No significant abnormality in the coagulation test (PT, APTT, TT, FIB).

2012/4/25 – 2012/5/6 Comprehensive Metabolic panel reports: hypoalbuminemia, others were normal

2012/5/2 blood test reports: FDP 6.5ug/ml, Antithrombin III 108.4%, D-dimer 4.4 ug/ml.

2012/5/18 blood test reports: FDP 5.3 ug/ml, Antithrombin III 146.5%, D-dimer 3.9 ug/ml.

2012/4/25 – 2012/5/2 no abnormally in the routine blood test.

2012/5/2 routine urine test is negative.

2012/4/25 troponin reports negative

2012/4/26 BNP 33.44 pg/ml.

2012/4/26 red blood cell ESR 25 mm

2012/4/26 IgM 2.98 (Normalcy: 0.4 – 2.3 g/L), Complimentary C 0.78 (Normalcy: 0.9 – 1.8 g/L)

2012/4/26 Result for Widal test and WFR are both negative.

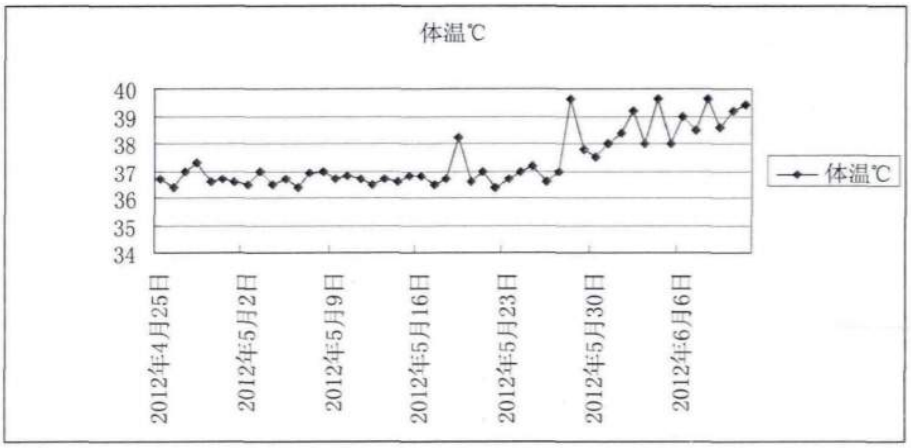
2012/4/26 Hepatitis study report: HBsAg quantity 157.5 ng/ml, HBeAb quantity 2.12 U/ml, HbcAb quantity 2.55 U/ml. HBsAg positive.

2012/4/26 PCR test: EBV positive 5200 (normalcy: 5000 measurement/ml).

2012/4/26 PCR test showed TB negative
2012/5/1 PCR rest showed HSV1 negative
T, B, NK cell percentage and count (see below):

日期 Date	CD3 阳性 T 淋巴细胞绝对值 Positive Aboslute Value of Lymphocyte	T 抑制细胞 Suppressor Cell CD3+CD8+双阳细胞绝对值 double positve cell absolute value	T 辅助细胞 supporting cell CD3+CD4+绝对值 absolute Value	CD3CD4 CD8 均为阳性细胞 Positvie cell 绝对值 absolute value	NK 细胞（CD16+CD56+ 双阳细胞） double positive cell	B 淋巴细胞（CD19+CD45+） Lymphocyt
4-26	361↓	166↓	[redacted]	[redacted]	128	[redacted]
5-8	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5-10	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5-14	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5-17	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
5-22	[redacted]	[redacted]	[redacted]	13	[redacted]	[redacted]
5-28	501	425	[redacted]	[redacted]	[redacted]	[redacted]
5-30	766	587	[redacted]	[redacted]	[redacted]	[redacted]
6-2	1011	711	[redacted]	[redacted]	[redacted]	[redacted]
6-4	324↓	243	[redacted]	[redacted]	[redacted]	[redacted]

Body Temperature (see below):



Prescription after being admitted to the hospital (some information is missing):

2012/4/25 – 2012/4/26 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h.

2012/5/2 – 2012/5/4 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h.

2012/4/25 – 2012/5/4 Ganciclovir injection 125mg x 2 shots, ivgtt, Q12h.

2012/4/26 – 2012/5/2 Meropenem 0.5g x 2 shots, ivgtt, Q8h.

2012/5/1 – 2012/5/2 L- Voriconazole 0.1g x 2 shots, ivgtt, Q12h.

Remote Meeting Minute 1

Meeting time: 2012/6/4

Meeting location: Number 1 hospital

Experts Attendee: Dr. Xie Can Mao , Chief Physician, Respiratory department of The First Affliated Hospital, Sun Yat-Sen University

After hearing the report of the medical history of the patient and other examination report, Dr. Xie diagnose: 1. Severe Pneumonia (possibly Fungus infection? Virus infection?); 2. Type I respiration failure 3. Sepsis 4. Hepatitis B.

The patient can complete the G test, and fiberoptic bronchoscopy examination. If the circumstances allow, we should also consider conducting biopsy of lung. However, the patient is on noninvasive ventilator, the biopsy is not appropriate. Treatment wise, Dr. Xie agrees with what we have done so far. He suggested that we should also prescribe 2 tablets of compound Sulfamethoxazole (oral), 3 times/ day. Fluconazole for the fungus and Thymosin for boosting up immune system.

Remote Meeting Minute 2

Meeting time: 2012/6/7

Meeting location: Number 1 hospital

Experts Attendee: Shi Jing, department of Occupation Toxicology, Shang Hai Pulmonary Hospital

After hearing the report of the medical history of the patient and other examination report, Dr. Shi suggests: 1. Have a consultation with the Toxicology department 2. Further treatment from the respiratory department 3. Do not take Pneumoconiosis into consideration. Dr. Shi also agrees with our treatment so far.

Discussion

The patient started working in the mining site on 2012/4/2 and last for 14 days.

The first day of hospitalization is 2012/4/25 and the day left is 2012/6/12, total of

48 days.

Discharge Diagnosis: 1. Asystole and stop breathing 2. Severe Pneumonia 3. Type I respiration failure 4.Sepsis 5.Hepatitis B

Discharge reason: death

According to CT and Chest radiograph, the illness was progressively developed.

As the analysis on the arterial blood gas shows, during hospitalization, the patient had Type I respiratory failure. Oxygenation index was poor. According to the “ARDS Berlin Criteria” in 2012, for sure it was ARDS. Consequentially, one of the causes of death could be respiratory failure.

During hospitalization, the T, B, NK Lymphocyte percentage and count of the patients were decreasing. It shows that the immune system of the patient was impaired, had poor resistant to the disease and could easily be infected by hospital-acquired infection.

After admitted to the hospital, suggested by the Hepatology, it could also be Hepatitis B.

(Some information of the patient is missing so we failed to do a thorough analysis)

Case Three

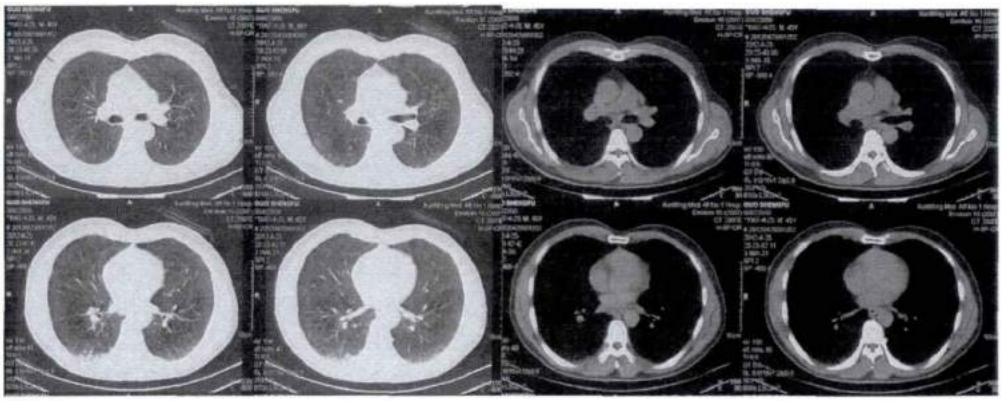
Patient, Mr. Guo, male, 45 years old, was admitted to the hospital. He had signs of coughing, productive cough, shortness of breath, and fever for two weeks. The patient went into a 150 meter deep cave 24 days ago. He continuously inhaled some unknown gas for 10 days. About two weeks ago, started having signs of coughing, tightness in chest, shortness of breath, fever, yellow and greenish mucus (about 2-3 times a day, about 5 ml each time). When he rests, he feels tightness in chest, shortness of breath and fever around 39 – 40 Celsius. Before the fever, there are no chills. Along with headache and soreness in limbs. After taking some antipyretics (not sure what kind), the body temp went back to normal. 10 days ago, the mucus turned white and with some blood string (light red, 2-3 times a day). Went to the local clinic for treatment and was prescribed antibiotics (not sure what kind). The coughing with blood stopped three days after but other symptoms remained the same. 2 days ago came to the emergency and was admitted by us. CT reports: lung marking increase, blurry, septal thickening. Multiple nodules and floccular exudate. Multiple inflamed lymph nodes in mediastinum. Was given Cefmenoxime 0.5g x 6, ivgtt, Qd and methylprednisolone 40mg, ivgtt, Qd for inflammation for two days. The patient was getting better and the body temperature was between 38 – 39 Celsius. For further treatment, the patient was admitted to our department for respiratory impairment. During the whole process, the patient did not have any chest pain, faint, coughing pink bubbly mucus or sign of paroxysmal dyspnea at night. The patient eat and sleep well. Normal bowel movement and urination. He lost 10 kilograms. Had a bowel obstruction surgery in 1985 (no further detail). No history of allergy to any medication. Physical examination: Body temperature 36.2 Celsius, pulse 96 times/minute, Respiration rate 20 times/minute, BP 120/85 mmHg, stay sharp, soft neck, no resistant, the lips and tip of the fingers appear cyanotic, the outline of the chest looks normal, no enlargement in between the ribs, no tenderness on the chest when pressured; oxygenation is 83% without inhaling, resonant to percussion over bilateral lung, rough breathing sounds, slightly moist crackles in lower right lung. Did not hear any dry crackle from either lung. No lump on the heart area, no apical impulse, normal cardiac boundary, heart rate 96 times/ minute, no murmurs or gallop. Abdomen soft, non-tender. No inflammation on the legs. Additional checkup: 2012/4/25 CT report: lung markings increased, blurry, septal thickening. Multiple nodules and floccular exudate. Multiple inflamed lymph nodes in mediastinum. 2012/4/25 our regular blood test report: WBC13.01 x 10^9/L, Percentage of Neutrophil is 70.3 %, ANC is 9.15 x 10^9/L, RBC 5.87 x 10^{12}/L, Hemoglobin 175 g/L, PLT 352 x 109/L. CRP 60mg/L.

Initial diagnosis after admission: 1. inhaling respiratory impairment (restrictive lung disease); 2. Severe Pneumonia

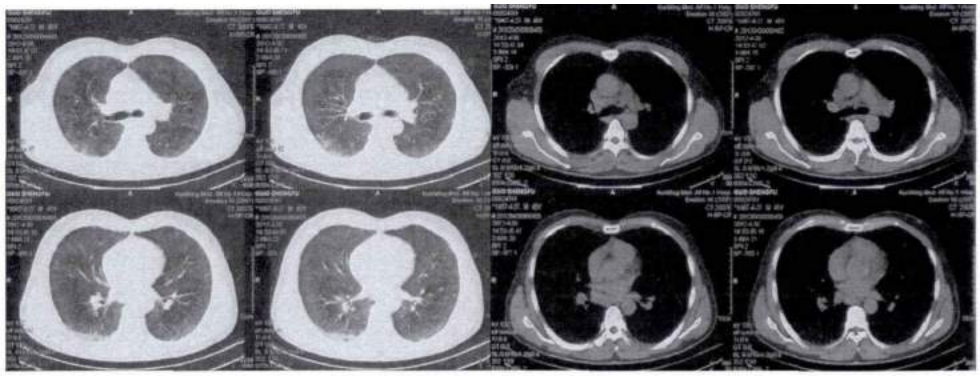
Method

After admission, more complete examination:

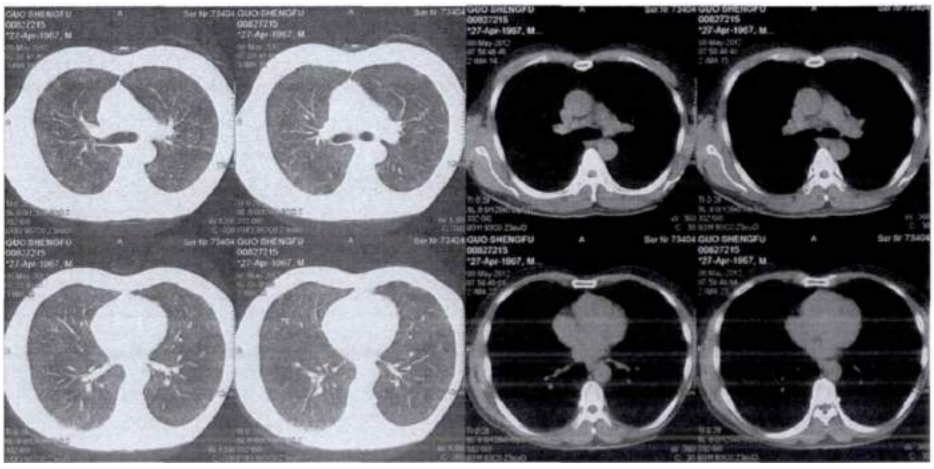
2012/4/25 CT reports: lung markings more numerous and prominent, septal thickening. Multiple nodules and floccular exudate; Multiple inflamed lymph nodes in mediastinum. The shadow of the heart remain normal; no effusion (see below).



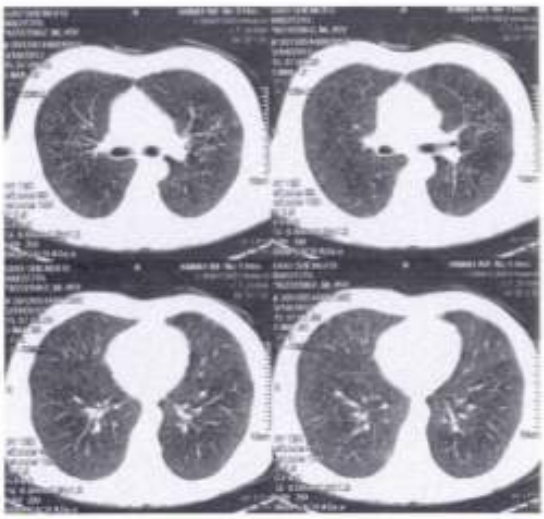
2012/4/30 CT reports: Compared to before, the lung markings are more numerous and prominent. Septal thickening, multiple nodules and floccular exudate; multiple inflamed lymph nodes in mediastinum. Others unchanged (See below).

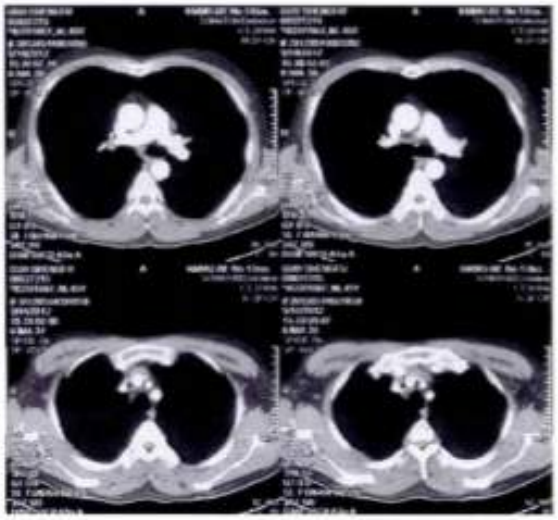


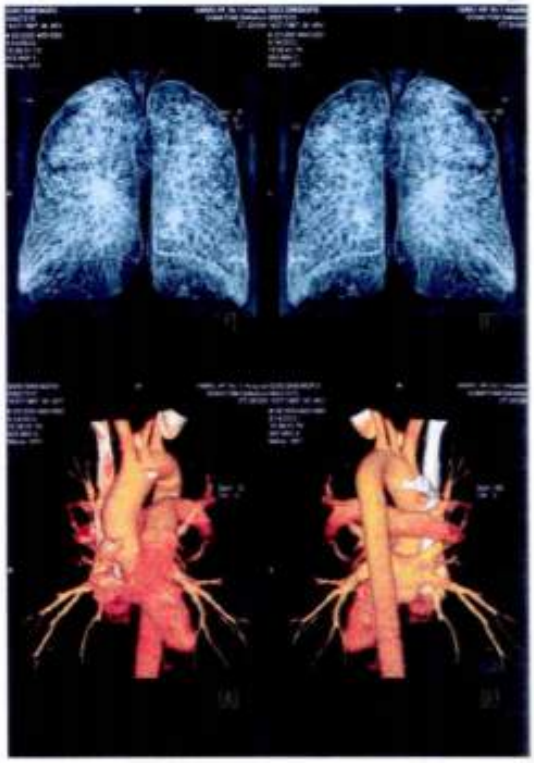
2012/5/6 CT: the exudation on the lower right lobe seems to be absorbed, others remained the same as before: multiple nodules and floccular exudate; multiple inflamed lymph nodes in the mediastinum (See below).



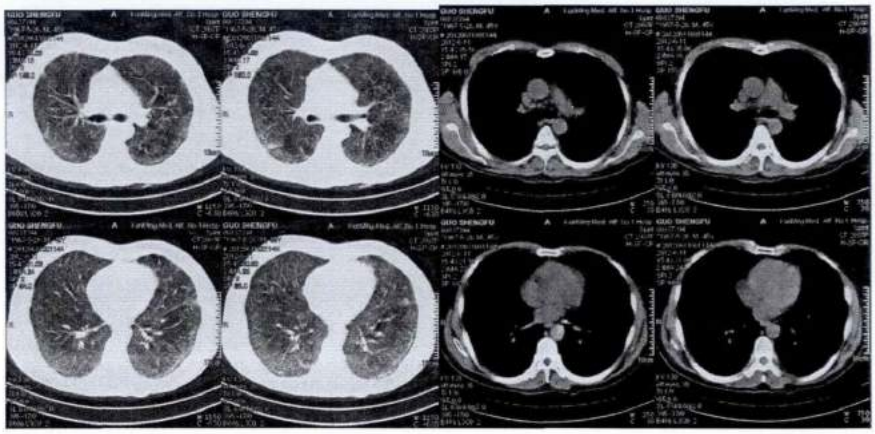
2012/5/14 intensified 3D CT: the lung marking was clearer: the flaky exudation on the lower right lobe of the lung seemed to absorb, the shadow of the multiple nodules and floccular exudation have also improved. The lymph nodes in the mediastinum remained the same. Whether the artery in the lung and its major branches were intact remained unknown.



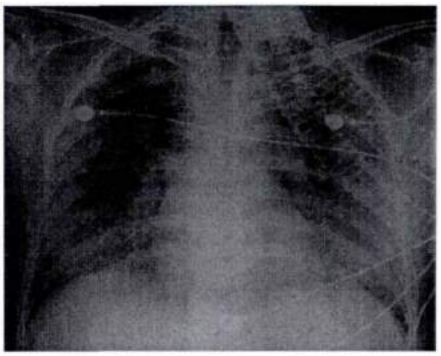




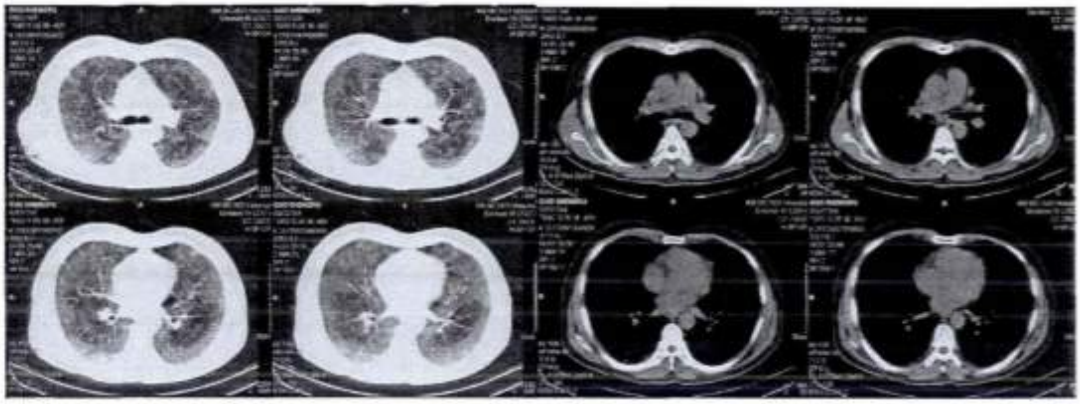
2012/5/26 CT: Clear increment of the lung marking, thickening, blurry. Overall thickening of the septum. Glassy and high density shadows in both lungs and partial pulmonary emphysema. Above are the substantial changes and may relate to infection or pneumoconiosis. Requested a check on the history of occupational disease (see below)



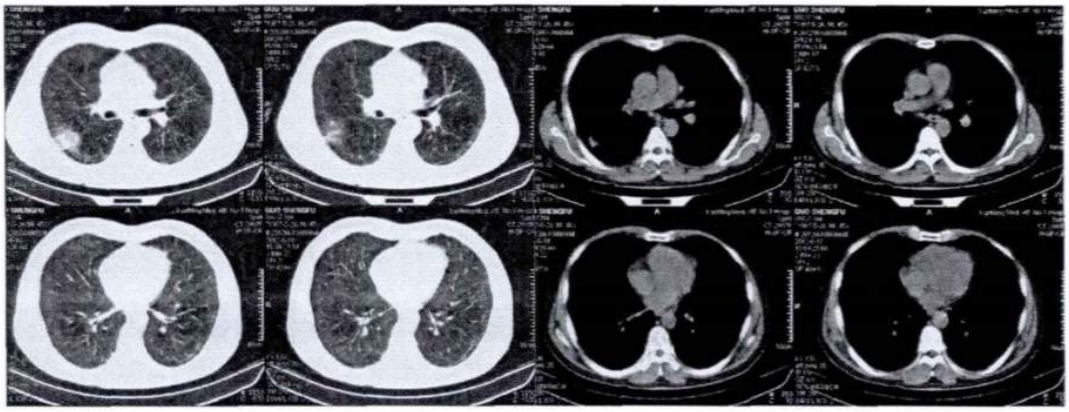
2012/6/3 Chest film reports: Compared to the films shot on 5/29, substantial changes in both lungs, and multiple scattered spotty shadows, partial lesion fusion. The shadow of both hila looks bigger and thicker. The illness progressed. Please work with the clinical for further diagnosis. (See below)



2012/6/7 CT reports: bilateral lung multiple patchy opacities and exudative consolidation, little fluid found in the left side, average amount of fluid in right side, possibly infection. Suggested double examination after treatment. Small mediastinal lymph nodes. Widening of the pulmonary artery. The shadow of the heart is enlarged. Calcification on the wall of the major artery. Found the shadow of the stent in the left coronary artery (see below).

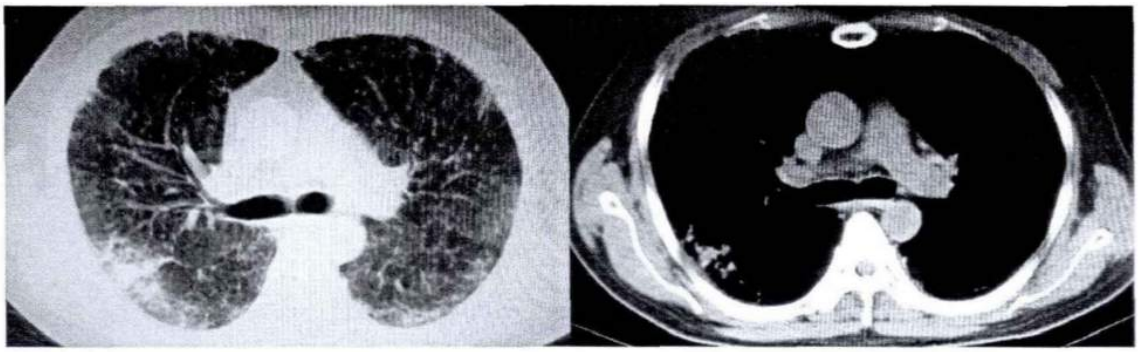


2012/6/18 CT Reports: Interstitial fibrosis in both lungs, pulmonary emphysema remained the same. Shadow of lumpy consolidation found on the right back side of the lower lobe and the upper lobe toward the end. Suggest a double checkup after treatment (see below).



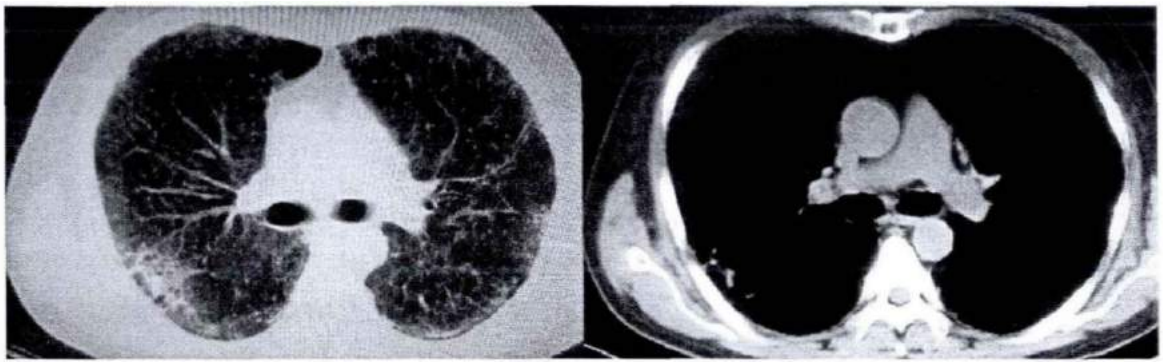
2012/7/1 CT reports: the pathological changes became more defined.

2012/7/8 CT reports: noticed diffused web-like shadow in both lungs. Multiple mediastinal lymph nodes were inflamed same as the CT report on 2012/7/1 (see below).



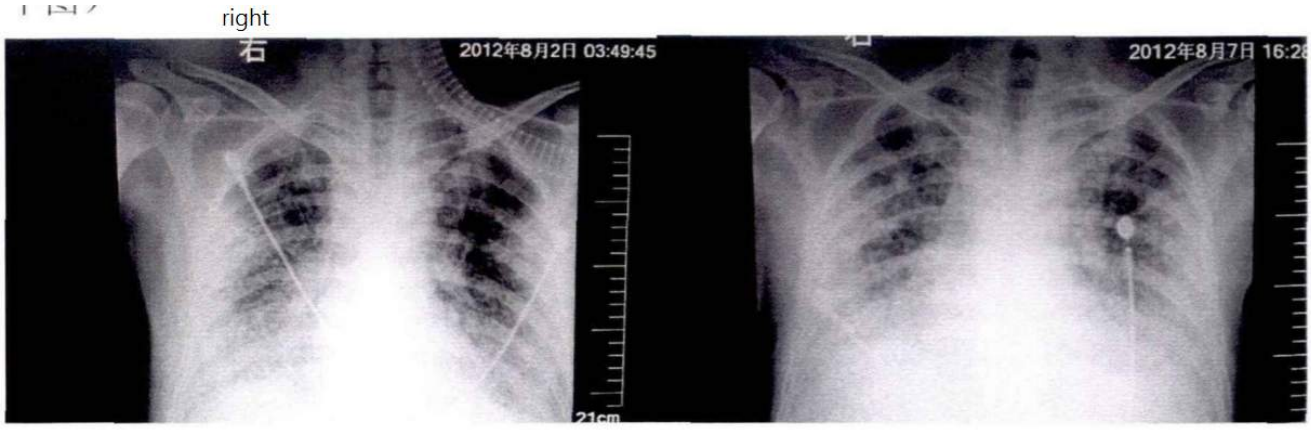
2012/7/11 Chest film indicates: interstitial changes in both lungs, spotty and flaky shadow diffused in both lungs, both hilar enlarged and murky. Possible infection. Other pathological changes need further confirmation, please work with clinical.

2012/7/14 Chest film indicates: highly density spotty and webbed shadow all over the lungs. Multiple mediastinal lymph nodes were inflamed same as the CT report on 2012/7/8 (see below).



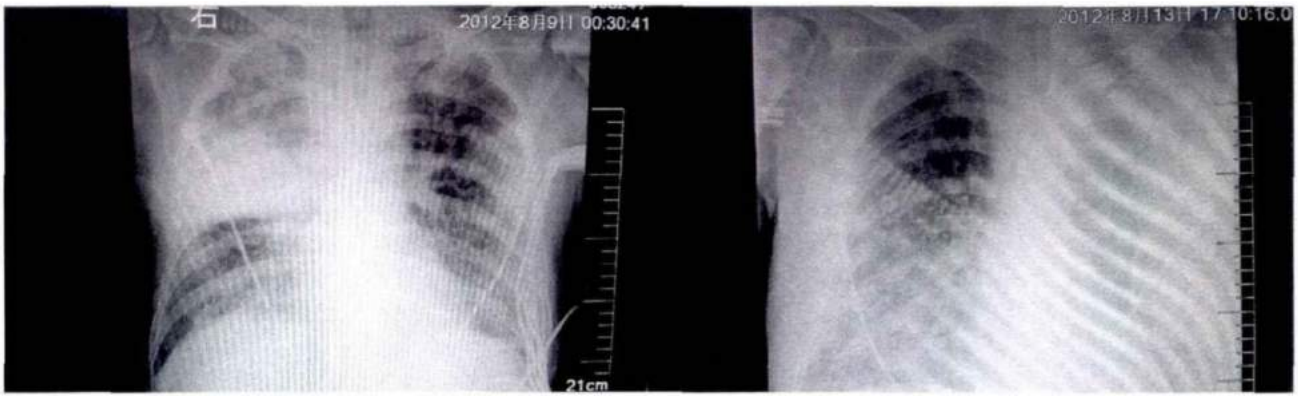
2012/7/26 CT reports: The symptom of Interstitial or fibrosis became more apparent, intensified heart, lung and mediastinum, others remain the same. Whether the lung artery and other major branches remain intact or not need to be confirmed.

2012/8/2 Chest film: interstitial changes in both lungs, flaky opacity at the bottom and on the ring of the upper lung. Compared to the 2012/7/24 film, the lesion has progressed. Please work with the clinical to do a thorough analysis (see the left picture below).



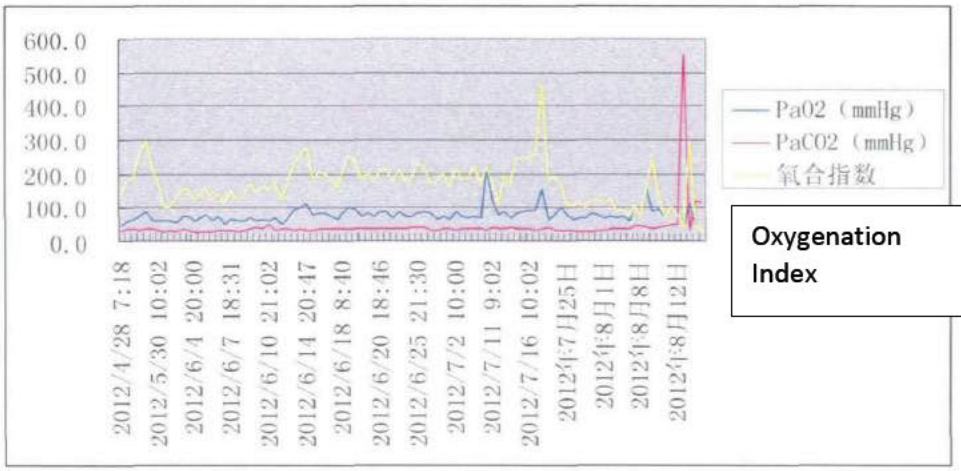
2012/8/7 Chest film: interstitial changes in both lungs, flaky opacity in the upper rings and lower lungs, lesion progressed. Please work with clinical (see the upper right picture).

2012/8/9 Chest film: the lung markings increased and murky, spotted shadow of the nodules. Increase flaky density in the lobe of the right lung. The lesion progress. Both hila remain bushy. The structure did not look clear. Please work with clinical (see the left picture below).

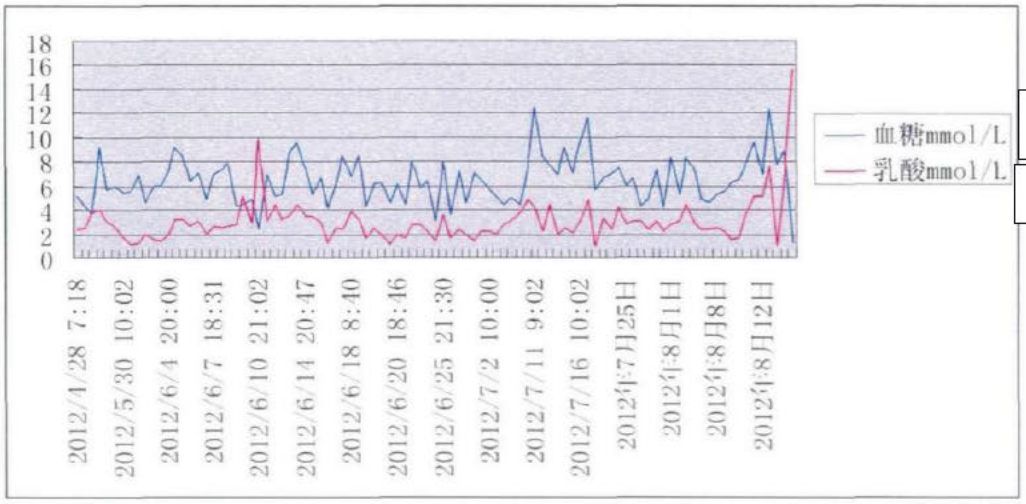


2012/8/13 Chest film: Compared to last time, the infected lesion in the upper right lung slightly absorb. The infected lesion in the lower right lobe progressed. Both hilar remain bushy, the structure is poorly defined. Please work with clinical. The infected lesion in the lobe of the left lung progressed. The left hilar, top of the diaphragm and costophrenic angle were unclear. The left chest was not visualized. Please work with clinical and make further examination if necessary (see the upper right picture).

2012/4/28 – 2012/8/13 Analysis of blood gas (see below):



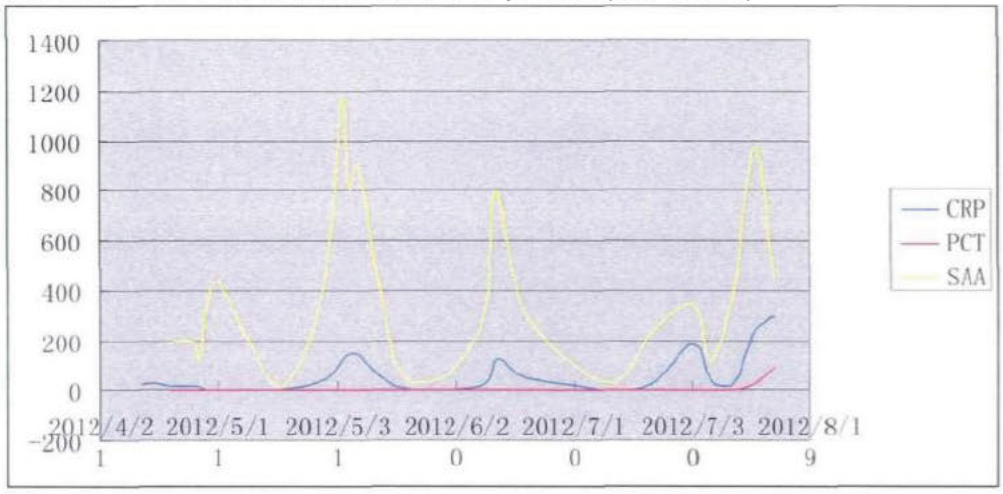
Oxygenation Index



Blood sugar

Lactic Acid

2012/4/25 – 2012/8/13 related infected protein (see below)



2012/5/15 Etiological examination: throat swab, complete blood test SARS-CoV, Hemorrhagic fever, Dengue fever, Japanese encephalitis, H5N1- negative

2012/4/27 PDD - negative

2012/4/28 Tumor protein chip: negative

2012/4/25 – 2012/8/13 Blood test: normal

2012/4/25 – 2012/7/23 Stool and urination test: normal

2012/4/25 – 2012/8/13 Coagulation test (PT, APTT, TT, FIB): normal

2012/4/25 – 2012/8/10 fiber blood test for three items: normal

2012/4/28 – 2012/8/13 Comprehensive metabolic panel: normal

2012/8/13 B-type Natriuretic peptide: 323.91 pg/ml

2012/8/12 B-type Natriuretic peptide: 252.60 pg/ml

2012/8/7 B-type Natriuretic peptide: 8.52 pg/ml

Percentage of T, B, NK cells and count (see below):

日期 Date	CD3 阳性 T 淋巴细胞绝对值 Positive Aboslute Value of Lymphocyte	T 抑制细胞 Suppressor Cell CD3+CD8+双阳细胞绝对值 double positve cell absoulute value	T 辅助细胞 supporting cell CD3+CD4+绝对值 absosolute Value	CD3CD4 CD8 均为阳性细胞 Positvie cell 绝对值 abosolute value	NK 细胞（CD16+CD56+双阳细胞） double positive cell	B 淋巴细胞 Lymphocyte（CD19+CD45+）
5-11	901	361	471	2↓	102	316
6-2	475↓	136↓	308↓	3↓	20↓	48↓
6-3	444↓	113↓	322↓	0↓↓	14↓↓	38↓
6-13	1578	669	933	1↓↓	84↓	347↓
6-18	1197	417	795	2↓	58↓	438↓
7-31	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
8-3	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
8-9	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

2012/6/2 Deep vein catheterization

2012/7/10 Deep vein catheterization

2012/8/8 Deep vein catheterization

2012/8/11 Picco 2 catheterization

2012/6/2 Noninvasive ventilator for aeration

2012/7/10 Noninvasive ventilator for aeration

2012/8/8 ventilator for breathing

2012/4/26 – 2012/5/29 mucus culture, sputum smear and blood culture: negative

2012/6/1 mucus culture smooth candida

2012/6/1 – 2012/7/1 mucus culture, sputum smear and blood culture: negative

2012/7/3 sputum smear shows Gram-positive bacteria and Gram-negative bacteria

2012/7/6 mucus culture Acinetobacter baumannii positive, only sensitive to levofloxacin and amikacin

2012/7/12 – 2012/7/28 mucus culture, sputum smear and blood culture: negative

2012/7/29 mucus culture positive

2012/7/29 mucus culture acinetobacter baumannii positive, only sensitive to levofloxacin and Tobramycin

2012/7/31 mucus culture acinetobacter baumannii positive, only sensitive to levofloxacin and Tobramycin

2012/8/1 – 2012/8/3 mucus culture and blood culture: negative

2012/8/5 mucus culture acinetobacter baumannii positive, only sensitive to levofloxacin

2012/8/10 mucus culture stenotropho monas maltophilia, multiple reactions

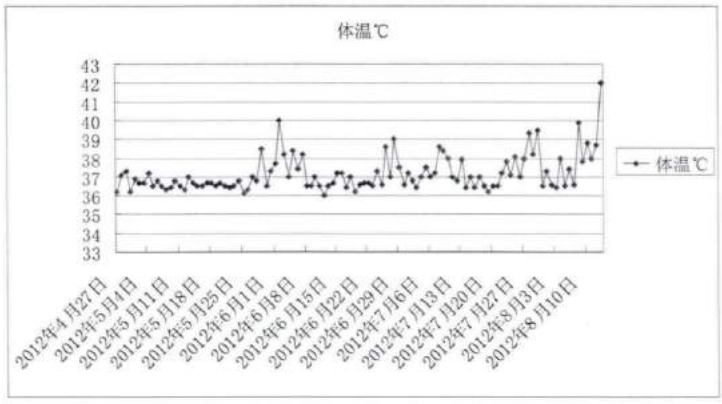
2012/8/11 mucus culture acinetobacter baumannii positive (twice).

2012/8/11 blood culture A.junni, multiple reactions to antibodies (twice).

2012/8/13 blood culture acinetobacter baumannii and candida negative

2012/8/13 mucus culture negative

Body temperature (see below):



Prescription during hospitalization:

2012/4/27 – 2012/4/28 Cefixime 0.5g x 2, ivgtt, Bid

2012/4/28 – 2012/5/4 Cefoperazon Sodium and Tazobactam sodium 2.25g, ivgtt, Q8h.

20125/4 – 2012/5/7 Z piperacillin sodium/tazobactam sodium 4.5g, ivgtt, Q8h.

2012/5/30 – 2012/6/3 Z piperacillin sodium/tazobactam sodium 4.5g, ivgtt, Q8h

2012/6/3 – 2012/6/19 Vancomycin 0.5g x 2, ivgtt, Q12h

2012/6/4 – 2012/6/28 Cefoperazon Sodium and Tazobactam sodium 1.5g x 2, ivgtt, Q12h.

2012/6/4 – 2012/6/28 Meropenem 0.5g x 2, ivgtt, Q8h.

2012/7/8 – 2012/7/17 levofloxacin 0.1g x 4, ivgtt, Qd.

2012/7/9 – 2012/7/19 Cefoperazon Sodium and Tazobactam sodium 2.25g, ivgtt, Q8h.

2012/7/26 – 2012/8/1 Cefoperazon Sodium and Tazobactam sodium 2.25g, ivgtt, Q8h.

2012/7/26 -2012/8/1 levofloxacin 0.5, po, Qd.

2012/7/28 – 2012/8/1 Fosfomycin 6g, ivgtt, Q8h.

2012/8/8 – 2012/8/10 Z piperacillin sodium/tazobactam sodium 4.5g, ivgtt, Q8h

2012/8/10 – death Fosfomycin 6g, ivgtt, Q8h.

2012/8/10 – death Tygecycline 50mg, ivgtt, Q12h.

2012/4/27 – 2012/5/2 (J) Methlyprednisolone injection 40mg, ivgtt, Qd

2012/5/2 – 2012/5/7 (J) Methlyprednisolone injection 30mg, ivgtt, Qd

2012/5/7 – 2012/5/21 (J) Methlyprednisolone injection 40mg, ivgtt, Q12d.

2012/5/21 – 2012/5/25 (J) Methlyprednisolone injection 30mg, ivgtt, Q12h

2012/5/25 – 2012/5/27 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h

2012/5/27 - 2012/6/6 Methlyprednisolone injection 40mg, po, Qd

2012/6/6 – 2012/6/7 Methlyprednisolone injection 40mg, po, Q12h

2012/6/7 – 2012/6/19 (J) Methlyprednisolone injection 40mg, iv, Q12h

2012/6/19 – 2012/6/23 (J) Methlyprednisolone injection 40mg, iv, Qd

2012/6/23 – 2012/6/26 (J) Methlyprednisolone injection 20mg, iv, Qd

2012/6/26 - 2012/6/3 Methlyprednisolone injection 80mg, po, Qd

2012/6/30 – 2012/7/4 Methlyprednisolone injection 40mg, po, Qd

2012/7/10 - 2012/7/17 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h

2012/7/17 – 20127/26 (J) Methlyprednisolone injection 40mg, ivgtt, Qd

2012/7/26 – 2012/7/30 prednisone 20mg, po, Qd

2012/7/30 – 2012/8/3 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h

2012/8/3 – 2012/8/7 (J) Methlyprednisolone injection 40mg, ivgtt, Qd

2012/8/11 – 2012/8/13 (J) Methlyprednisolone injection 80mg, ivgtt, Q8h

2012/8/13 – death (J) Methlyprednisolone injection 40mg, ivgtt, Q8h

2012/6/3 - 2012/7/9 Caspofungin 50mg, ivgtt, Qd

2012/6/5 – 2012/6/19 Fluconazole 40mg, ivgtt, Qd

2012/7/13 – 202/8/1 Micafungin 150 mg, ivgtt, Qd

2012/8/1 – death Fluconazole 0.2g, po, Q12h

2012/5/7 - 2012/5/28 Ganiciclovir 0.3g, ivgtt, Q12h

2012/8/11 – death Qseltamivir 75mg, po, Bid

2012/8/13 – death Ganiciclovir 0.3g, ivgtt, Q12h

2012/6/6 – 2012/6/14 a - Thymosin 1.6mg, ih, Qod

2012/8/8 – 2012/8/10 a – Thymosin 1.6mg, ih, Qod

Remote Meeting Minute

Time: 2012/6/4

Location: First Affiliated Hospital

Expert Attendee: Dr. Xie Can Mao , Chief Physician, Respiratory department of The First Affliated Hospital, Sun Yat-Sen University

After learning the report of the patient and related information, Dr. Xie diagnose: Interstitial pneumonia, great possibility for fungi infection. Have the patient to complete the G examination, and fiber bronchoscope checkup. If the circumstances allow, we should also consider conducting biopsy of lung. However, the patient is on noninvasive ventilation, the biopsy is not appropriate. Treatment wise, Dr. Xie agrees with what we have done so far. He suggested that we should also prescribe 2 tablets of compound Sulfamethoxazole (oral), 3 times/ day. Fluconazole for the fungus and Thymosin for boosting up immune system.

Reported back to Dr. Qian. After Dr. Qian Chuan Yun, Wang Yun Hui and Liu Rong's discussion, they decided to use Caspofungin and Fluconazole for fungi treatment. Also, prescribe some compound Sulfamethoxazole and thymosin for treatment. The patient is having fever, possible a sign of merged infection. Prescribe Vancomycin, sulbactam and cefoperazone and Meropenem for infection.

Remote Meeting Minute 2

Time: 2012/6/19

Location: First Affiliated Hospital

Expert Attendee: Dr. Zhong Nan Shan, Respiratory department of The First Affliated Hospital, Sun Yat-Sen University

After learning the report of the patient and related information, Dr. Zhong diagnose: 1.Interstitial pneumonia, great possibility for virus infection. 2. Invasive pulmonary aspergillosis (secondary infection). Suggestion: 1. Went to the animal lab in Kun Ming to confirm the type of the bat; 2. Did a throat swab and SARS antibody examination; 3.Prescribe Caspofungin, sulbactam and cefoperazone and Meropenem for treatment; 4. Intensify airway monitor, use fiber bronchoscope to clear out the mucus (do not wash by water). Basically agree with our treatment so far.

After Dr. Qian Chuan Yun, Wang Yun Hui and Liu Rong's discussion, they decided to use Caspofungin, sulbactam and cefoperazone and Meropenem for treatment.

Discussion

The patient started to work in the mining filed on April 2, 2012, for up to 14 days.

Day of Admission to the Hospital: 2012/4/27

Discharge Day: 2012/8/13, total of 109 days

Discharge diagnosis: 1. Severe Pneumonia 2.Multiple organs failure 3.ARDS 4. Inhaling Lung Impairment 5. Interstitial pneumonia (Virus related) 6. Invasive pulmonary aspergillosis (secondary infection).

Discharge reason: death

According to Chest film and CT, the illness recurred itself and developed in fluctuation. Finally, the lungs suffered from fibrosis.

The artery blood gas analysis indicated that the patient went through Type I respiration failure, poor oxygenation index. According to the "ARDS Berlin Criteria" in 2012, for sure it was ARDS. Consequentially, one of the causes of death could be respiratory failure.

the T, B, NK Lymphocyte percentage and count of the patients were decreasing. It shows that the immune system of the patient was impaired, had poor resistant to the disease and could easily be infected by hospital-acquired infection. During hospitalization, the patient had deep vein cauterization for four times. The blood culture and mucus culture in the later stage both suggested Acinetobacter baumannii. Before death, the infection related protein PCT reports 92.09ng/ml, therefore, one of the causes of the death could be infectious shock (induced by severe pneumonia).

According to the “Guideline and Diagnosis of invasive fungal infection” published in 2007 by Critical care branch of the Chinese medical association, we should also consider the secondary infection of invasive pulmonary aspergillosis

Prescription: five days after the suspension of Meropenem on 2012/6/28 and sulbactam and cefoperazone on 2012/7/26, the patience started to have high fever while continuously taking Methlyprednisolone and Micafungin. It shows that the possibility of secondary infection is high, the application of antibiotics is necessary.

After the patient passed away, we suggested to do an autopsy surgery to identify actual cause of the death. The families of the patient refused.

Analysis of the death of cause: the immune system was going down. The resistant to the disease was weak. The disease was acute and aggressive. Caught hospital-acquired infection in the later stage.

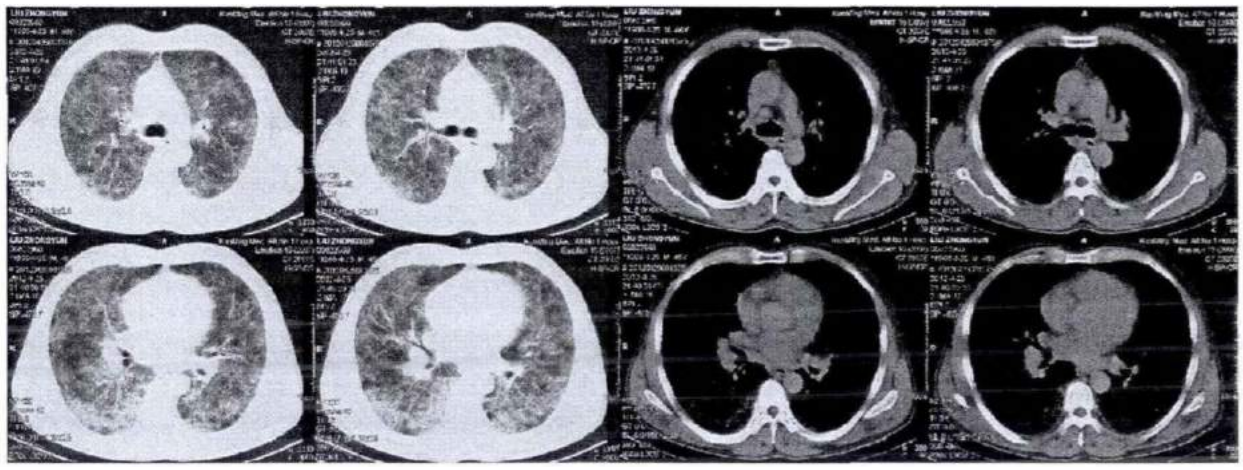
Case Four

Patient, Mr. Liu, male, 46 years old. He had sign of coughing, coughing with mucus, fever for 10 days and difficulty in breathing for three days and was admitted to the hospital on 2012/4/26. He worked in the mining well 10 days ago and was exposed to large amount of bats and their feces. He had cough, productive cough and hemoptysis (small amount), fever (highest to 39 Celsius) 10 days ago. He denied chest pain. He started to feel difficulty in breathing three days ago and went to the local hospital for treatment. The actual prescription remained unknown. For further treatment, he was admitted to our hospital. Since the illness started, he lost his appetite and felt drowsy. No significant change in bowel movement and urination. Used to be healthy. Denied high blood pressure, diabetes, heart disease or other chronic illness. He had been to Mo River. Prior to the illness, he worked in the mining well and was exposed to large amount of bats and their feces. Five of his colleagues had similar illness. Denied history of hepatitis, Typhoid or any other contagious disease. No history of blood transmission, allergy, typhoid or Tuberculosis. No other injuries, blood transmission, medical related allergy reaction. The vaccination record remained unknown. Physical examination: Body temperature 37.1 Celsius, Pulse 90 times/ minute, respiratory rate 18 times/ minute, BP 120/80 mmHg, considered poor performance, the pupils are round and dilated with 2.5 mm diameter. Sensitive to light. Softness in neck. The lips and tip of the fingers appear cyanotic, The breathing sound from both lungs were rough. Moist crackle sound from both lower part of the lungs. HR 90 times/ minute, regular, no murmur, rub or gallop. Abdomen soft, non-tender. Bowel sounds: 5 times/ minute. The limbs function okay and so do the muscle strength and stretch. Babinski on both sides. 2012/4/25 CT reports: Increase, thickening and blurring of the lung markings. Large parcel consolidation exudation across both lungs. Initial diagnosis: 1. ARDS; 2. Need more examination on the pathological changes of the bilateral lungs?

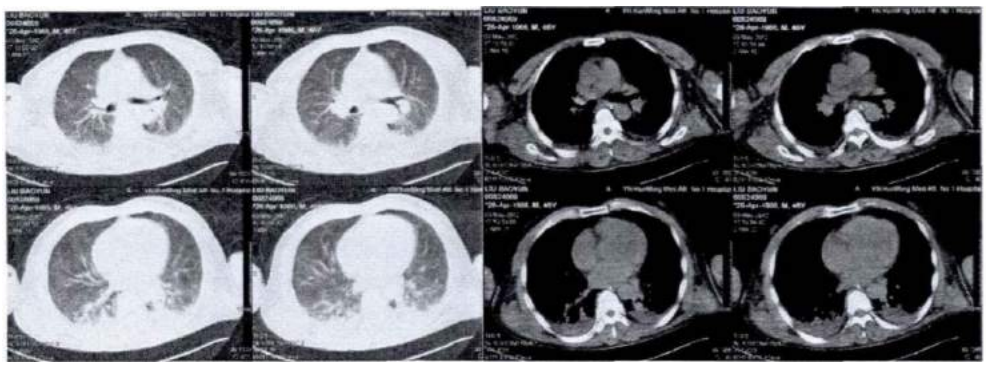
Method

Complete examination after hospitalization

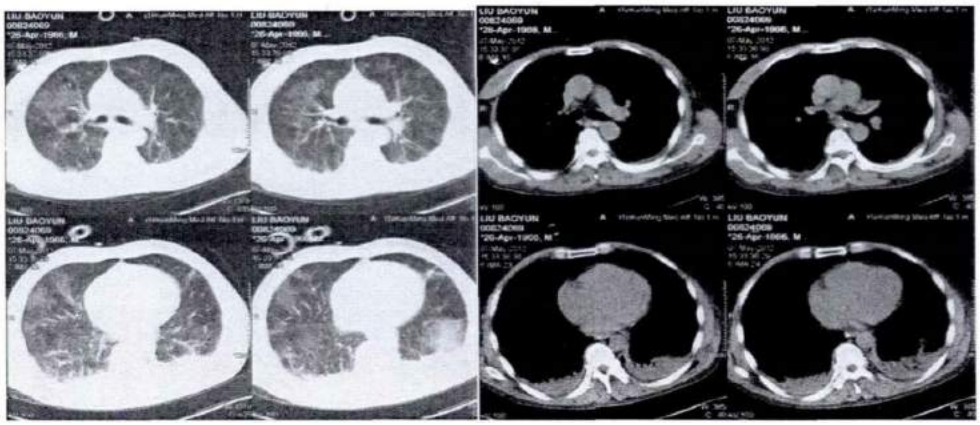
2012/4/29 CT reports: increased in lung marking of both lungs and opacity. Multiple patchy opacity and exudative consolidation, especially in the lower lobes. It is recommended to have a second checkup. Pleural effusion found in both lungs (see below).



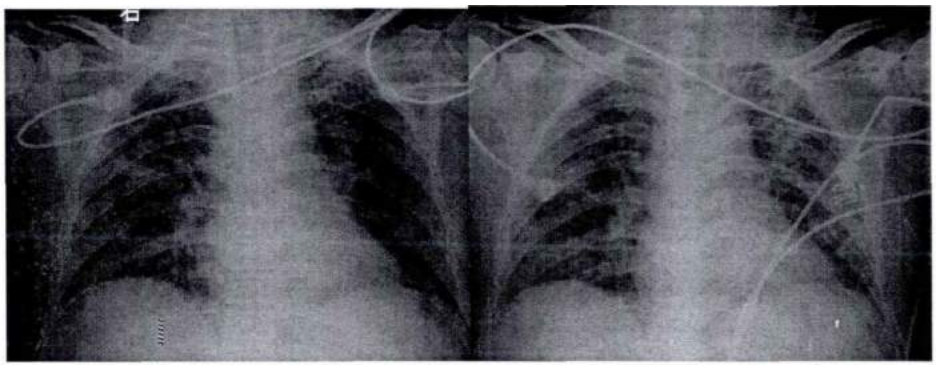
2012/5/3 CT reports: compared to the CT on 2012/4/29, the lung marketing has increased and more opacity. The multiple flaky consolidation exudation seemed to be absorbed in both lungs, so did the effusion (see below).



2012/5/7 Intensified CT reports: screen the artery more, the left and right artery appeared normal. Low density filling defect in bilateral pulmonary arteries, possibly acute pulmonary embolism. Please work with clinical. Multiple glassy exudation and consolidation in both lungs. Little effusion on both sides (see below).

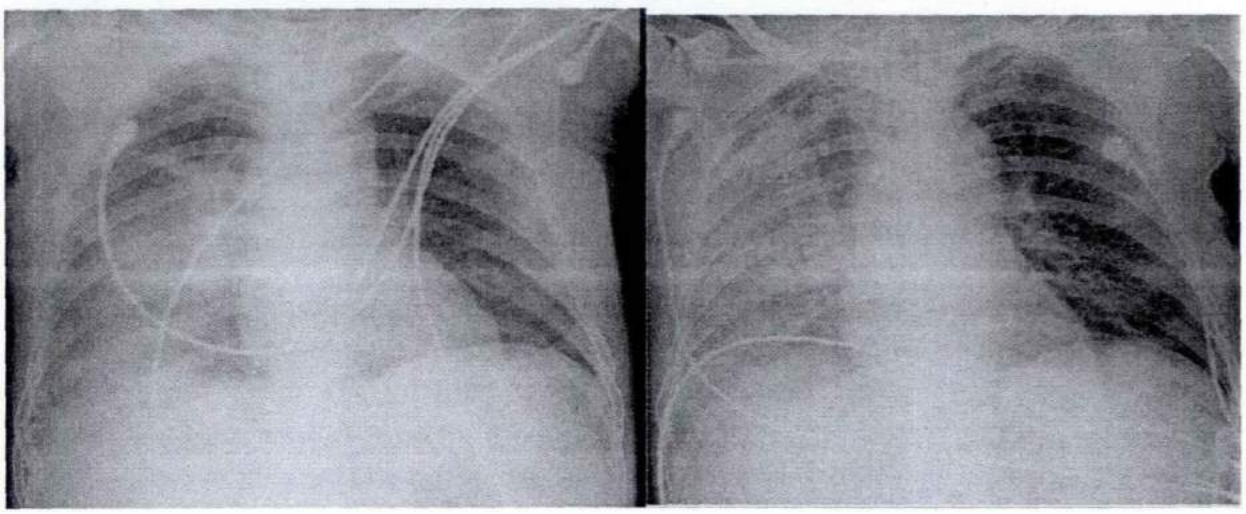


2012/5/8 Chest film: lung marking increased, hila looked normal, more markings in the lower lobe and appear to be blurry and some spotty, flaky and blurry shadow. In the lower lobe of the right lung, there were patchy and blurry shadow (see the left picture below).



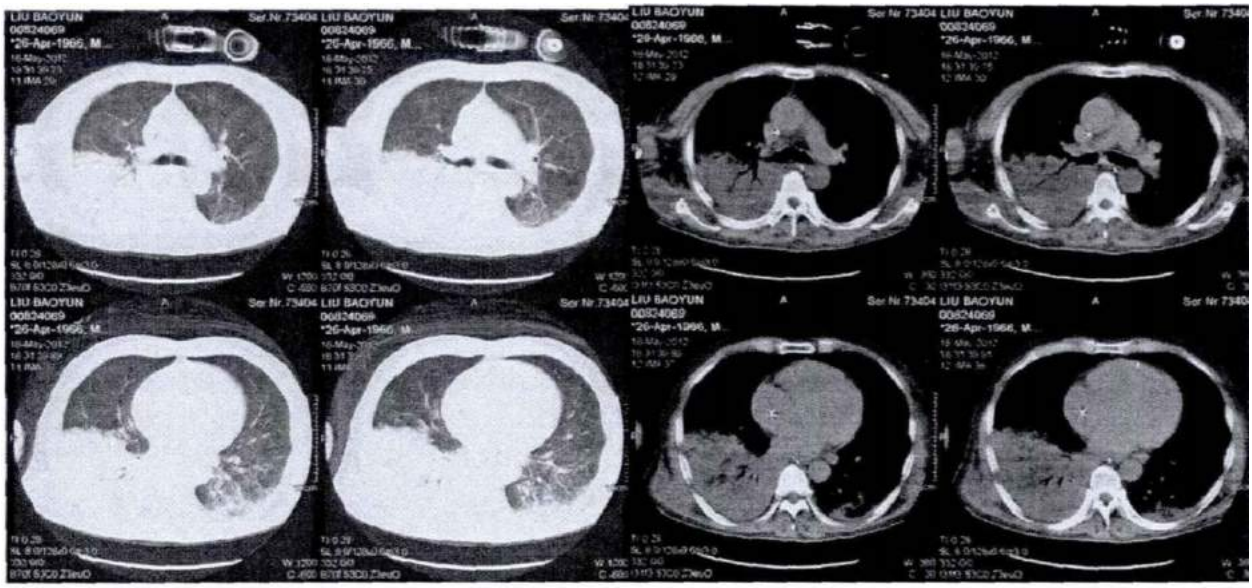
2012/5/12 Chest film: infection in both lungs, work with clinical for periodical checkup (see the right picture above)

2012/5/15 Chest film: Compared to the chest film on 5/13, the exudation on the right lung seemed worse. The left seemed slightly improved (see the left picture below).

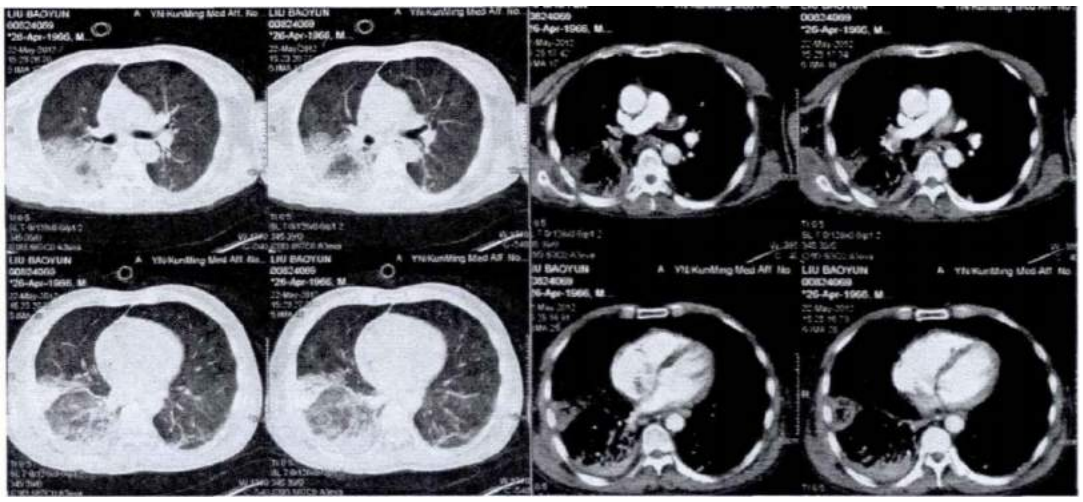


2012/5/18 Chest film: Compared to 2012/5/16, the exudation on both sides had slightly absorbed. Please work with clinical (see the right picture above)

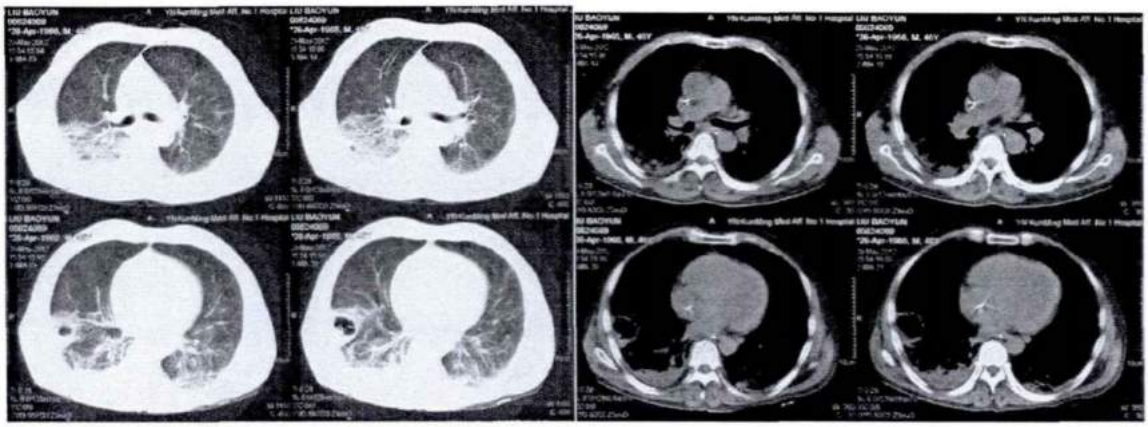
2012/5/18 Intensive CT: The lesion on the left lung decreased substantially. The consolidation exudation on the right need further confirmation (see the picture below).



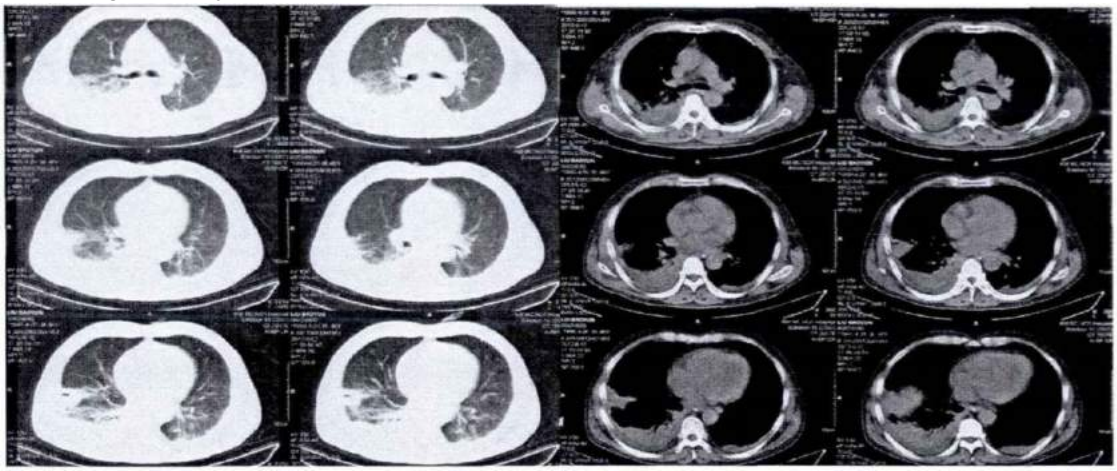
2012/5/22 intensive CT: Compared to 2012/5/18, the consolidation slightly absorbed. Glassy-like dense shadow in both lungs, possibly exudation. The intensive screen did not spot any abnormally (see the picture below).



2012/5/29 CT film: Compared to the film on 5/22, the consolidation and hollow on the right had slightly absorbed. The glassy-like dense shadow is smaller and less dense. Recommend continue treatment and a follow up checkup (see the picture below).

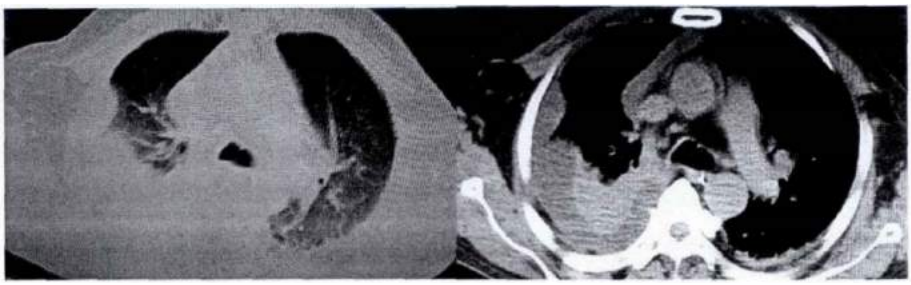


2012/6/12 CT film: the consolidation on the right become heavier and the hollow seemed absorbed slightly. The glassy-like dense shadow has decreased and less dense. The effusion on the right cavity has increased. The heart and mediastinum remain the same (see below).



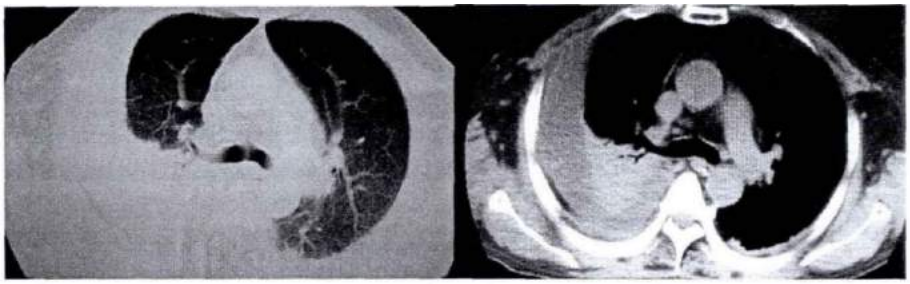
English translation of the MSc: "The Analysis of Six Patients With Severe Pneumonia Caused By Unknown Viruses" By Li Xu of Kunming Medical University, 2013. Translation completed: Jun 23rd 2020 (https://www.independentsciencenews.org/)

2012/6/20 CT: Compared to 2012/6/12, the lung markings become blurrier, the consolidation in the right lung is more aggressive, and the area of exudation in the left lung has enlarged. The effusion in the right cavity increased. The shadow of the heart increased. The mediastinum remain the same (see below).

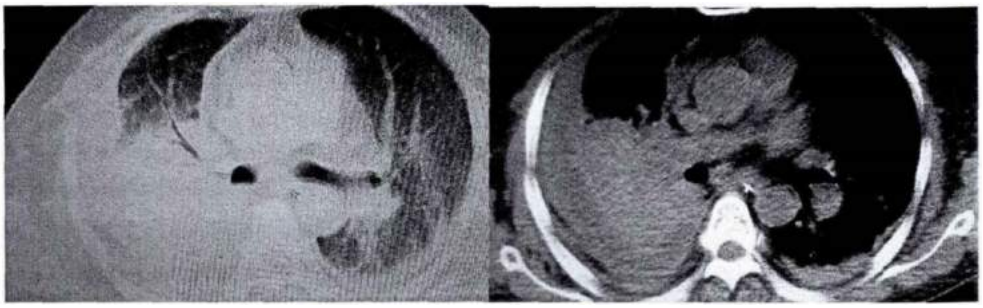


2012/6/27 Chest film: flaky consolidation exudation in the right lung and effusion in the right cavity.

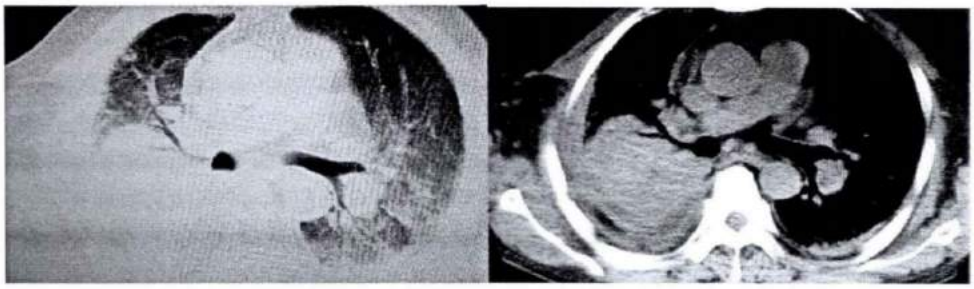
2012/6/28 CT scan: lung marking increased and blurry. Noticed flaky and floccular blurry shadow at the lower part of the lungs. The functioning area in the right lung has decreased. Effusion in both cavities. The widest effusion in the right cavity is 3.1 cm and large patchy dese consolidation shadow in lower right lobe. Sign of air bronchogram inside. Saw the drain in the right cavity (see below).



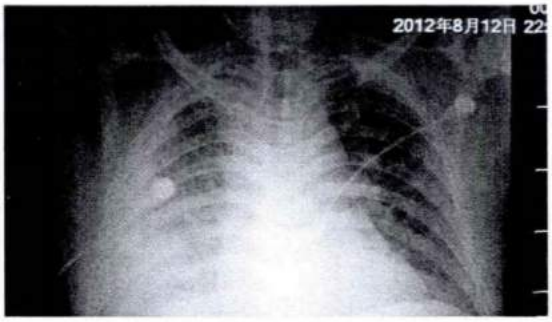
2012/7/6 CT scan: lung marking increased and blurry, ground-glass exudation in both lungs. Consolidation in the upper and lower lobe of the right lung. The airway and bronchus work well. Please work with the clinic. Moderate amount of effusion in the right side and less amount in the left. Multiple big inflamed lymph nodules in mediastinum (see below).



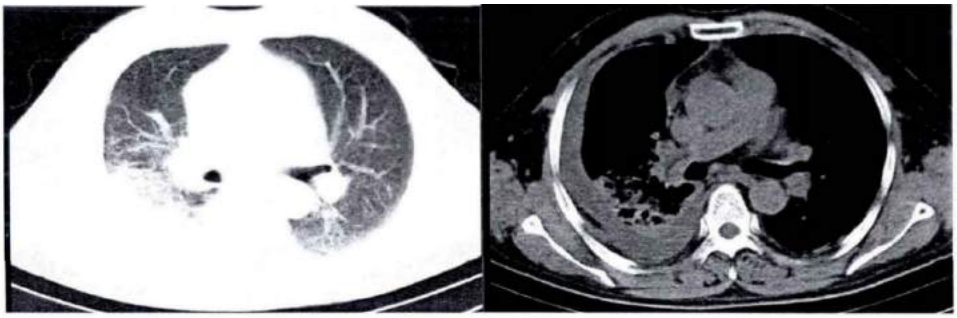
2012/7/11 CT scan: increased lung marking and blurry, ground-glass exudation same as above, the consolidation of the upper and lower right lung remain the same. Moderate amount of effusion in the right side and the left remain the same as before (see below).



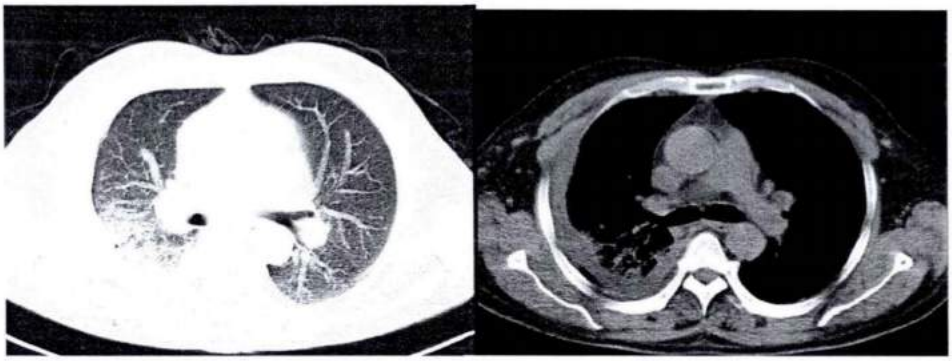
2012/8/12 Chest film: exudation lesion in both lungs have slightly absorb, the right side is more obvious, possible infection. Possibly effusion in right cavity (see below).



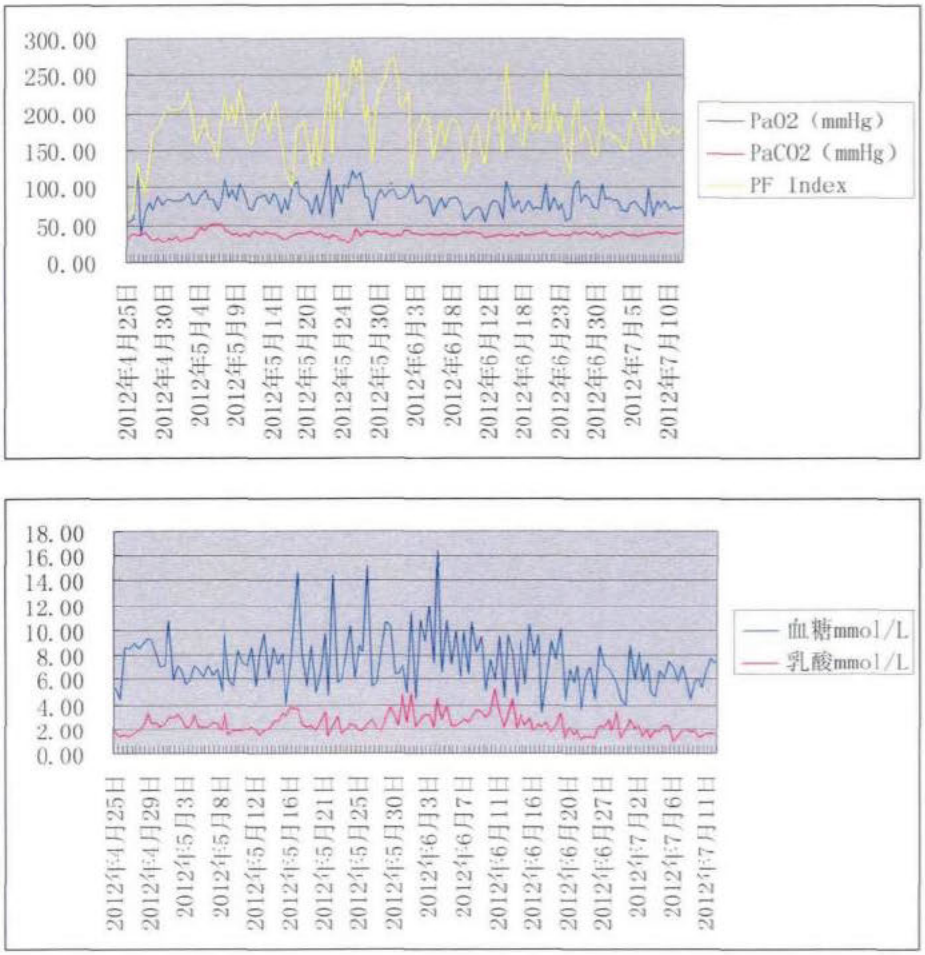
2012/8/14 CT scan: large consolidation exudation in the right lung, Sign of air bronchogram inside. Noticed shadow spotty, flaky exudation and stripe exudation. Little amount of effusion in both lungs, atelectasis due to extrinsic pressure. Multiple lymph nodules in mediastinum. The shadow of the heart and the artery remain normal (see below).



2012/8/23 CT scan: effusion, consolidation and atelectasis remain the same (see below).



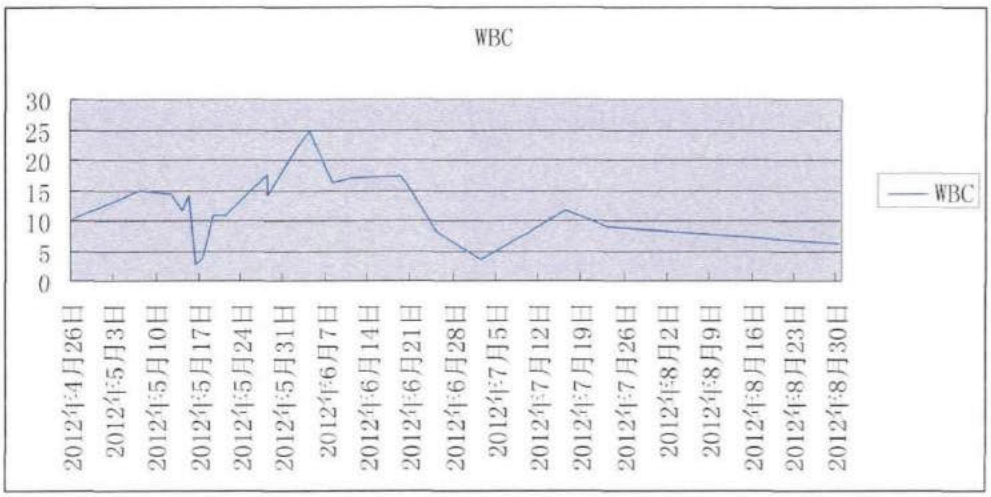
2012/4/25 – 2012/7/26 Analysis of Artery Blood gas (see below):



Blood sugar

Lactic Acid

2012/4/26 – 2012/8/30 Blood test: line chart of the white blood cell, the rest of the result remain normal (see below)



2012/4/26 – 2012/5/15 CK, AST, LDH, CK-MB and BNP test: normal

2012/4/27 immunoglobulin and complement test: C3 0.76g/L

2012/4/27 Hepatitis Virus and HIV test: negative

2012/5/7 Herpes Simplex virus DNA + Cytomegalovirus DNA + HPV DNA test: Negative

2012/5/9 Implement Picco2

2012/5/19 Conduct Tracheotomy

2012/5/20 Center of Disease Control in Chendu city Army reservation conducted an Aetiology test (swab and blood test): negative

2012/6/27 Ultra sound guided thoracentesis

2012/6/28 effusion test: bloody; Rivalta test: positive, red blood cell 60000 x 10^6 / L, White blood cell 2830 x 10^6 / L, Percentage of Monocytes - 14%, Percentage of giant cell – 86%

2012/6/28 effusion test: Adenosine deaminase 16.8 U/L, Total protein 39.9 g/L, Glucose 1.3 mmol/ L, Chlorine 101.4 mmol/L

2012/6/29 Cerebrospinal fluid test: increase of Neutrophil

2012/7/2 Cerebrospinal fluid test: Mixed cell reaction

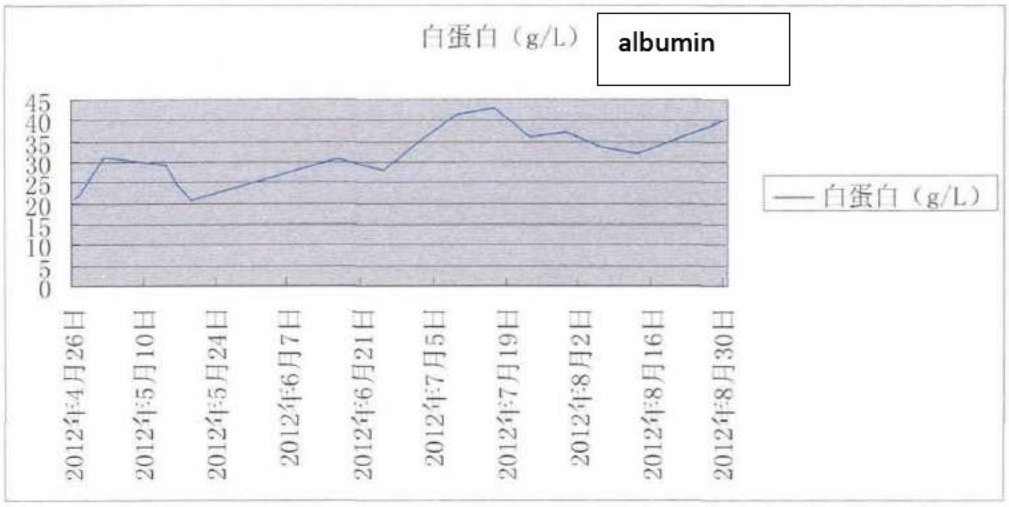
2012/4/26 Urinary test: Ketones1+, Urine Occult Blood 3+

2012/5/12 Urinary test: Urine Occult Blood 3+

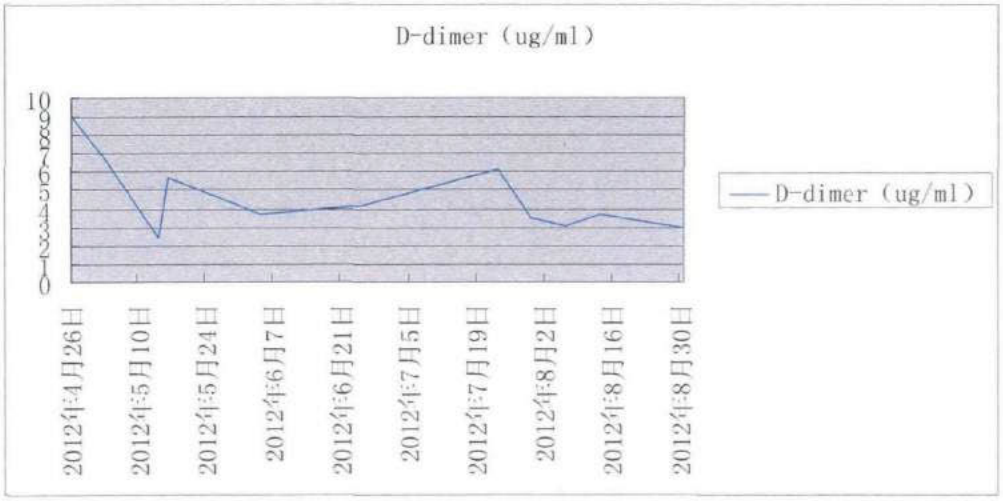
2012/5/29 Stool test: Occult blood positive

2012/6/18 Urinary test: negative

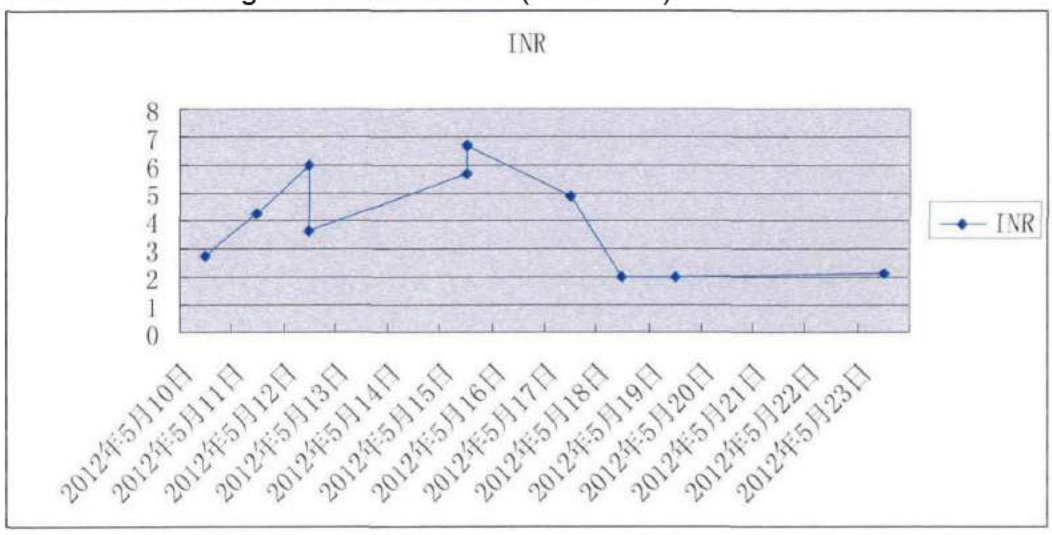
2012/4/26 – 2012/8/30 albumin development (see below), other metabolite index remain normal.



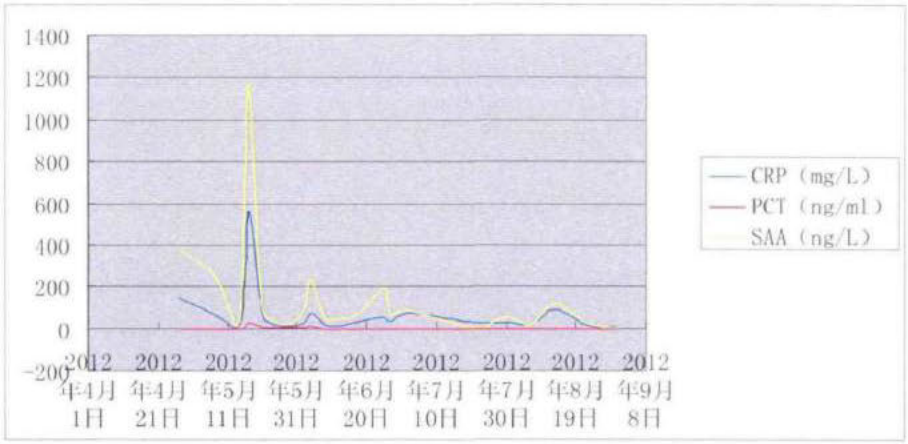
2012/4/26 – 2012/8/30 D- dimer (see below):



2012/4/26 – 2012/8/30 Anticoagulant treatment INR (see below):



2012/4/27 – 2012/8/30 infection related protein (see below):



Percentage and count of T, B, NK cell (see below):

日期 Date	CD3 阳性 T 淋巴细胞绝对值 Positive Aboslute Value of Lymphocyte	T 抑制细胞 Suppressor Cell CD3+CD8+双阳细胞绝对值 double positve cell absoulute value	T 辅助细胞 supporting cell CD3+CD4+绝对值 abosolute Value	CD3CD4 CD8 均为阳性细胞绝对值 Positvie cell abosolute value	NK 细胞（CD16+CD56+双阳细胞） double positive cell	B 淋巴细胞 Lymphocyte（CD19+CD45+）
4-27	483↓	110↓	200↓↓	0↓↓	15↓↓	40↓↓
5-3	401↓	150↓	240↓↓	0↓↓	15↓↓	58↓↓
5-11	901	361	471	2↓	102	316↓
6-2	475↓	136↓	308↓	3↓	20↓↓	48↓↓
6-3	444↓	113↓	322↓	0↓↓	14↓↓	38↓↓
6-13	1578	669	933	1↓↓	84↓	347↓
6-18	1197	417	795	2↓	58↓	438↓

2012/4/27 mucus culture: negative

2012/5/16 blood culture: negative

2012/5/18 mucus culture: acinetobacter baumannii

2012/5/18 mucus culture: acinetobacter baumannii, allergic reaction to Amikacin

2012/5/26 mucus culture: acinetobacter baumannii, allergic reaction to Amikacin

2012/5/28 mucus culture: acinetobacter baumannii

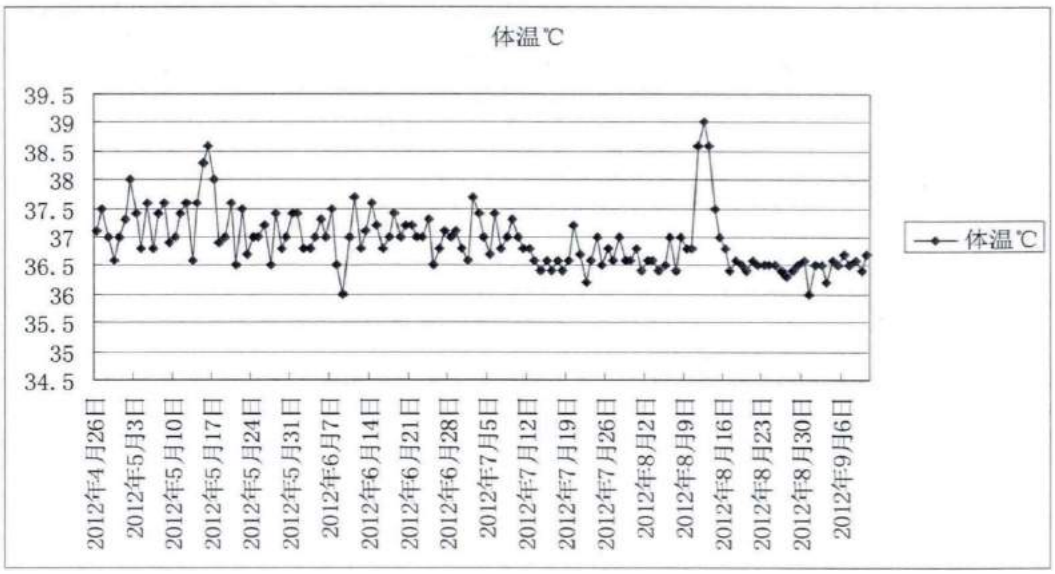
2012/5/28 mucus culture: acinetobacter baumannii, E.coli

2012/6/26 mucus culture: acinetobacter baumannii

2012/7/2 blood culture: klebsiella pnuemoniae subsp. Pneumoniae, KPP

2012/8/15 blood culture (Oxygen demand + anaerobic): negative

Body Temperature (see below):



Prescription after hospitalization:

2012/4/26 – 2012/4/30 (J) Methlyprednisolone injection 80mg, ivgtt, Q12h

2012/4/30 – 2012/5/4 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h

2012/5/4 – 2012/5/10 (J) Methlyprednisolone injection 40mg, ivgtt, Qd

2012/5/10 – 2012/5/17 (J) Methlyprednisolone injection 40mg, ivgtt, Q12 h

2012/5/17 – 2012/5/21 (J) Methlyprednisolone injection 80mg, ivgtt, Q12h

2012/5/21 – 2012/5/25 (J) Methlyprednisolone injection 40mg, ivgtt, Q8h

2012/5/25 – 2012/6/1 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h

2012/6/1 – 2012/6/19 (J) Methlyprednisolone injection 40mg, ivgtt, Qd

2012/6/19 – 2012/6/26 (J) Methlyprednisolone injection 20mg, ivgtt, Qd

2012/6/26 – 2012/6/30 Prednisone Acetate Tablets 10mg, po, Qd

2012/6/30 – 2012/7/4 Prednisone Acetate Tablets 5mg, po, Qd

2012/4/26 – 2012/5/2 Ganciclovir 0.3g, ivgtt, Q12h

2012/5/7 – 2012/5/10 Aciclovir 0.25g x 3, ivgtt, Q8h

2012/5/10 – 2012/5/21 Ganciclovir 0.3g, ivgtt, Q12h

2012/4/26 – 2012/5/14 L – Voriconazole, 0.4g, ivgtt, Q12h

2012/6/2 – 2012/6/4 (J) Itraconazole capsule 600 mg, po, Qd

2012/6/5 – 2012/6/19 Fluconazole 400mg (double the initial intake), ivgtt, Qd

2012/6/5 – 2012/6/6 Caspofungin 70mg, ivgtt, Qd

2012/6/6 – 2012/7/12 Caspofungin 50mg, ivgtt, Qd

2012/7/12 - 2012/8/16 Itraconazole tablet 100 mg, po, Bid

2012/7/17 -2012/9/5 Fluconazole 0.2g, po, Bid

2012/4/26 – 2012/5/7 Moxifloxacin 0.4g, ivgtt, Qd

2012/5/17 – 2012/6/2 Meropenem 0.5g x 2, ivgtt, Q8h

2012/5/17 – 2012/5/30 Linezolid 0.6g, ivgtt, Q12h

2012/5/21 – 2012/6/2 Cefoperazone sulbactam 1.5g x 2, ivgtt, Q12h

2012/6/2 – 2012/6/5 Cefoperazone sulbactam 2.25g, ivgtt, Q8h

2012/6/5 – 2012/6/28 Cefoperazone sulbactam 1.5g x 2, ivgtt, Q12h

2012/6/19 – 2012/6/28 Meropenem 0.5g x 2, ivgtt, Q8h

2012/8/14 – 2012/8/22 Z- Piperacillin tazobactam 4.5g, ivgtt, Q8h

2012/8/14 – 2012/8/27 Levofloaxacin tablets 0.5g, po, Qd

2012/5/7 – 2012/5/8 low molecular weight heparin 0.4 ml, ih, Qd

2012/5/8 – 2012/5/11 Warfarin Tablet 6mg, po, Qd

2012/5/11 – Discharge Warfarin Tablet 3mg, po, Qd

2012/5/18 – Discharge low molecular weight heparin 0.6 ml, ih, Qd

2012/5/16 VitKl 10mg, im, st

2012/5/24 Haloperidol 50mg, im, st

2012/6/4 – 2012/6/26 a – Thymosin injection 1.6mg, im, Qod

Discussion

The patient started to work in the mining well since 2012/4/2 for up to 14 days.

The day the patient was admitted: 2012/4/26, day of discharge: 2012/9/10, total of 107 days.

Discharge diagnose: 1. Interstitial pneumonia 2. Severe Pneumonia, ARDS 3. Low Proteinuria

Discharge reason: recovery

According to the analysis of the artery blood gas line chart, the beginning of the hospitalization is Type I respiratory failure, oxygenation index is low. According to the “ARDS Berlin Criteria” in 2012, it was confirmed as ARDS.

The illness was more severe at the beginning. It started to get better after the tracheal intubation and the aid from ventilation. However, the oxygenation index dropped again on May 4. Correspondently, the parameter of the ventilation was adjusted, yet the oxygenation index was still low. The D-dimer was 8.9 ug/ml on April 26, 6.9 ug/ml on May 2. The reason for the drop remained unknown. Therefore, did an emergency intensive CT on May 7 and it suggested that the artery and branches on the top and the bottom part of the lungs were in low density and filling defect, considering acute pulmonary embolism. We immediately prescribe low molecular weight heparin and Warfarin for two days. The breathing has improved significantly, indicated that anticoagulation and antithrombosis treatment were effective. During the treatment of anticoagulation, according to INR, we adjusted the amount of warfarin. During the adjustment, we noticed a INR 6.03 and immediately used VItkl for treatment.

On May 16, the oxygenation index dropped again and the body temperature rose sharply. Since the admission on April 26, the patient kept taking Fluconazole, Ganciclovir and Methlyprednisolone for treatment. On May 7, the patient stop taking Moxifloxacin and did not take any antibodies afterward. So we suspected that the malfunctioning of the breathing was caused by the intensifying lung infection. On May 17, PCT reports 24.05 ng/ml, so the patient took Meropenem and Itraconazole right away. As suggested by the CT on May 18, there was consolidation in large area in the right lung. On May 18, the mucus culture came back with acinetobacter baumannii positive twice. The blood culture was also positive. After prescription, the body temperate has dropped. On May 21, PCT was 1.63ng/ml. Indicated by the Intensive CT on May 22, the consolidation of the right lung has absorbed and the breathing was getting better.

2012/5/29 CT reports: There were frosty glass like density increased and hollows in both lungs. The temperature fluctuate between 36.8 – 37.4 Celsius. Possibly having secondary infection caused by Invasive pulmonary aspergillosis. On June 2, PCT reports 5.38 ng/ml, added Itraconzaole capsule, oral treatment. On 6/3, the oxygenation index dropped again, Since the diagnoses of acute pulmonary embolism on May 7, we apply anticoagulation treatment every day. Based on the report on 6/4, the D-dimer is 3.7 ug/ml and PCT is 14.02ng/ml, we predict the likelihood of having another acute pulmonary embolism is low, yet the possibilities of having severe pneumonia infection is bigger. Because the patient has been in critical medical condition and the diagnosis remain unclear, we sought out advice from Dr. Xie.

On 2012/6/4, Dr. Xie Can Mao, Chief Physician, Respiratory department of The First Affliated Hospital, Sun Yat-Sen University, gave us some suggestions in a remote meeting. He diagnosed: 1. Interstitial pneumonia, great possibility for fungal infection. 2. Invasive pulmonary aspergillosis (secondary infection). 3. pulmonary embolism. The patient could take a more complete G examination and and fiber bronchoscope checkup. If the circumstances allow, we should also consider conducting biopsy of lung. However, the patient is on noninvasive ventilator, the biopsy is not appropriate. Treatment wise, Dr. Xie agrees with what we have done so far. He suggested that we should also prescribe 2 tablets of compound Sulfamethoxazole (oral), 3 times/ day. Fluconazole for the fungus and Thymosin for boosting up immune system. Our department agree with using Fluconazole for 14 days. For the antifungal medicine, we agreed to switch to Caspofungin and Fluconazole for treatment. On 6/8, PCT was 0.61ng/ml and on 6/11 was 0.11 ng/ml. The CT scan on 6/12, the hollows in the right lungs were slightly absorbed. The frosty glass like density has decreased and less dense. The improvement reflects on the effectiveness of fungal treatment.

During hospitalization, the body temperature of the patient fluctuate between 37 – 37.3 Celsius. With the help of increasing nutrients, prone position and treatment for swollen lung, the patient still couldn't get rid of the ventilation machine. On June 19, we had Dr. Zhong Nan Shan from the Respiratory department of The First Affiliated Hospital, Sun Yat-Sen University to join our team remotely. He diagnosed: 1. Interstitial pneumonia, great possibility for virus infection. 2. Invasive pulmonary aspergillosis (secondary infection). He suggested 1. Visit the Animal lab in Kun Ming to confirm the species of the bat. 2. Conduct a swab test and SARS antibody examination. 3. Prescribe Caspofungin, Cefoperazone sulbactam and Meropenem for tratement. 4. Intensify airway monitoring, use fiber bronchoscope to clear out the mucus (do not wash by water), try to suspend the usage of ventilation machine. He basically agreed with our treatment so far.

2012/6/20 Chest CT plain scan, the lung marking become blurry, the consolidation in the right lung is more aggressive, and the area of exudation in the left lung has enlarged. The effusion in the right cavity increased. On 6/27, we conducted ultrasound assisted thoracoscopic thymectomy and extracted some pink effusion for further examination. It was exudate (nontuberculous or tumorous). Continue the treatment from the remote meeting. On 7/6 and 7/11, CT reports: consolidation in the upper and lower lobes of the right lung, average amount of effusion in right cavity and less effusion in left cavity. Continuously envelope pleural effusion drainage. At the same time, keep close attention to the hyoalbuminemia.

On 7/6, the oxygenation index was around 200. The blood flow is steady and can breathe on his own. After the breathing and airway evaluation, we successfully remove the metal tube.

On 8/12, the temperature of the patient spiked but could not find the cause. On 8/13, the infection related protein reports: CRP 90.8 mg/L, PCT 0.72 ng/ml. Given the patient was on the antifungal med, we did not prescribe any antibiotics. Instead, we prescribed Z- Piperacillin tazobactam and Levofloxacin tablets. After 2 days treatment, his body temperature went back to normal. In the later stage, CT plain scan suggested the consolidation, atelectasis and effusion in the right lung were slightly absorbed, yet on the back of the left lung.

There were still parts of consolidation exudation.

The percentage and counts for T, B, NK lymph cells is lower in the early and middle stage of the illness. Because of the treatment, the immune system of the patient has improved. In the later stage, the index went back to normal.

During hospitalization, we carefully monitor patient's random blood sugar in between 6-10 mmol/L. We tried to minimize the blood sugar variation.

On 8/15, blood culture (oxygen demand and anaerobic) reports negative. On 8/30, the infection related protein test: CRP 12.5 mg/L, PCT 0.04 ng/ml, SAA 3.22ng/L, the upper part of the lungs basically back to normality. The body temperature remained around 36.5 Celsius. Besides, the symptom of coughing, coughing with mucus, difficulty in breathing and soreness in limbs is gone. We decided to suspend every other medicine besides the anticoagulation one. The patient was discharged on 2012/9/10.

Case Five

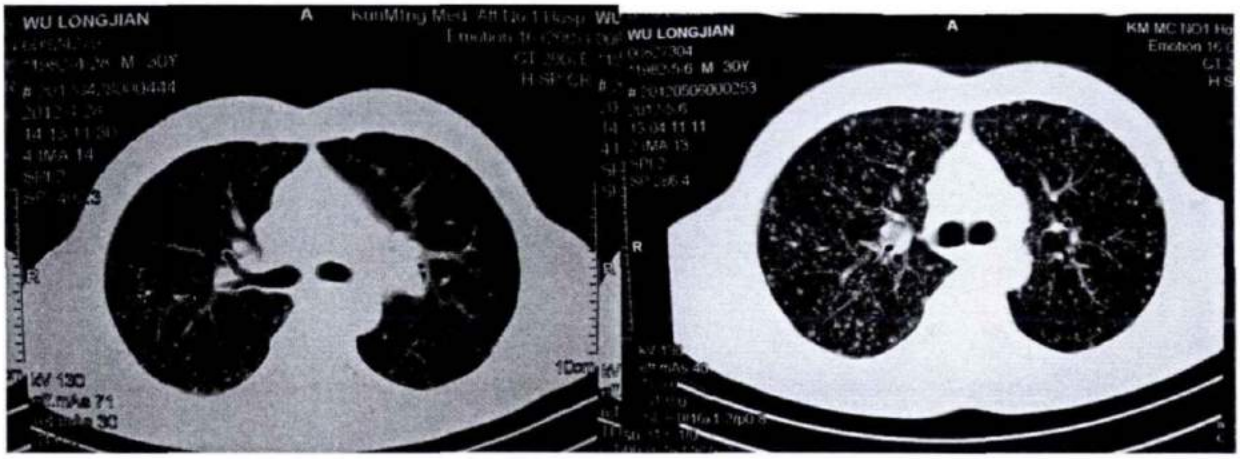
Patient, Mr. Wu, male, 30 year old, was admitted to the hospital on May 2, 2012. He had signs of coughing, coughing with mucus, fever, chest tightness and shortness of breath for five days. Dry cough most of the time, sometimes with white slimy mucus and the mucus came out easily. Chills and fever. There was no observable pattern for the fever. The highest is 39.0 Celsius, accompany with headache, soreness in limbs, chest tightness and short of breath after some light exercise. No symptom of hemoptysis, dizziness and palpitation. Sweating, dizziness, loss of strength, sign of paroxysmal dyspnea at night and edema. No specific treatment after onset of illness. Admitted to our ER last night for further treatment. Exudation and shadow of nodules found in the initial diagnosis. Sleeps and eats well. Normal bowel movement and urination. Used to work in the mining field for about 20 years. He has been to a big cave (about 150 meters deep) to work and was exposed to feces of bats for 4 days. No record of special diseases. No history of allergic reaction. Physical examination: temperature – 36.4 Celsius, Pulse 78 times/ minute, Respiration rate 19 times/ minute, BP 118/60mmHg, alert, No sign of cyanosis on the tip of the fingers or lips; the outline of the chest remains normal. No pain in the chest when pressured. Without inhaling, the oxygenation in the blood is 88%. No white spots in oral mucosa. Resonant to percussion over bilateral lung. Rough breathing sound. Little moist crackles sound from the lower left lung. Did not heard any dry crackle sound from both lungs. The heart rate is 78 times/ minute. No murmurs. No cardiomegaly. The abdominal is soft and flat. No pain when pressure or reflex. The examination did not involve liver, spleen and ribs. No edema in the legs. CT on 2012/4/28: chestnut shaped nodules in both lungs, shadow of multiple exudation.

Initial diagnosis after admission: Further confirmation on the exudation and shadow of the nodules in the lungs (possibly inhaling pneumonia, check with pneumoconiosis)

Method

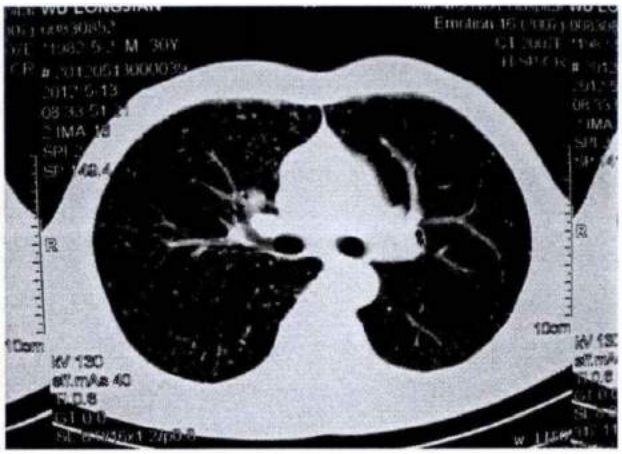
Assisted examination after admission:

2012/4/28 CT: multiple chestnut shaped nodules, shadows of exudation in both lungs. Multiple inflamed big lymph nodules in mediastinum (see below).



2012/5/6 CT: found chestnut-shaped nodules in both lungs, the exudation is more apparent in the lower lungs (see the upper right picture)

2012/5/13 CT: diffusive lesion in both lungs seemed to improved. The lymph nodules in the mediastinum decreased (see below)



2012/5/2 – 2012/5/24 regular blood test, blood biochem test and artery gas analysis, CK, AST, LDH, CK-MB test, PT, APTT, TT, FIB test, BNP and D-dimer: Normal.

2012/5/2 PPD test: negative.

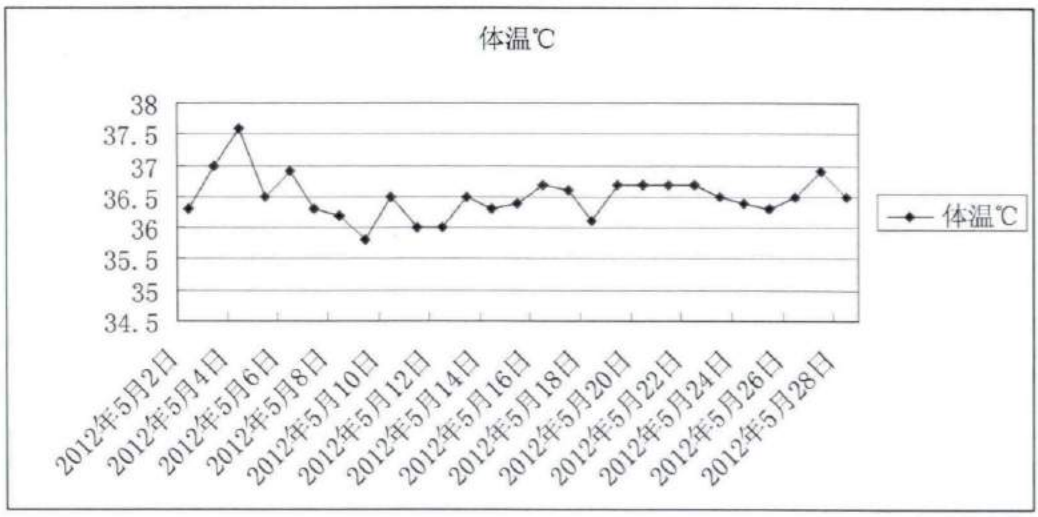
2012/5/2 ECG test reports sinus bradycardia and others were normal

Infection related protein: CRP 21.3 mg/L (May 2), PCT 0.67 mg/ml (May 3), PCT 0.75 mg/ml (May 7), CRP 12.6 mg/L, PCT 0.04 ng/ml, SAA 44.10 mg/L (May 9), PCT reports < 0.1 ng/ml (May 18), CRP 0.8 mg/L, PCT 0.04 ng/ml, SAA 2.82 mg/L (May 21).

Percentage and count of cell T, B, NK (see below):

日期	CD3 阳性 T 淋巴细胞绝对值	T 抑制细胞 CD3+CD8+双阳细胞绝对值	T 辅助细胞 CD3+CD4+绝对值	CD3CD4 CD8 均为阳性细胞绝对值	NK 细胞（CD16+CD56+ 双阳细胞）	B 淋巴细胞（CD19+CD45+）
5-18	683↓	355	288↓	6	139	120↓

Body temperature (see below):



Prescription after hospitalization:

2012/5/2 – 2012/5/10 Sulbencillin 1.0 g x 4 shots, ivgtt, Q8h

2012/5/7 – 2012/5/27 L – Fluconazole 0.2 g x 1, ivgtt, Q12h

2012/5/7 – 2012/5/9 (J) Methlyprednisolone injection 40mg x 1 shot, ivgtt, Qd

2012/5/9 – 2012/5/14 Prednisolone 10mg x 3 shots, ivgtt, Qd

2012/5/14 – 2012/5/15 Prednisolone 10mg x 2 shots, ivgtt, Qd

2012/5/15 – 2012/5/21 Prednisone Acetate tablet 20mg, po, Qd

2012/5/21 – Discharge, Prednisone Acetate tablet 15mg, po, Qd

2012/5/22 – Discharge, Thymosin, 1.0 mg x 2 shots, ivgtt, Qd

Discussion

The patient started to work in the mining cave on 2012/4/22 for up to 4 days.

First day of hospitalization: 2012/5/2; Day of Discharge: 2012/5/28, total of 26 days

Discharge diagnosis: Multiple nodules in the lungs, need further confirmation for the exudation (possibly Histoplasmosis also need to check for the possibility for pneumoconiosis)

Discharge reason: recovery

The patient is young adult. After taking anti-infection and antifungal treatment, the disease was under control while hospitalization. No reoccurrence of fever, coughing, coughing with mucus, tightness of chest and short in breath. The patient did not take any anti-virus medicine during rehabilitation, yet he has recovered. It indicates that his own immune system play a big role in fighting the disease.

On May 6, according to the CT plain scan, the illness was getting worse. Therefore, we prescribed the antifungal medication and some hormone. The consolidation exudation in the upper lung has improved five days after. The temperature has dropped to normal. It indicates that antifungal med and hormones were effective.

The cause of recovery: The patient is younger with stronger immune system. In addition, he did not spend a long time in the mining field, The treatment was immediate and effective.

Case Six

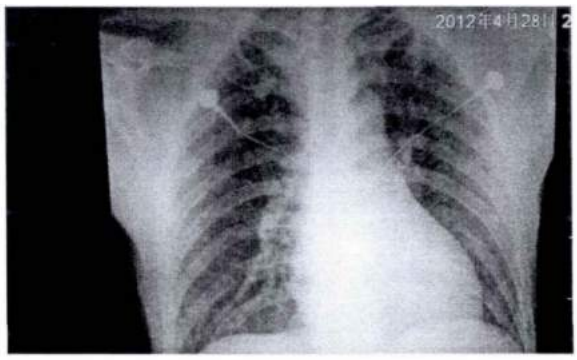
Patient Li, male, 32 year old, has been admitted to the hospital on 2012/4/26. He had sign of coughing, coughing with mucus, fever and difficulty in breathing for four days. He worked in the mining well four days ago. There were many bats and their feces in the well. Four days ago, he started to show sign of coughing, coughing with mucus (white and slimy) and fever. It smelled really bad in the well. His temperature went up to 39 Celsius. When he coughed, he had difficulties in breathing. No chest pain or coughing up blood. No sign of paroxysmal dyspnea at night. No stomach ache or diarrhea. He went to the local hospital for treatment but no documentation. His symptom had improved but wanted further treatment. He was healthy. No history of high blood pressure, diabetes, heart disease or any other chronic illness. He worked in the mining well before and was exposed to big amount of bats' feces. He had inhaled much irritating gas. No history of hepatitis, Typhoid or any other contagious disease or in contact with such diseases. No medical or food allergy. The vaccination report remained unknown. Physical checkup: temperature: 37 Celsius, pulse 74 times/minute, respiration rate 24 times/ minute, blood pressure 137/ 72 mmHg. In moderate health. No yellowing of skin and mucous membranes. Did not feel any lymph nodules on the superficial level. No abnormality in the head structure. The pupils were round and equal sized. Sensitive to the light. No sign of cyanosis on the tip of the fingers or lips. No resistance in the neck. The airway was in the middle. The thyroid was normal. The outline of the chest looked symmetric. The breathing sound from the lungs was rough. Did not hear any moist or dry crackle. Did not see any abnormality in heart and abdominal checkup. No sign of edema in legs. No abnormality in spine and limbs. Regular active and normal muscle strength. React to reflex and no any pathological reflex. Assistive checkup: CT reports: lung markings thickening and increased. Noticed multiple chestnut-shaped nodules. Need further confirmation on possibilities for Pneumoconiosis, acute pulmonary tuberculosis or other illnesses. Noticed multiple inflamed lymph nodules in mediastinum.

Initial diagnosis: 1. Cause of fever (possibly lung infection). 2. Inhaling lung impairment 3. Hypokalemia.

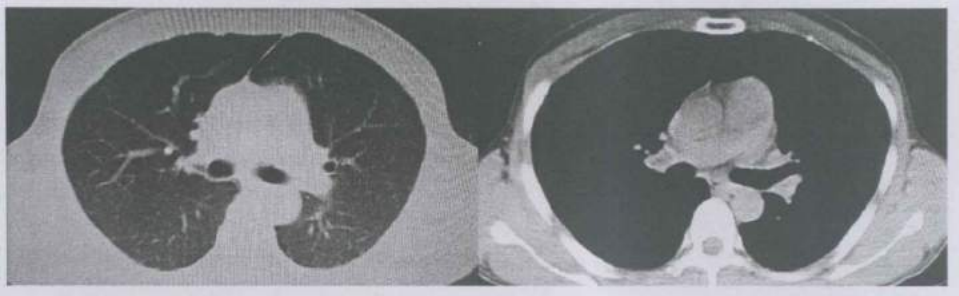
Method

After hospitalization, a complete examination:

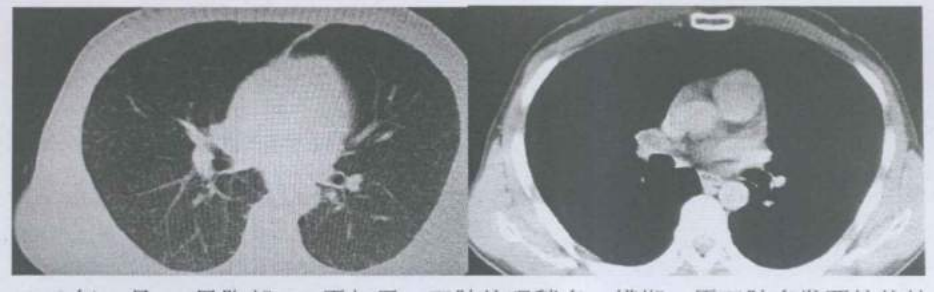
2012/4/28 Chest plain film: lungs marking messy and murky. Chest-nut shaped nodules all over bilateral lungs. Please work with the clinical for further confirmation. The heart and diaphragm remained normal (see below).



2012/4/29 CT chest plain scan: lung markings have increased and become blurrier in both lungs. Decrease amount of chestnut-shaped nodules shadows in both lungs. Noticed few strip shadows at the bottom part of the lower lobes in both lungs. Thickening on the left back side of the pulmonary pleurae.

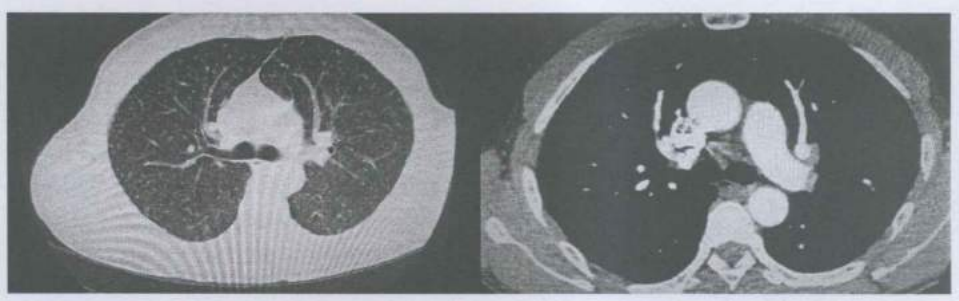


2012/5/7 CT plain scan: Compared to the scan on 2012/4/29, the lung marking has increased and blurry. The shadow of chestnut-shaped nodules has decreased. Less strip at the bottom of the lower lobes. The local emphysema, and bullae on the ring remained the same as before. The shadow of the heart looked normal. Noticed multiple inflamed lymph nodules in mediastinum (see below).



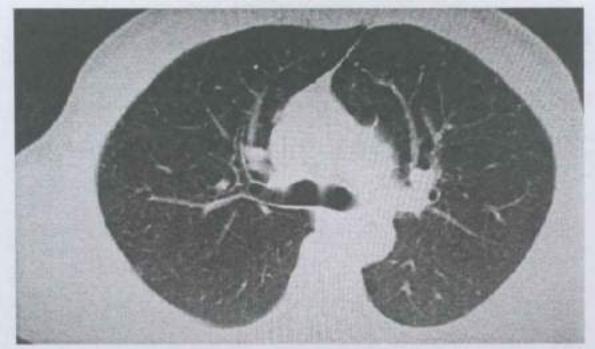
2012/5/14 CT plain scan: lung marking has increased and blurry. The chestnut shaped nodules remain the same. Noticed few strip shadow at the bottom of the lower lobes, local emphysema and bullae on the ring.

2012/5/18 intensive CT: 1. Diffuse pulmonary lesions (tuberculosis?) in both lungs, the change of the lesions was not as apparent as before. 2. The lung artery has thickened (see below).



2012/5/28 CT plain scan: the lung marking has slightly increased and blurry. Fewer shadow of chestnut-shaped nodules. Noticed few strip shadow at the bottom of the lower lobes, local emphysema and bullae on the ring.

(see below)



2012/4/26 Regular blood test, bio-Chem blood test, PT, APTT, TT, FIB and CK, AST, LDH, CK-MB: normal

2012/4/27 Bio-Chem blood test: CRP 34.2 mg/L, SAA 79.00 ng/L

2012/4/27 Hepatitis virus examination, regular urinary test, PT, APTT, TT, FIB: normal

2012/5/7 NK and PCR: normal

2012/5/17 Regular blood test, Bio-Chem blood test, CK, AST, LDH, CK-MB, blood culture: normal

2012/5/18 Artery blood gas analysis: PaO2 56.9mmHg, PaCO2 32.9 mmHg, Oxygenation Index (PF index) 270.8, Blood sugar 5.7 mmol/ L, Lactic Acid 1.4 mmol/L

2012/5/19 Artery gas Analysis: PaO_2 76.2 mmHg, $PaCo_2$ 36.7 mmHg, Oxygenation Index (PF index) 363.0, Blood sugar 7.9 mmol/ L, Lactic Acid 3.0 mmol/L

2012/5/18 Blood test: EDP 5.3 ug/ml, Antithrombin III 146.5 %, D-dimer 3.9 ug/ml

2012/5/18 Infection related protein: CRP 66.3 mg/L, PCT 0.04 ng/ml, SAA 230.00 ng/L

Body temperature chart (see below):

Prescription during hospitalization:

2012/5/17 – 2012/5/21 Ganciclovir 150 mg x 2 shots, ivgtt, Q12h.

2012/5/17 – 2012/5/24 Piperacillin Sodium and Tazobactam Sodium 4.5g, ivgtt, Q8h

2012/5/17 – 2012/5/21 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h

2012/5/21 – 2012/5/26 (J) Methlyprednisolone injection 20mg, ivgtt, Q12h

Discussion

The patient started to work in the mining cave since 2012/4/22 and a total of 4 days.

Day admitted to the hospital: 2012/4/26; Day of discharge: 2012/5/28, total of 24 days

Discharge diagnose: 1. Lung infection 2. Inhaling lung impairment 3. Hypokalemia

Discharge reason: recovery

The patient is a young adult. After receiving the anti-infection, anti-inflammation and antivirus treatment, the patient has started to recover. The body temperature was kept in the normal range. No reoccurrence of coughing, coughing with mucus or any difficulty in breathing. The patient did not receive any anti-fungal medicine for treatment, yet still recovered. This suggested that the possibility of the illness being triggered by fungal infection is slim.

Compared the CT at the beginning and in the end, it showed that the treatment was effective.

The cause of recovery: the patient was young and with a stronger immune system. He did not spend a long time in the mining well. The treatment was immediate and effective.

Comprehensive Analysis

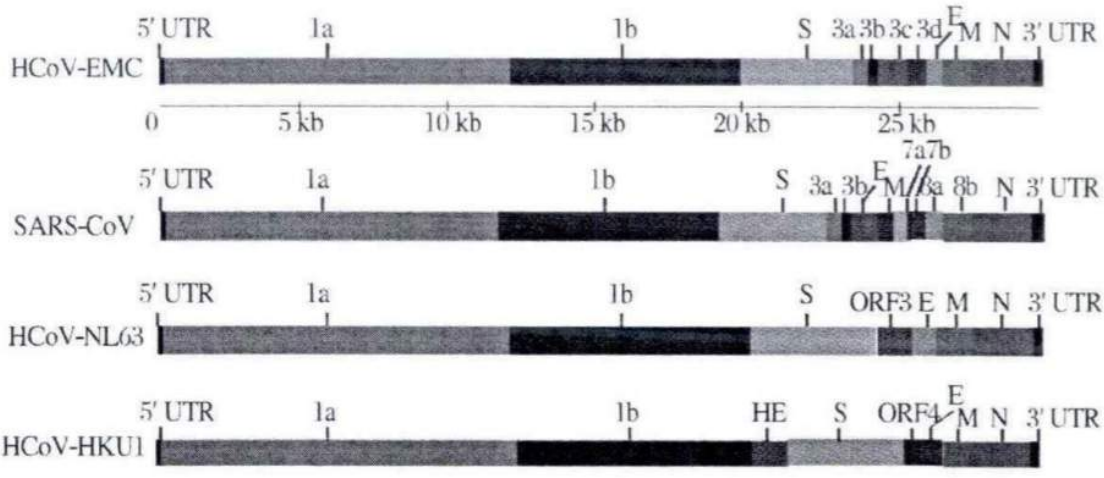
I. Etiology

Virus is a small, simple structure non-cellular life with only one type of Nucleic acid (DNA or RNA). To multiply itself, it has to parasite with a live cell. According to the type and the structure of Nucleic acid, virus is sorted into two kinds: DNA and RNA. Among RNA virus, based on different shapes, it can be categorized into: Paramyxoviridae, Orthomyxoviridae, Retrovirus, Picornaviridae, Coronaviridae, Arenavirus, Rhabdovirida, Filoviridae and so forth.

Based on the categorization, coronavirus belongs to Coronaviridae. One of its varieties is what caused SARS. According to the analysis on the sequence of the nucleic acids, in the ninth report from the International committee on taxonomy of viruses (ICTV), corona virus has four categories: a, β, γ and a presumably new one. β -coronavirus mainly includes severe acute respiratory syndrome (SARS), SARS-like CoV and Chinese rufous horseshoe bat virus Rf1, HKU3, HKU4, HKU5, leopard cat virus and so forth.

About SARS-like-CoV:

In November, 2002, as a new corona virus, SARS had a first outbreak in Guang Dong Province and had spread out in a short timeframe. Because the main symptom is severe acute respiratory illness, it is named SARS-CoV or contagious non-traditional pneumonia. The real host of SARS-CoV had not been found. However, in the process of tracing SARS-CoV, scientists have dissected multiple corona viruses from different kinds of bats. The genetic structure and feature of the corona virus from the Chinese rufous horseshoe bat is similar to SARS-CoV. They have the comparable similarity in Nucleotide, it was between 82 % - 92 %. Hence, this virus was named SARS-like CoV or Bats kind SARS-like Corona Virus [reference 3].



In the previous research, SARS-like CoV [reference 4] was found in the Chinese rufous horseshoe bat in Hong Kong (by bio-chemistry scientist Yuan Guo Yong, Chinese Hong Kong Univeristy), Greater horseshoe bat and Big-eared horseshoe bat in Tian Jing (Li Wen Dong), Rhinolophus Pearsonii in Guang Xi Nan Ning by using RT-PCR examination. If the bats carry SARS-CoV or SARS-like CoV, then very likely they can transmit the disease to human and other animals. In that way, the virus is transferred across different species. However, from other researches, it indicates that when compared the genetic sequence, the SARS-CoV from SARS patients and other animals is more advanced than the SARS-like CoV from the bat. The figures suggested that SARS – CoV, which caused SARS in 2002-2003, is from the evolution group related bats virus [Reference 4]. Therefore, bats corona virus has become the hot topic of international virus study.

II. "Horizontal" Analysis:

1. All 6 patients worked in the same mining cave in different times. The main duty was "cleaning the bats' feces inside the cave", then they all immediately have the illness with "similar syndrome in different degrees".
2. After five patients were admitted into our department in different times (Mr. Wu was admitted to respiratory department), the doctor on duty immediately reported to the medical office about the circumstance in case of an outburst of disease.
3. Four patients were in severe condition when they got admitted to our department. They were in Type I respiration failure, meaning gas exchange function was failing. Hence the reflection of interstitial lung disease and alveoli lesion.
4. After admitted to the hospital, the percentage and count for T, B, NK cells were all substantially low, which means the immune system of the patients were in severe impairment and created chances for multiple infections. In 2011, a scholar mentioned the importance of low CD4 + T lymph in virus infection [reference 5]. Therefore, presume that all 6 patients were infected by the virus.
5. After admission, Patient Guo and Liu did test for etiology (swabs and blood) for SARS-CoV, hemorrhagic fever, Dengue fever, Japanese encephalitis, Influenza A virus and other related virus by Chen Du army reserved Center for Disease Prevention and Control, the result were all negative. A negative on a onetime etiology test could not exempt other related virus.
6. According to Table 1: The major clinical syndrome of the six patients was "coughing, coughing with mucus and fever", some other accompanied syndromes were "difficulty in breathing, soreness in limbs, cough up blood and headache".
7. According to Table 2: The longer the time spent in the mining cave, the likelihood of death is higher. At the same time, the older patient died sooner. In terms of recovery, the fewer the working hours, the younger the patient, the better the recovery. They spend less time in the hospital.
8. According to Table 3: In the first infection related protein test of all 6 patients, SAA were noticeably increasing,

PCT remained in the normal range. It suggested that the six patients possibly had virus infection.

The syndromes of the six patients

表格 1 Table 1 6 位患者入院主诉及伴随症状

症状 / 患者	咳嗽 Coughi	咳痰 Coughi	发热 ≥39℃ Fever	呼吸困难 Difficulty	四肢酸痛 Soreness	血性痰 Bloody	头痛 Headac	胸痛 Chest
Patient Zhou 周 XX	+	+	+	+	+	-	+	+
Patient Lu 吕 XX	+	+	+	+	+	+	-	-
Patient Guo 郭 XX	+	+	+	+	+	+	+	-
Patient Liu 刘 XX	+	+	+	+	+	+	-	+
Patient Wu 吴 XX	+	+	+	+	+	-	+	-
Patient Li 李 XX	+	+	+	-	-	-	-	-

表格 2 Table 2 相关重要信息 Related Important Info

情况 / 患者	入院时间 Date admitted to Hospital	住院天数 Total days of hospitalization	出院情况 Discharge reason	下洞穴工作天数 Number of days spend in the cave	性别 Sex	年龄（岁） Age
Patient Zhou 周 XX	4-26	12	死亡	14	男	63
Patient Lu 吕 XX	4-25	48	死亡	14	男	42
Patient Guo 郭 XX	4-27	109	死亡	14	男	45
Patient Liu 刘 XX	4-26	107	好转	14	男	46
Patient Wu 吴 XX	5-2	26	好转	4	男	30
Patient Li 李 XX	4-26	24	好转	4	男	32

表格 3 Table 3 入院后首次感染相关蛋白 Initial infection related protein test

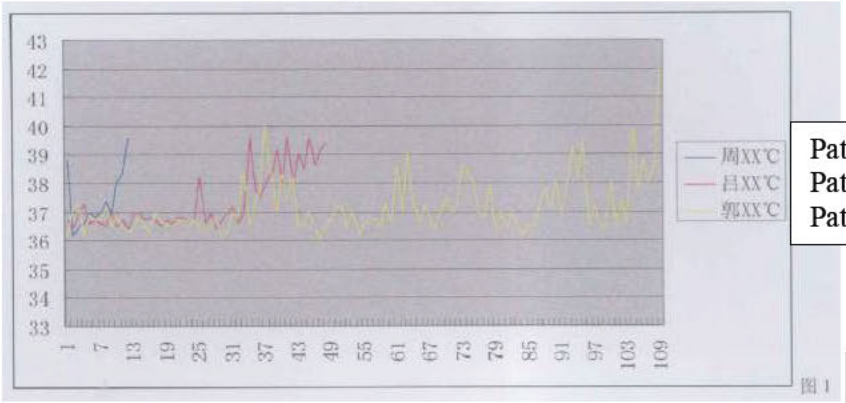
姓名	时间	CRP mg/L	PCT ng/ml	SAA mg/L
Patient Zhou 周 XX	4-27	82.1	0.40	198.00
Patient Lu 吕 XX	4-26	117.0	0.04	398.00
Patient Guo 郭 XX	4-28	23.8	0.04	434.00
Patient Liu 刘 XX	4-27	145.0	0.47	380.00
Patient Wu 吴 XX	5-9	12.6	0.04	44.10
Patient Li 李 XX	4-27	34.2	0.04	79.00

（现院 PCT 用胶体金比色法（B.R.A.H.M.SPCT-Q-半定量快速实验）测得，结果分为四级：正常<0.5ng/mL；轻度升高>0.5ng/mL；明显升高>2ng/mL；显著升高>10ng/mL。）

(For PCT, we used colloidal gold colorimetric (B.R.A.H.M. SPCT-Q Semi-quantitative speedy exam). There are four levels: normal < 0.5 ng/ml; slightly higher > 0.5 ng/ml, substantial higher > 2ng/ml; noticeably higher > 10 ng/ml)

English translation of [illegible] Li Xu of Kunming Medical Un[illegible]

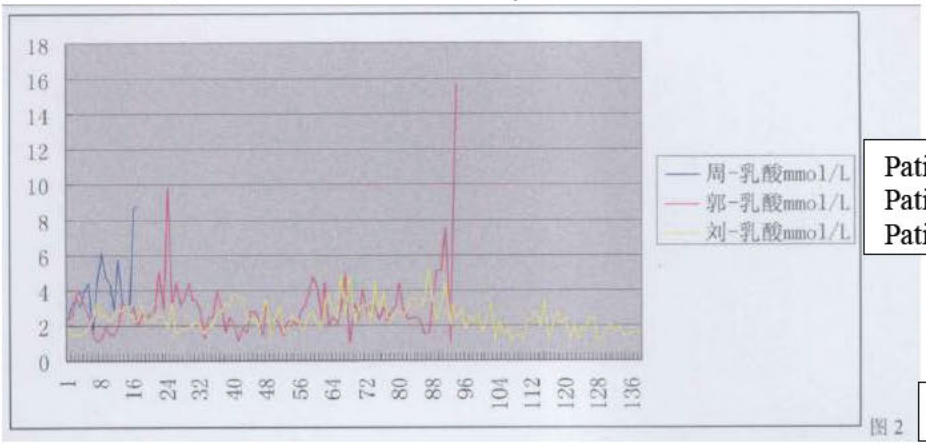
9. Picture 1 shows the temperature line chart of the three dead patients. It suggested three of them were all in high fever.



Patient Zhou
Patient Lu
Patient Guo

Picture 1

10. Picture 2 shows the lactic acid of the three patients in critical stage (Because some of the Lu's information was missing, I wasn't able to do the comparison). According to international and domestic researches, lactic acid is a critical index for monitoring the illness of the patients in critical stage. It is useful in evaluating the severity of hypoxia during shock, tissue hypoperfusion and so forth. It can also predict the possibility of recovery [reference 6]. In our case, the level of lactic acid is related to the rate of death, which resonates with the previous researches.



Patient Zhou
Patient Guo
Patient Liu

Picture 2

12. Phone counselling after the discharge: Patient Liu, has been discharged for 240 days, he was still resting at home. He said his immune system is weak, which makes him catch a cold very easily. He worked out at home to boost up his immune system. The two young adult patients, Patient Wu and Li, both were doing fine after discharge, but also have poor body resistant.
13. Patient Liu was the only recovery case for critical condition patient, we conclude the success of the treatment is: This is a comprehensive treatment as we provided supports in breathing, circulation and nutrients. At the same time, closely monitored the functions of each organs and kept the balance of PH and electrolyte. We

prepared for and immediately took care of any complication, especially any hospital acquired infections.

14. Gaps and failings: (1) Initially, the patients were tested for etiology (swabs and blood) by Chen Du army reserved Center for Disease Prevention and Control and the result was negative. However, a negative on a onetime etiology test could not exempt the possibility of infections caused by other related viruses. In the later stage, we worked with Dr. Zhong Nan Shan and did some sampling. The patient tested positive for Serum IgM by the WuHan Institute of Virology. It suggested the existence of virus infection. Therefore, in the future, if there is any more unknown virus related severe pneumonia or severe group lung infection cases in clinical, we need to be alert to the possibilities of contagiousness and work closely with local center for disease control. That way, we can ensure the prevention, clinical and research for similar kinds of disease. (2) We had three patients died this time. We had considered a lung biopsy before, but we did not do one in the end for various reasons. Currently, diagnosis rate done by biopsy is around 94%. For patients in critical condition, the risk of doing a biopsy with the assistance of ultrasound or CT is very high. Doctors should consider doing fiberoptic bronchoscopy instead. The diagnosis rate is not as high as biopsy but is worth trying. (3) The work of preventing hospital acquired infection should be the priority of ICU. (4) Given all six patients had the same disease but to different degrees, it is important to do autopsy on those who died. Autopsy and Etiology are important for the advancement in medical field. The reluctance of patients' families stands in the way of better understanding the disease. In the future, for unknown and possibly contagious disease, there should be a law which allows immediate autopsy for further examination. (5) For the first two dead patients, we failed to take any blood sampling when they died for the purpose of related examination and scientific research. (6) Given all of the six patients were exposed to huge amount of bats and their feces, also inhaling the smell of the feces, it is important to go sampling the live bats and their feces in the same cave.

III. Future Research

1. About SAA: Recently, there were many researches, internationally and domestically, indicate the increment of SAA during virus or bacterial infection, however, CRP does not increase or the increment is not noticeable in virus infection [reference 7]. Testing for both SAA and CRP can increase the rate of diagnosis for virus infection in the early stage. The testing is also valuable for determining the kinds of virus or bacterial infection and treatment [reference 8-9]. At recent years, the pervasiveness of PCT and its credible application shows that PCT has become the critical index in determining severe bacterial infection [reference 10-11].
2. About Bats: The research on SARS is still ongoing. In the international arena, scholars from Hong Kong are highly respected. They have discovered that the Chinese rufous horseshoe bat plays an important role in understanding the transmission of SARS-CoV.

3. With the Kunming Institute of Zoology, we confirmed that the six patients were exposed to Chinese rufous horseshoe bat, which caused the disease. However, a paper published in *Science* magazine in 2005 by Scientist Shi Zheng Li and Zhang Shu Yi from Wuhan Institute of Virology under Chinese Academy of Science, concluded that the SARS-like-CoV carried by bats is not contagious to humans. This contradiction indicates the importance of these six cases: the severe pneumonia caused by the unknown virus and the bats in the cave merit further investigation and research.

IV. Conclusion

Based on the above mentioned cases and related researches, the unknown virus lead to severe pneumonia could be: The SARS-like-CoV from the Chinese rufous horseshoe bat or Bats kind SARS-like CoV.

参考文献

[1] Virus taxonomy, classification and nomenclature of viruses: ninth report of the International Committee on Taxonomy of Viruses. San Diego, CA: Academic Press, 2012.

[2] World Health Organization(WHO).WHO final summary SARS, 15 August 2003: Summary table of SARS cases by country, 1 November 2002-7 August 2003. Geneva, WHO, 2003.

[3] Lau S K, Woo P C ,Li K S, et al. Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats[J]. Proc Natl Acad Sci, USA, 2005, 102:14040-14045.

[4] Li W, Shi Z, Yu M, et al. Bats are natural reservoirs of SARS-like coronaviruses Science, 2005, 310(5748): 676-679.

[5]Fahey LM, Wilson EB. Viral persistence redirects CD4 T cell differentiation toward T follicular helper cells [J]. Exp Med, 2011, 208(5):987-99.

[6]蒋文中,汤彦.危重病乳酸增高机制及其在预后中价值[J].临床荟萃, 2004, 19(7): 405-407.

[7]Urieli-Shoval S,Linke RP,Matzner Y.Expression and function of serum amyloid A, a major acutephase protein, in normal and disease states[J].Curr Opin Hematol,2000,7(1):64-69.

[8]Lannergard A,Larsson A,Friman G,et al.Human serum amyloid A (SAA) and high sensitive C-reactive protein (hsCRP) in preterm newborn infants with nosocomial infections[J].Acta Paediatr,2008,97(8):1061-1065.

[9]Lannergard A,Larsson A,Cars O,et al.The time course of body temperature, serum amyloid A protein,C-reactive protein and interleukin-6 in patients with bacterial infection during the initial 3 days of antibiotic therapy[J].Scand J Infect Dis,2009,41(9):663-671.

[10]Schuetz P, Christ-Crain M, Thomann R, et al. Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: the ProHOSP randomized controlled trial [J]. JAMA, 2009, 302(10): 1059-1066.

[11]Riedel S, Melendez JH, An AT, et al. Procalcitonin as a marker for the detection of bacteremia and sepsis in the emergency department[J]. Am J Clin Pathol, 2011, 135(2): 182-189.

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English translation of the MSc: "The Analysis of Six Patients With Severe Pneumonia Caused By Unknown Viruses" By Li Xu of Kunming Medical University, 2013. Translation completed: Jun 23rd 2020 (https://www.independentsciencenews.org/)

攻读硕士学位期间发表文章情况

李旭，钱传云，吴海鹰. PiCCO监测血管外肺水对ARDS的指导性治疗[J]. 昆明医科大学学报，2012，(2B)：387-389.

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English translation of the MSc: "The Analysis of Six Patients With Severe Pneumonia Caused By Unknown Viruses" By Li Xu of Kunming Medical University, 2013. Translation completed: Jun 23rd 2020 (https://www.independentsciencenews.org/)

致　谢

时光如梭，白驹过隙，三年的硕士研究生学习生涯即将结束之际，谨对诸多年来给予我关心、支持和帮助的良师益友和亲人们致以最诚挚的谢意。

首先要真诚的感谢我的导师钱传云教授三年来对我的培养。恩师学识渊博、胸襟广阔，他平易近人、和蔼可亲的待人风格；严谨求实的治学态度，丰富的临床经验，精湛的诊疗技术，敏锐活跃的创新思维，敢于创新的科研精神，对医疗事业的无私奉献以及对学生亲切而无私的关怀，都使我铭记于心，是我一生学习的典范，我为一生中有这样的恩师而幸运，在这三年中我的所学所得都离不开恩师的辛勤教诲，在此谨向导师致以最诚挚的感谢，并祝愿导师身体健康，万事如意!

感谢王云徽主任、刘荣副教授、吴海鹰副主任医师、张玮副主任医师、王锦医师、喻雯医师、夏婧医师等在学习、工作中给予的细心指导和帮助。在此，谨向老师们致以最诚挚的感谢！

感谢我的师姐刘金金、朱妮妮，师兄杨耀鹏、洛祖骞，同门唐世凯，师妹张杰、李雪娇、柳金玲，师弟王枭、宋光宇、李正超、杨德兴给予的大力帮助和支持，虽然我们将工作、生活在各自的城市，但我会永远记得你们！

感谢陪伴我度过三年硕士生涯的同寝室友们，我不会忘记和你们共同度过的那些美妙的夜晚。

衷心感谢我的家人，你们永远是我的榜样和拼搏的动力！

感谢昆明医科大学研究生部、昆明医科大学附属第一医院科教处的全体老师三年来的悉心培养、关心和照顾，向你们付出的巨大劳动致以崇高的敬意！

感谢所有关心和帮助过我的老师和同学！

最后衷心地向各位评审老师致以最诚挚的谢意！

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English translation of the MSc: "The Analysis of Six Patients With Severe Pneumonia Caused By Unknown Viruses" By Li Xu of Kunming Medical University, 2013. Translation completed: Jun 23rd 2020 (https://www.independentsciencenews.org/)

From: Lauer, Michael (NIH/OD) [E]
To: Bulls, Michelle G. (NIH/OD) [E]
Cc: Ta, Kristin (NIH/OD) [E]; Lauer, Michael (NIH/OD) [E]
Subject: Re: Draft Package - FW: Follow-up (ROI for Wuhan)
Date: Monday, March 1, 2021 7:35:53 PM
Attachments: ROI - Wuhan Institute of Virology (OPERA DRAFT)[4].doc
ROI - Wuhan - Attachments[2].zip
Wuhan Cable 4f90a905-2b3f-44e0-8cb5-2d9ea5dfc62a..pdf

Hi Michelle – agree, this looks strong.

I found the State Department cable, which should be included. However, before going further, let me discuss with Larry.

Many thanks to you and to Joel.

Mike

From: "Bulls, Michelle G. (NIH/OD) [E]" (b) (6)
Date: Monday, March 1, 2021 at 10:02 AM
To: "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: "Bulls, Michelle G. (NIH/OD) [E]" (b) (6), "Ta, Kristin (NIH/OD) [E]" (b) (6)
Subject: Draft Package - FW: Follow-up (ROI for Wuhan)

Hi Mike,

Joel completed the S&D package for WIV. He outlined the fact that he was not able to use the article pieces as they appeared to be opinions and not factual narrative. He used much of the information that you outlined in the official files and the fact that none of our biosafety concerns have been addressed. I think he pulled together a nice package that outlines the serious nature of biosafety concerns with an apparatus around it which highlights policy, regs, and directions for what we need and they have yet to respond. Please take a look at it and let me know what you think. If you're good with content, I will finalize and send to Tiffani.

Thanks!
Michelle

From: Lauer, Michael (NIH/OD) [E] (b) (6)
Sent: Thursday, February 25, 2021 3:28 PM
To: Bulls, Michelle G. (NIH/OD) [E] (b) (6)
Cc: Lauer, Michael (NIH/OD) [E] (b) (6); Ta, Kristin (NIH/OD) [E] (b) (6)
Subject: Follow-up

Hi Michelle – phone call disconnected. In any case, here's the additional material.

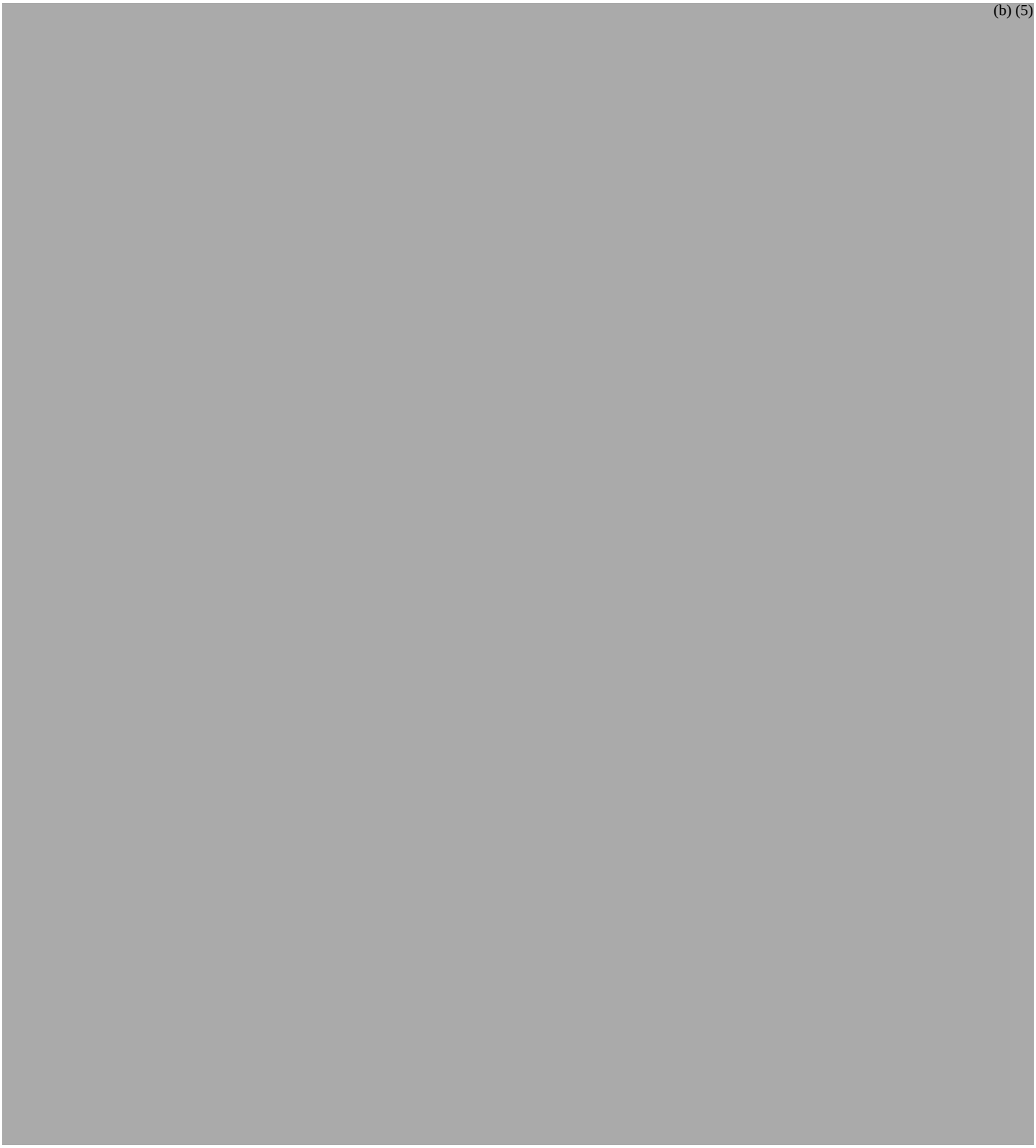
Many thanks, Mike

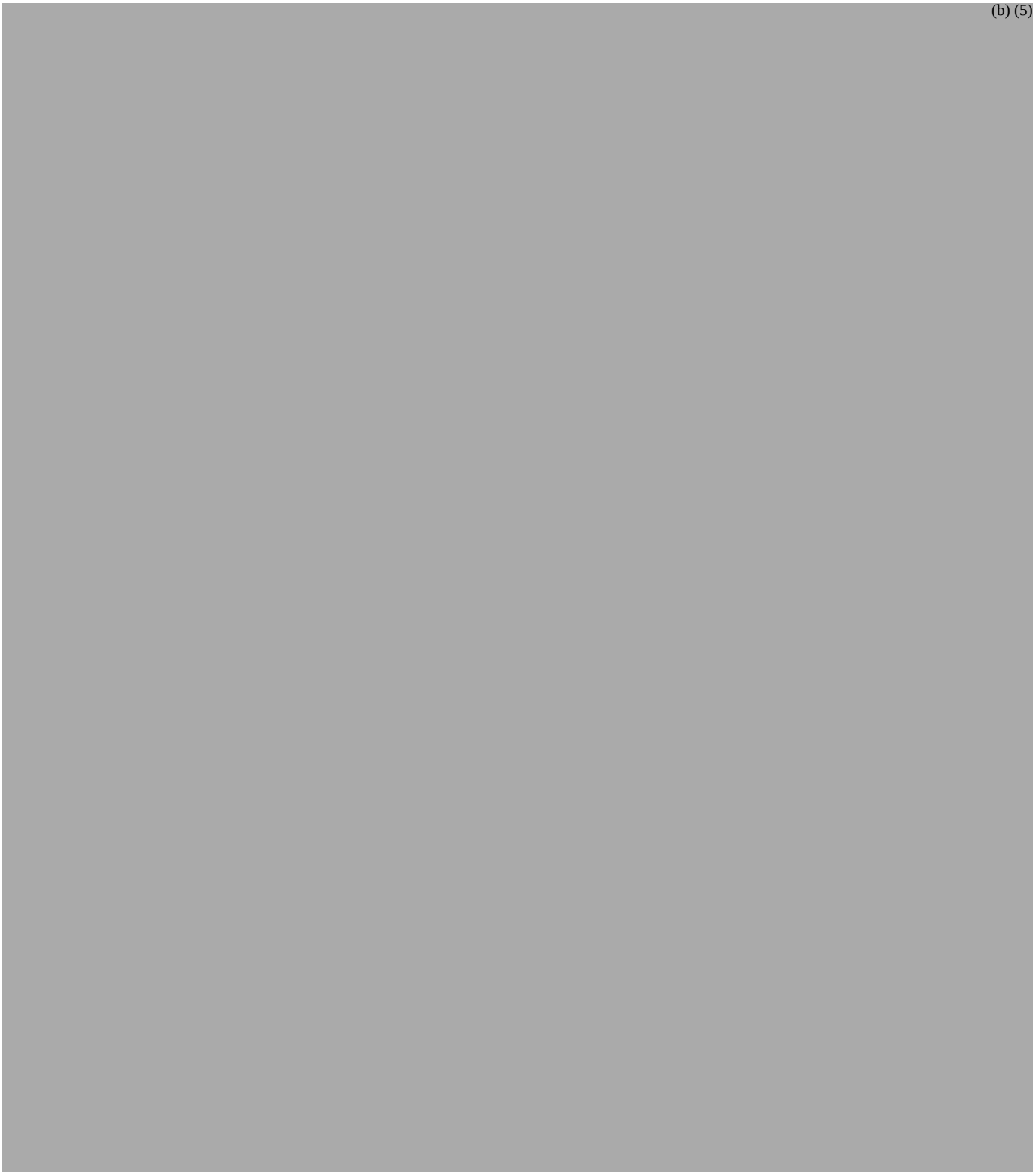
DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

(b) (5)




(b) (5)

RESEARCH
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 07/13/2020

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 2R01AI110964-06 REVISED
FAIN: R01AI110964

Principal Investigator(s):
PETER DASZAK, PHD

Project Title: Understanding the Risk of Bat Coronavirus Emergence

Dr. Daszak, Peter
PD/PI
460 West 34th Street
Suite 1701
New York, NY 100012320

Award e-mailed to: (b) (6)

Period Of Performance:
Budget Period: 07/24/2019 – 06/30/2021
Project Period: 06/01/2014 – 06/30/2025

Dear Business Official:

The National Institutes of Health hereby revises this award to reflect an increase in the amount of $369,819 (see “Award Calculation” in Section I and “Terms and Conditions” in Section III) to ECOHEALTH ALLIANCE, INC. 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 R01AI110964. 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,

Emily Linde
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 2R01AI110964-06 REVISED

Award Calculation (U.S. Dollars)

Salaries and Wages	$170,325
Fringe Benefits	$53,654
Personnel Costs (Subtotal)	$223,979
Consultant Services	$49,809
Materials & Supplies	$20,170
Travel	$15,045
Subawards/Consortium/Contractual Costs	$229,923
Federal Direct Costs	$538,926
Federal F&A Costs	$123,054
Approved Budget	$661,980
Total Amount of Federal Funds Obligated (Federal Share)	$661,980
TOTAL FEDERAL AWARD AMOUNT	$661,980
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$369,819

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
6	$661,980	$661,980
7	$637,980	$637,980
8	$637,980	$637,980
9	$637,980	$637,980
10	$637,980	$637,980

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Allergy and Infectious Diseases Research
CFDA Number:	93.855
EIN:	1311726494A1
Document Number:	RAI110964B
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019	2021	2022	2023	2024
AI	8472364	$661,980	$637,980	$637,980	$637,980	$637,980

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C B / **OC**: 41022 / **Released**: (b) (6) 07/13/2020
Award Processed: 07/15/2020 12:00:48 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 2R01AI110964-06 REVISED

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 – 2R01AI110964-06 REVISED

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).

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) R01AI110964. 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/.

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 – 2R01AI110964-06 REVISED

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.

REVISED AWARD: Pursuant to the letter to EcoHealth Alliance, Inc. dated July 8, 2020, this award has been reinstated; however, all activities are suspended until such time as these concerns in the letter have been addressed to NIH's satisfaction.

Supersedes previous Notice of Award dated 04/27/2020. All other terms and conditions still apply to this award.

REVISED AWARD: This award is revised to adjust the budget in accordance with the letter from Aleksei Chmura/ECOHealth Alliance.

Supersedes previous Notice of Award dated **07/24/2019**.

****
This Notice of Award (NoA) includes funds for activity with **The University of North Carolina at Chapel Hill** in the amount of **$77,750** (**$50,000** direct costs + **$27,750**F&A costs).

This Notice of Award (NoA) includes funds for activity with **Wuhan Institute of Virology** in the amount of **$76,301** (**$70,649** direct costs + **$5,652** F&A costs).

This Notice of Award (NoA) includes funds for activity with **Institute of Pathogen Biology** in the amount of **$75,600** (**$70,000** direct costs + **$5,600** F&A costs).

****
The Research Performance Progress Report (RPPR), Section G.9 (Foreign component), includes reporting requirements for all research performed outside of the United States. Research conducted at the following site(s) must be reported in your RPPR:

Wuhan Institute of Virology, CHINA

Institute of Pathogen Biology, CHINA

East China Normal University, CHINA

Duke-NUS Medical School, SINGAPORE

****
This award reflects current Federal policies regarding Facilities & Administrative (F&A) Costs for foreign grantees including foreign sub-awardees, and domestic awards with foreign sub-awardees. Please see: Chapter 16 Grants to Foreign Organizations, International Organizations, and Domestic Grants with Foreign Components, Section 16.6 "Allowable and Unallowable Cost" of the NIH Grants Policy.

****
This award may include collaborations with and/or between foreign organizations. Please be advised that short term travel visa expenses are an allowable expense on this grant, if justified as critical and necessary for the conduct of the project.

****
The budget period anniversary start date for future year(s) will be **July** 1.

****

N H NGA R | Version: 56 - 12/26/2018 2 22:00 PM| Generated on: 7/15/2020 12:00:48 AM

Dissemination of study data will be in accord with the Recipient's accepted genomic data sharing plan as stated in the page(s) **203** of the application. Failure to adhere to the sharing plan as mutually agreed upon by the Recipient and the NIAID may result in Enforcement Actions as described in the NIH Grants Policy Statement.

****

This award is subject to the Clinical Terms of Award referenced in the NIH Guide for Grants and Contracts, July 8, 2002, NOT AI-02-032. These terms and conditions are hereby incorporated by reference, and can be accessed via the following World Wide Web address: https://www.niaid.nih.gov/grants-contracts/niaid-clinical-terms-award All submissions required by the NIAID Clinical Terms of Award must be forwarded electronically or by mail to the responsible NIAID Program Official identified on this Notice of Award.

****

Awardees who conduct research involving Select Agents (see 42 CFR 73 for the Select Agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens at http://www.selectagents.gov/Regulations.html) must complete registration with CDC (or APHIS, depending on the agent) before using NIH funds. No funds can be used for research involving Select Agents if the final registration certificate is denied.

Prior to conducting a restricted experiment with a Select Agent or Toxin, awardees must notify the NIAID and must request and receive approval from CDC or APHIS.

****

Select Agents:
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: Shaun W Gratton
Email: (b) (6) **Phone**: (b) (6)

Program Official: Erik J. Stemmy
Email: (b) (6) **Phone**: (b) (6)

SPREADSHEET SUMMARY
GRANT NUMBER: 2R01AI110964-06 REVISED

INSTITUTION: ECOHEALTH ALLIANCE, INC.

Budget	Year 6	Year 7	Year 8	Year 9	Year 10
Salaries and Wages	$170,325	$170,123	$170,123	$170,123	$170,123
Fringe Benefits	$53,654	$53,590	$53,590	$53,590	$53,590
Personnel Costs (Subtotal)	$223,979	$223,713	$223,713	$223,713	$223,713
Consultant Services	$49,809	$49,750	$49,750	$49,750	$49,750
Materials & Supplies	$20,170	$14,850	$14,850	$14,850	$14,850
Travel	$15,045	$15,027	$15,027	$15,027	$15,027
Subawards/Consortium/Contractual Costs	$229,923	$229,651	$229,651	$229,651	$229,651
Publication Costs		$6,000	$6,000	$6,000	$6,000
TOTAL FEDERAL DC	$538,926	$538,991	$538,991	$538,991	$538,991
TOTAL FEDERAL F&A	$123,054	$98,989	$98,989	$98,989	$98,989
TOTAL COST	$661,980	$637,980	$637,980	$637,980	$637,980

Facilities and Administrative Costs	Year 6	Year 7	Year 8	Year 9	Year 10
F&A Cost Rate 1	32%	32%	32%	32%	32%
F&A Cost Base 1	$384,547	$309,340	$309,340	$309,340	$309,340
F&A Costs 1	$123,054	$98,989	$98,989	$98,989	$98,989

Date: April 19, 2020

From: Michael S Lauer, MD
NIH Deputy Director for Extramural Research

To: Kevin Olival, PhD
Vice-President for Research
EcoHealth Alliance
(b) (6)

Naomi Schrag, JD
Vice-President for Research Compliance, Training, and Policy
Columbia University
(b) (6)

Subject: Project Number 2R01AI110964-06

Dear Dr. Olival and Ms. Schrag:

EcoHealth Alliance, Inc. is the recipient, as grantee, of an NIH grant entitled "Understanding the Risk of Bat Coronavirus Emergence." It is our understanding that one of the sub-recipients of the grant funds is the Wuhan Institute of Virology ("WIV"). It is our understanding that WIV studies the interaction between corona viruses and bats. The scientific community believes that the coronavirus causing COVID-19 jumped from bats to humans likely in Wuhan where the COVID-19 pandemic began. There are now allegations that the current crisis was precipitated by the release from WIV of the coronavirus responsible for COVID-19. Given these concerns, we are pursuing suspension of WIV from participation in Federal programs.

While we review these allegations during the period of suspension, you are instructed to cease providing any funds from the above noted grant to the WIV. This temporary action is authorized by 45 C.F.R. § 75.371(d) ("Initiate suspension or debarment proceedings as authorized under 2 C.F.R. part 180"). The incorporated OMB provision provides that the funding agency may, through suspension, immediately and temporarily exclude from Federal programs persons who are not presently responsible where "immediate action is necessary to protect the public interest." 2 C.F.R. § 180.700(c). It is in the public interest that NIH ensure that a sub-recipient has taken all appropriate precautions to prevent the release of pathogens that it is studying. This suspension of the sub-recipient does not affect the remainder of your grant assuming that no grant funds are provided to WIV following receipt of this email during the period of suspension.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

24 April 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: Termination of NIH Grant R01 AI 110964

Dear Drs. Chmura and Daszak:

I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS) has elected to terminate the project *Understanding the Risk of Bat Coronavirus Emergence*, funded under grant R01 AI110964, for convenience. This grant project was issued under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284). This grant was funded as a discretionary grant as outlined in the NIH Grants Policy Statement, which states that the decision not to award a grant, or to award a grant at a particular funding level, is at the discretion of the agency, in accordance with NIH's dual review system.

At this time, NIH does not believe that the current project outcomes align with the program goals and agency priorities. NIAID has determined there are no animal and human ethical considerations, as this project is not a clinical trial, but rather an observational study.

As a result of this termination, a total of $369,819.56 will be remitted to NIAID and additional drawdowns will not be supported. The remaining funds have been restricted in the HHS Payment Management System, effective immediately.

Please let me know if you have any questions concerning the information in this letter.

Sincerely,

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy
Ms. Emily Linde

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

8 July 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

In follow-up to my previous letter of April 24, 2020, I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS), has withdrawn its termination of grant R01AI110964, which supports the project *Understanding the Risk of Bat Coronavirus Emergence*. Accordingly, the grant is reinstated.

However, as you are aware, the NIH has received reports that the Wuhan Institute of Virology (WIV), a subrecipient of EcoHealth Alliance under R01AI110964, has been conducting research at its facilities in China that pose serious bio-safety concerns and, as a result, create health and welfare threats to the public in China and other countries, including the United States. Grant award R01AI110964 is subject to biosafety requirements set forth in the NIH Grants Policy Statement (e.g., NIH GPS, Section 4.1.24 "Public Health Security") and the Notice of Award (e.g., requiring that "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]."). Moreover, NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients. 45 C.F.R. § 75.101.

As the grantee, EcoHealth Alliance was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). We have concerns that WIV has not satisfied safety requirements under the award, and that EcoHealth Alliance has not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance.

Moreover, as we have informed you through prior Notices of Award, this award is subject to the Transparency Act subaward and executive compensation reporting requirement of 2 C.F.R. Part

170. To date you have not reported any subawards in the Federal Subaward Reporting System.

Therefore, effective the date of this letter, July 8, 2020, NIH is suspending all activities related to R01AI110964, until such time as these concerns have been addressed to NIH's satisfaction. This suspension is taken in accordance with 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable in accordance with 42 C.F.R. § 50.404 and the NIH GPS Section 8.7, Grant Appeals Procedures. However, EcoHealth Alliance has the opportunity to provide information and documentation demonstrating that WIV and EcoHealth Alliance have satisfied the above-mentioned requirements.

Specifically, to address the NIH's concerns, EcoHealth must provide the NIH with the following information and materials, which must be complete and accurate:

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.
3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.
4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.
5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.
6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.
7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

During this period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further asses compliance by EcoHealth Alliance and WIV, including compliance with other terms and conditions of award that may be implicated. Additionally, during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the

recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. Once the original award is reinstated, NIH will take additional steps to restrict all funding in the HHS Payment Management System in the amount of $369,819. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 CFR Part 75, including, but not limited to, terminating the grant award. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

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Sincerely,

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy
Ms. Emily Linde

UNCLASSIFIED
SBU

MRN:	18 BEIJING 138
Date/DTG:	Jan 19, 2018 / 190739Z JAN 18
From:	AMEMBASSY BEIJING
Action:	WASHDC, SECSTATE *ROUTINE*
E.O.:	13526
TAGS:	SHLH, ETRD, ECON, PGOV, CN
Captions:	SENSITIVE
Reference:	17 WUHAN 48
Subject:	China Opens First Bio Safety Level 4 Laboratory

1. (SBU) **Summary and Comment:** The Chinese Academy of Sciences (CAS) has recently established what is reportedly China's first Biosafety Level 4 (BSL-4) laboratory in Wuhan. This state-of-the-art facility is designed for prevention and control research on diseases that require the highest level of biosafety and biosecurity containment. Ultimately, scientists hope the lab will contribute to the development of new antiviral drugs and vaccines, but its current productivity is limited by a shortage of the highly trained technicians and investigators required to safely operate a BSL-4 laboratory and a lack of clarity in related Chinese government policies and guidelines. (b)(5)

(b)(5)

(b)(5) **End Summary and Comment.**

China Investing in Infectious Disease Control

2. (U) Between November 2002 and July 2003, China faced an outbreak of Severe Acute Respiratory Syndrome (SARS), which, according to the World Health Organization, resulting in 8,098 cases and leading to 774 deaths reported in 37 countries. A majority of cases occurred in China, where the fatality rate was 9.6%. This incident convinced China to prioritize international cooperation for infectious disease control. An aspect of this prioritization was China's work with the Jean Merieux BSL-4 Laboratory in Lyon, France, to build China's first high containment laboratory at Wuhan's Institute of Virology (WIV), an institute under the auspices of the Chinese Academy of Sciences (CAS). Construction took 11 years and $44 million USD, and construction on the facility was completed on January 31, 2015. Following

two years of effort, which is not unusual for such facilities, the WIV lab was accredited in February 2017 by the China National Accreditation Service for Conformity Assessment. It occupies four floors and consists of over 32,000 square feet. WIV leadership now considers the lab operational and ready for research on class-four pathogens (P4), among which are the most virulent viruses that pose a high risk of aerosolized person-to-person transmission.

Unclear Guidelines on Virus Access and a Lack of Trained Talent Impede Research

3. (SBU) In addition to accreditation, the lab must also receive permission from the National Health and Family Planning Commission (NHFPC) to initiate research on specific highly contagious pathogens. According to some WIV scientists, it is unclear how NHFPC determines what viruses can or cannot be studied in the new laboratory. To date, WIV has obtained permission for research on three viruses: Ebola virus, Nipah virus, and Xinjiang hemorrhagic fever virus (a strain of Crimean Congo hemorrhagic fever found in China's Xinjiang Province). Despite this permission, however, the Chinese government has not allowed the WIV to import Ebola viruses for study in the BSL-4 lab. Therefore, WIV scientists are frustrated and have pointed out that they won't be able to conduct research project with Ebola viruses at the new BSL-4 lab despite of the permission.

(b)(6)

(b)(6) Thus, while the BSL-4 lab is ostensibly fully accredited, its utilization is limited by lack of access to specific organisms and by opaque government review and approval processes. As long as this situation continues, Beijing's commitment to prioritizing infectious disease control - on the regional and international level, especially in relation to highly pathogenic viruses, remains in doubt.

(b)(6) noted that the new lab has a serious shortage of appropriately trained technicians and investigators needed to safely operate this high-containment laboratory. University of Texas Medical Branch in Galveston (UTMB), which has one of several well-established BSL-4 labs in the United States (supported by the National Institute of Allergy and Infectious Diseases (NIAID of NIH)), has scientific collaborations with WIV, which may help alleviate this talent gap over time. Reportedly, researchers from GTMB are helping train technicians who work in the WIV BSL-4 lab. Despite this, (b)(6) they would welcome more help from U.S. and international organizations as they establish "gold standard" operating procedures and training courses for the first time in China. As China is building more BSL-4 labs, including one in Harbin Veterinary Research Institute subordinated to the Chinese Academy of Agricultural Sciences (CAAS) for veterinary research use (b)(6) the training for technicians and investigators working on dangerous pathogens will certainly be in demand.

Despite Limitations, WIV Researchers Produce SARS Discoveries

6. (SBU) The ability of WIV scientists to undertake productive research despite limitations on the use of the new BSL-4 facility is demonstrated by a recent publication on the origins of SARS. Over a five-year study, (b)(6) (and their research team) widely sampled bats in Yunnan province with funding support from NIAID/NIH, USAID, and several Chinese funding agencies. The study results were published in PLoS Pathogens online on Nov. 30, 2017 (1), and it demonstrated that a SARS-like coronaviruses isolated from horseshoe bats in a single cave contain all the building blocks of the pandemic SARS-coronavirus genome that caused the human outbreak. These results strongly suggest that the highly pathogenic SARS-coronavirus originated in this bat population. Most importantly, the researchers also showed that various SARS-like coronaviruses can interact with ACE2, the human receptor identified for SARS-coronavirus. This finding strongly suggests that SARS-like coronaviruses from bats can be transmitted to humans to cause SARS-like disease. From a public health perspective, this makes the continued surveillance of SARS-like coronaviruses in bats and study of the animal-human interface critical to future emerging coronavirus outbreak prediction and prevention. (b)(5) (b)(5) WIV scientists are allowed to study the SARS-like coronaviruses isolated from bats while they are precluded from studying human-disease causing SARS coronavirus in their new BSL-4 lab until permission for such work is granted by the NHFCP.

1. Hu B, Zeng L-P, Yang X-L, Ge X-Y, Zhang W, Li B, et al. (2017) Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. PLoS Pathog 13(11): e1006698. https://doi.org/10.1371/journal.ppat.1006698

Signature:	BRANSTAD
Drafted By:	(b)(6)
Cleared By:	
Approved By:	
Released By:	
Info:	CHINA POSTS COLLECTIVE *ROUTINE*
Dissemination Rule:	Archive Copy

UNCLASSIFIED
SBU

From:	Lauer, Michael (NIH/OD) [E]
To:	Wojtowicz, Emma (NIH/OD) [E]; Kosub, David (NIH/OD) [E]; OER Press Group
Cc:	Myles, Renate (NIH/OD) [E]; Fine, Amanda (NIH/OD) [E]; Lauer, Michael (NIH/OD) [E]
Subject:	Re: Media Inquiry from PolitiFact
Date:	Wednesday, February 3, 2021 10:30:05 PM
Attachments:	Re Media Response Review Politifact - Difference in EcoHealth Alliance Grants.msg

Hi Emma – sorry, see attached. My apologies, I'm a bit confused by the different email trails.

Mike

From: "Wojtowicz, Emma (NIH/OD) [E]" (b) (6)
Date: Wednesday, February 3, 2021 at 6:45 PM
To: "Kosub, David (NIH/OD) [E]" (b) (6), OER Press Group (b) (6), "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: "Myles, Renate (NIH/OD) [E]" (b) (6), "Fine, Amanda (NIH/OD) [E]" (b) (6)
Subject: RE: Media Inquiry from PolitiFact

+Mike, thanks for your review on the other EcoHealth inquiry.

Sorry to keep nudging, (b) (5). Do you think you will be able to get back to us tonight with the language we asked for?

Thank you!
Emma

From: Kosub, David (NIH/OD) [E] (b) (6)
Sent: Wednesday, February 3, 2021 2:45 PM
To: Wojtowicz, Emma (NIH/OD) [E] (b) (6); OER Press Group (b) (6)
Cc: Myles, Renate (NIH/OD) [E] (b) (6); Fine, Amanda (NIH/OD) [E] (b) (6)
Subject: RE: Media Inquiry from PolitiFact

Hi yes, working on it. sorry for radio silence.
D

From: Wojtowicz, Emma (NIH/OD) [E] (b) (6)
Sent: Wednesday, February 3, 2021 2:40 PM
To: OER Press Group (b) (6)
Cc: Myles, Renate (NIH/OD) [E] < (b) (6); Fine, Amanda (NIH/OD) [E] (b) (6)
Subject: RE: Media Inquiry from PolitiFact

Hi All-

Sorry to ping you, but I wanted to make sure that you saw my email below and will get back to us soon with language. We also are waiting to hear back on the other EcoHealth inquiry that we sent to Mike this morning, please see attached.

Thank you-
Emma

From: Wojtowicz, Emma (NIH/OD) [E]
Sent: Wednesday, February 3, 2021 12:44 PM
To: OER Press Group (b) (6)>
Cc: Myles, Renate (NIH/OD) [E] (b) (6); Fine, Amanda (NIH/OD) [E] (b) (6)
Subject: FW: Media Inquiry from PolitiFact

Hello OER-

As you are aware, we have been receiving many inquiries about EcoHealth as a result of Fox segment reporting that the original grant supported gain-of-function research. Please see the inquiry below from PolitiFact asking for clarification on the relationship between the grants. Can you please help us and provide language explaining how the original grant was for 5 years and renewed in 2019 and what that means. Once we have this language we will go back to Fox as well.

Thank you in advance for your help-
Emma

From: Noah Kim <(b) (6)
Sent: Wednesday, February 3, 2021 11:46 AM
To: Wojtowicz, Emma (NIH/OD) [E] (b) (6)
Cc: Myles, Renate (NIH/OD) [E] (b) (6); Fine, Amanda (NIH/OD) [E] (b) (6)
Subject: Re: Media Inquiry from PolitiFact

Hi Emma,

Thanks a lot for this, I really appreciate it. Would you mind explaining the difference between grants 1R01AI110964-01 and 2R01AI110964-06? My guess is that grant 1R01AI110964-01 is a sub-award of the larger grant 2R01AI110964-06, but it would be good to get some clarification.

For context, the Fox segment we're looking into addresses a similar statement that the NIH sent them. The Fox commentator claims that the NIH addressed his questions about project 2R01AI110964-06 even though he had asked about project 1R01AI110964-01. He then goes onto claim that project 1R01AI110964-01 included gain-of-function research at the Wuhan Institute,

but not 2R01AI110964-06. The relevant clip starts around 10:22 in this video.

In order to debunk this, I'm hoping to address the specific allegations made by the commentator, and it would be very helpful to get some clarification.

Best,
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> Thanks for checking with us. Attributable to NIH generally:
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> EcoHealth Alliance Inc. is the grantee organization, which made sub-awards to Wuhan Institute of Virology (Wuhan), East China Normal University (Shanghai), the Institute of Pathogen Biology (Beijing), and Duke-NUS Medical School (Singapore). Publicly available information about the grant to EcoHealth Alliance Inc. is available on NIH RePORTER at this link. For Information about the distribution to sub-awardees please visit USASpending.gov and switch from "Prime Awards" to "Sub-Awards" in the upper right corner.
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> To clarify, the research supported under the grant to EcoHealth Alliance Inc. characterized the function of newly discovered bat spike proteins and naturally occurring pathogens and did not involve the enhancement of the pathogenicity or transmissibility of the viruses studied. Therefore, after review NIAID determined the awards were not subject to either the Gain-of-Function Research Funding Pause or its successor, the DHHS Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens.
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> For additional background, here is the Director's statement about NIH lifting the pause on gain-of-function research: https://www.nih.gov/about-nih/who-we-are/nih-director/statements/nih-lifts-funding-pause-gain-function-research.
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> The Office of the Director of National Intelligence issued a statement on their investigation into the origins of the outbreak. Any questions related to the origins of the outbreak should be directed to ODNI.
>
> Thank you-
> Emma
>
> **Emma Wojtowicz**
> Public Affairs Specialist

National Institutes of Health
Tel: (b) (6)
Email: (b) (6)
Web: http://www.nih.gov

NIH . . . Turning Discovery Into Health

From: Noah Kim (b) (6)
Sent: Wednesday, February 3, 2021 10:11 AM
To: Wojtowicz, Emma (NIH/OD) [E] (b) (6)
Subject: Media Inquiry from PolitiFact

Hi Emma,

My name is Noah Kim, and I'm a reporter with PolitiFact.

We're trying to debunk a viral claim that's circulating social media about Dr. Fauci. It's a variation on other conspiracy theories that have cropped up over the source of this pandemic.

The thrust of the claim is that Dr. Fauci advocated for gain-of-function research in 2011. This appears to be true. However, the claim goes further than that, saying that "Fauci's National Institute of Allergy and Infectious Diseases" funded gain-of-function research at the Wuhan Institute of Virology, and that it is a "near certainty" that Sars-Cov-2 was lab-made.

I was wondering if you'd mind sending me a statement/any materials pushing back on these claims.

I'd be especially curious to know if there's any truth to the fact that the NIH funded the Wuhan Institute of Virology. (This wouldn't establish the veracity of the conspiracy theory, but it would allow me to share with our readers how this conspiracy theory may have originated from a germ of truth.) I'd also be curious to know the scientific basis behind why we know it is extremely unlikely that Sars-Cov-2 was manufactured or engineered at the Wuhan Institute.

Thanks a lot for your time and help,
Noah

From:	Lauer, Michael (NIH/OD) [E]
To:	Rabin, Elise (NIH/OD) [E]; Kosub, David (NIH/OD) [E]; Bulls, Michelle G. (NIH/OD) [E]; Wojtowicz, Emma (NIH/OD) [E]
Cc:	OER Press Group; Ta, Kristin (NIH/OD) [E]; Lauer, Michael (NIH/OD) [E]
Subject:	Re: Media Response Review: Politifact - Difference in EcoHealth Alliance Grants
Date:	Wednesday, February 3, 2021 10:29:02 PM

Thanks Elise – looks fine. I'm looping in Emma. Sorry if I'm confused by different email trails.

Mike

From: "Rabin, Elise (NIH/OD) [E]" (b) (6)
Date: Wednesday, February 3, 2021 at 6:58 PM
To: "Lauer, Michael (NIH/OD) [E]" (b) (6), "Kosub, David (NIH/OD) [E]" (b) (6), "Bulls, Michelle G. (NIH/OD) [E]" (b) (6)
Cc: OER Press Group (b) (6), "Ta, Kristin (NIH/OD) [E]" (b) (6)
Subject: RE: Media Response Review: Politifact - Difference in EcoHealth Alliance Grants

Hi Mike –

This addresses only part one of the question, and is OPERA's proposed response after revising David's original language:

(b) (5)

We believe that part two of the reporter's question (all the way at the bottom of this message) pertaining to gain of function should go to NIAID and OSP for review and response. Thoughts – recognizing that Emma is waiting?

- Elise

From: Lauer, Michael (NIH/OD) [E] (b) (6)
Sent: Wednesday, February 3, 2021 5:40 PM
To: Kosub, David (NIH/OD) [E] (b) (6); Bulls, Michelle G. (NIH/OD) [E]

(b) (6)
Cc: OER Press Group (b) (6); Ta, Kristin (NIH/OD) [E] (b) (6); Lauer, Michael (NIH/OD) [E] (b) (6)
Subject: Re: Media Response Review: Politifact - Difference in EcoHealth Alliance Grants

Many thanks – could you send me the proposed response? I'm having trouble figuring it out.

Mike

From: "Kosub, David (NIH/OD) [E]" (b) (6)
Date: Wednesday, February 3, 2021 at 5:10 PM
To: "Bulls, Michelle G. (NIH/OD) [E]" (b) (6), "Lauer, Michael (NIH/OD) [E]" (b) (6)
Cc: OER Press Group (b) (6), "Ta, Kristin (NIH/OD) [E]" (b) (6)
Subject: RE: Media Response Review: Politifact - Difference in EcoHealth Alliance Grants

Thanks Michelle.
Mike, appreciate any additional thoughts you may have on Michelle's revised response. OCPL is hoping for a response on this and the other request Emma made earlier (which I can re-forward to you).

Thanks
David

From: Bulls, Michelle G. (NIH/OD) [E] (b) (6)
Sent: Wednesday, February 3, 2021 4:50 PM
To: Kosub, David (NIH/OD) [E] (b) (6); Lauer, Michael (NIH/OD) [E] (b) (6)
Cc: OER Press Group < (b) (6); Ta, Kristin (NIH/OD) [E] (b) (6); Bulls, Michelle G. (NIH/OD) [E] (b) (6)
Subject: RE: Media Response Review: Politifact - Difference in EcoHealth Alliance Grants

Hi David,
Just seeing this, (b) (5). See below for possible revisions.

From: Kosub, David (NIH/OD) [E] (b) (6)
Sent: Wednesday, February 3, 2021 2:32 PM
To: Lauer, Michael (NIH/OD) [E] (b) (6); Bulls, Michelle G. (NIH/OD) [E] (b) (6)
Cc: OER Press Group (b) (6); Ta, Kristin (NIH/OD) [E] (b) (6)
Subject: Media Response Review: Politifact - Difference in EcoHealth Alliance Grants

Good day Mike and OPERA,

A reporter with Politifact would like NIH to explain the difference between 1R01AI110964-01 and 2R01AI110964-06 awarded to EcoHealth Alliance. Though we can help the reporter decipher the relationship between the grants as requested by OCPL (i.e. difference between -01 original award and -06 renewal), we were wondering if the rest of the question should perhaps go to NIAID and/or OSP to explain the difference in the actual research being supported by each award (and if GOF was involved). This question stems from a Fox segment reporting that the original grant supported gain-of-function research. Appreciate your thoughts.

Proposed Response for the first part of the question:

(b) (5)

From: Wojtowicz, Emma (NIH/OD) [E] (b) (6)
Sent: Wednesday, February 3, 2021 12:44 PM
To: OER Press Group (b) (6)
Cc: Myles, Renate (NIH/OD) [E] (b) (6); Fine, Amanda (NIH/OD) [E] (b) (6)
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Emma Wojtowicz
Public Affairs Specialist
National Institutes of Health
Tel: (b) (6)
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NIH . . . Turning Discovery Into Health

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From: Lauer, Michael (NIH/OD) [E]
To: Tabak, Lawrence (NIH/OD) [E]
Cc: Lauer, Michael (NIH/OD) [E]
Subject: FW: Meeting about ECCO health
Date: Sunday, January 31, 2021 3:00:22 PM
Attachments: NIH Response to EcoHealth Response to Suspension_10_23_20.pdf
Daszak 7 8 20.pdf
Did the Coronavirus Escape From a Lab.pdf
The World Needs a Real Investigation Into the Origins of Covid-19 - WSJ.pdf
29246.full-2.pdf

Hi Larry – materials that might be helpful.

Thanks, Mike

From: "Tabak, Lawrence (NIH/OD) [E]" (b) (6)
Date: Sunday, January 31, 2021 at 2:35 PM
To: "McManus, Ayanna (NIH/OD) [E]" (b) (6), "Wood, Gretchen (NIH/OD) [E]" (b) (6)
Cc: "Lauer, Michael (NIH/OD) [E]" (b) (6), "Wolinetz, Carrie (NIH/OD) [E]" (b) (6)
Subject: Meeting about ECCO health

Francis would like a meeting with Mike, Carrie, and me about ECCO health, this week or next.
30 min should suffice.
Thanks
Larry

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

23 October 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

I am following up on Mr. Krinsky's August 13, 2020, letter on behalf of EcoHealth Alliance, Inc. ("EcoHealth") responding to NIH's suspension of grant R01AI110964, which funds the project *Understanding the Risk of Bat Coronavirus Emergence* (the "Project"). Per my letter of July 8, 2020, NIH reinstated the grant but suspended all award activities because we have concerns that the Wuhan Institute of Virology (WIV), which previously served as a subrecipient of the Project, had not satisfied safety requirements that applied to its subawards with EcoHealth, and that EcoHealth had not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance. EcoHealth objected to the suspension on the grounds that WIV has no *current* connection to the Project or EcoHealth's research, and EcoHealth had not issued any subawards in connection with the Grant *at the time of the suspension*.

The fact that EcoHealth does not currently have a subrecipient relationship with WIV and had not issued subawards to WIV at the time of suspension does not absolve EcoHealth of any past non-compliance with the terms and conditions of award for grant R01AI110964. While EcoHealth did not issue a subaward to WIV for year 6 of the grant, WIV served as a subrecipient for years 1 through 5. NIH awarded EcoHealth grant R01AI110964 in 2014, with a project period of June 1, 2014, through June 30, 2024, as renewed. In EcoHealth's grant application, EcoHealth listed Drs. Zheng Li Shi and Xing Yi Ge of WIV as co-investigators and senior/key personnel. It stated that "Drs. Shi, Zhang, and Daszak have collaborated together since 2002 and have been involved in running joint conferences, and shipping samples into and out of China." EcoHealth listed WIV as a Project/Performance Site Location. In describing WIV's facilities, EcoHealth described WIV as China's premier institute for virological research" and touted WIV's "fully equipped biosafety level 3 laboratory" and "a newly opened BLS-4 laboratory." In support of the application, Dr. Zheng Li Shi's personal statement indicated that "My lab will be responsible for diagnosis, genomics and isolation of coronavirus from wild and domestic animals in Southern China and for analyzing their receptor binding domains." The application stated that "Wuhan Institute of Virology and the Wuhan University Center for Animal Experiment BSL-3

lab have an Internal Biosafety Committee and are accredited BSL-2 and BSL 3 laboratories. All experimental work using infectious material will be conducted under appropriate biosafety standards. Disposal of hazardous materials will be conducted according to the institutional biosafety regulations."

EcoHealth requested funding specifically for activities to be carried out by WIV. NIH awarded EcoHealth a total of $749,976 for WIV's work in the following annual amounts for years 1 through 5:

	-Yr 1	-Yr 2	-Yr 3	-Yr 4	-Yr 5
Total Direct Costs	$123,699	$128,718	$147,335	$147,335	$147,335
F&A Costs @ 8%	$9,896	$10,297	$11,787	$11,787	$11,787
TOTAL COSTS	$133,595	$139,015	$159,122	$159,122	$159,122

As stated in the Notices of Award for each budget period of the grant, the awards were subject to terms and conditions, which include the NIH Grants Policy Statement (GPS) and applicable HHS grant regulations. As I indicated in my letter of July 8, 2020, as a term and condition of award EcoHealth was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). See also, 45 C.F.R. § 75.342(a) ("The non-Federal entity is responsible for oversight of the operations of the Federal award supported activities."). Moreover, EcoHealth was required to "Establish and maintain effective internal control over the Federal award that provides reasonable assurance that the non-Federal entity is managing the Federal award in compliance with Federal statutes, regulations, and the terms and conditions of the Federal award[.]" 45 C.F.R. § 75.303(a). The Notice of Award stated that as a term and condition of award, "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]." Moreover, the NIH GPS provides that NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients, so these terms applied to WIV. 45 C.F.R. § 75.101.

As I stated, NIH has concerns of non-compliance with terms and conditions of award—namely, that WIV had not satisfied safety requirements under the award and that EcoHealth Alliance had not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance. Accordingly, NIH suspended all activities related to R01AI110964, pursuant to 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare.

In my letter of July 8, 2020, I provided EcoHealth with the opportunity to object and to provide information and documentation challenging the suspension. Specifically, I sought information and materials that speak to WIV's lab safety and EcoHealth's oversight of its subrecipient, and an inspection of WIV's laboratory records and facilities. I indicated that as a specific condition of award, during the period of suspension, EcoHealth Alliance may not allow research under this

project to be conducted and that no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients.

EcoHealth objected to the requests on the grounds that "NIAID is not authorized under 45 CFR§§ 75.371, 75.205, and 75.207, entitled *Specific Award Conditions*, to impose, *inter alia*, conditions that consist of demands for information regarding entities that are neither subrecipients of grant funds nor project affiliates."

These provisions are irrelevant to NIH's requests. NIH is required to permit the opportunity for recipients to object and provide information and documentation challenging a suspension, 45 C.F.R. § 75.374, so we specifically gave EcoHealth the opportunity to provide information that speaks to NIH's concerns. Moreover, as a granting agency, NIH is required to "manage and administer the Federal award in a manner so as to ensure that Federal funding is expended and associated programs are implemented in full accordance with U.S. statutory and public policy requirements: Including, but not limited to, those protecting public welfare [and] the environment[.]" 45 C.F.R. § 75.300(a). In addition to seeking information that speaks to compliance with terms and conditions of award, NIH is entitled to "make site visits as warranted by program needs." 45 C.F.R. § 75.342. As a term and condition of award, NIH "must have the right of access to any documents, papers, or other records of the non-Federal entity which are pertinent to the Federal award, in order to make audits, examinations, excerpts, and transcripts" (45 C.F.R. § 75.364); and must have "timely and reasonable access to the non-Federal entity's personnel for the purpose of interview and discussion related to such documents" (id.). These requirements flow down to subawards to subrecipients. 45 C.F.R. § 75.101. "Non-Federal entities must comply with requirements in [45 C.F.R. Part 75] regardless of whether the non-Federal entity is a recipient or subrecipient of a Federal award." 45 C.F.R. 75.101. As the grantee, EcoHealth was required to have in place, "A requirement that the subrecipient permit the pass-through entity and auditors to have access to the subrecipient's records and financial statements as necessary for the pass-through entity to meet the requirements of this part." 45 C.F.R. § 75.352(a)(5). For each of these reasons, NIH is justified in seeking the materials, information, and a site visit specified in my letter of July 8, 2020.

In addition to objecting to NIH's authority to seek the materials, information, and a site visit, EcoHealth has responded that it lacks knowledge or information regarding the requests; that it is not in possession, custody, or control of the specified items; and that it has no authority to grant NIAID and the U.S. National Academy of Sciences access to WIV's facility to conduct an inspection. EcoHealth's responses have not satisfied NIH's concerns that EcoHealth had failed to adequately monitor the compliance of its subrecipient, and that the subrecipient, WIV, had failed to comply with safety requirements.

Notwithstanding this, NIH is providing an additional opportunity for EcoHealth to provide information and documentation challenging these concerns of non-compliance. Accordingly, in addition to reiterating our prior requests (1) through (6) per our letter of July 8, 2020, NIH requests the following information and materials, which must be complete and accurate:

1. Provide copies of all EcoHealth Alliance – WIV subrecipient agreements as well as any other documents and information describing how EcoHealth Alliance monitored WIV's compliance with the terms and conditions of award, including with respect to biosafety.
2. Describe EcoHealth's efforts to evaluate WIV's risk of noncompliance with Federal statutes, regulations, and the terms and conditions of the subaward.
3. Provide copies of all WIV biosafety reports from June 1, 2014 through May 31, 2019.

During the ongoing period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further assess whether EcoHealth Alliance and WIV complied with the terms and conditions of award, including compliance with other terms and conditions of award that may be implicated. We remind you that during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the continued suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 C.F.R. Part 75, including, but not limited to, terminating the grant award or disallowing costs. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

Sincerely,

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy (NIAID)
Ms. Emily Linde (NIAID)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Allergy
and Infectious Diseases
Bethesda, Maryland 20892

8 July 2020

Drs. Aleksei Chmura and Peter Daszak
EcoHealth Alliance, Inc.
460 W 34th St
Suite 1701
New York, NY 10001

Re: NIH Grant R01AI110964

Dear Drs. Chmura and Daszak:

In follow-up to my previous letter of April 24, 2020, I am writing to notify you that the National Institute of Allergy and Infectious Diseases (NIAID), an Institute within the National Institutes of Health (NIH), under the Department of Health and Human Services (HHS), has withdrawn its termination of grant R01AI110964, which supports the project *Understanding the Risk of Bat Coronavirus Emergence*. Accordingly, the grant is reinstated.

However, as you are aware, the NIH has received reports that the Wuhan Institute of Virology (WIV), a subrecipient of EcoHealth Alliance under R01AI110964, has been conducting research at its facilities in China that pose serious bio-safety concerns and, as a result, create health and welfare threats to the public in China and other countries, including the United States. Grant award R01AI110964 is subject to biosafety requirements set forth in the NIH Grants Policy Statement (e.g., NIH GPS, Section 4.1.24 "Public Health Security") and the Notice of Award (e.g., requiring that "Research funded under this grant must adhere to the [CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL)]."). Moreover, NIH grant recipients are expected to provide safe working conditions for their employees and foster work environments conducive to high-quality research. NIH GPS, Section 4. The terms and conditions of the grant award flow down to subawards to subrecipients. 45 C.F.R. § 75.101.

As the grantee, EcoHealth Alliance was required to "monitor the activities of the subrecipient as necessary to ensure that the subaward is used for authorized purposes, in compliance with Federal statutes, regulations, and the terms and conditions of the subaward . . ." 45 C.F.R. § 75.352(d). We have concerns that WIV has not satisfied safety requirements under the award, and that EcoHealth Alliance has not satisfied its obligations to monitor the activities of its subrecipient to ensure compliance.

Moreover, as we have informed you through prior Notices of Award, this award is subject to the Transparency Act subaward and executive compensation reporting requirement of 2 C.F.R. Part

170. To date you have not reported any subawards in the Federal Subaward Reporting System.

Therefore, effective the date of this letter, July 8, 2020, NIH is suspending all activities related to R01AI110964, until such time as these concerns have been addressed to NIH's satisfaction. This suspension is taken in accordance with 45 C.F.R. § 75.371, Remedies for Noncompliance, which permits suspension of award activities in cases of non-compliance, and the NIH GPS, Section 8.5.2, which permits NIH to take immediate action to suspend a grant when necessary to protect the public health and welfare. This action is not appealable in accordance with 42 C.F.R. § 50.404 and the NIH GPS Section 8.7, Grant Appeals Procedures. However, EcoHealth Alliance has the opportunity to provide information and documentation demonstrating that WIV and EcoHealth Alliance have satisfied the above-mentioned requirements.

Specifically, to address the NIH's concerns, EcoHealth must provide the NIH with the following information and materials, which must be complete and accurate:

1. Provide an aliquot of the actual SARS-CoV-2 virus that WIV used to determine the viral sequence.
2. Explain the apparent disappearance of Huang Yanling, a scientist / technician who worked in the WIV lab but whose lab web presence has been deleted.
3. Provide the NIH with WIV's responses to the 2018 U.S. Department of State cables regarding safety concerns.
4. Disclose and explain out-of-ordinary restrictions on laboratory facilities, as suggested, for example, by diminished cell-phone traffic in October 2019, and the evidence that there may have been roadblocks surrounding the facility from October 14-19, 2019.
5. Explain why WIV failed to note that the RaTG13 virus, the bat-derived coronavirus in its collection with the greatest similarity to SARS-CoV-2, was actually isolated from an abandoned mine where three men died in 2012 with an illness remarkably similar to COVID-19, and explain why this was not followed up.
6. Additionally, EcoHealth Alliance must arrange for WIV to submit to an outside inspection team charged to review the lab facilities and lab records, with specific attention to addressing the question of whether WIV staff had SARS-CoV-2 in their possession prior to December 2019. The inspection team should be granted full access to review the processes and safety of procedures of all of the WIV field work (including but not limited to collection of animals and biospecimens in caves, abandoned man-made underground cavities, or outdoor sites). The inspection team could be organized by NIAID, or, if preferred, by the U.S. National Academy of Sciences.
7. Lastly, EcoHealth Alliance must ensure that all of its subawards are fully reported in the Federal Subaward Reporting System

During this period of suspension, NIH will continue to review the activities under this award, taking into consideration information provided by EcoHealth Alliance, to further asses compliance by EcoHealth Alliance and WIV, including compliance with other terms and conditions of award that may be implicated. Additionally, during the period of suspension, EcoHealth Alliance may not allow research under this project to be conducted. Further, no funds from grant R01AI110964 may be provided to or expended by EcoHealth Alliance or any subrecipients; all such charges are unallowable. It is EcoHealth Alliance's responsibility as the

recipient of this grant award to ensure that the terms of this suspension are communicated to and understood by all subrecipients. EcoHealth Alliance must provide adequate oversight to ensure compliance with the terms of the suspension. Any noncompliance of the terms of this suspension must be immediately reported to NIH. Once the original award is reinstated, NIH will take additional steps to restrict all funding in the HHS Payment Management System in the amount of $369,819. EcoHealth Alliance will receive a revised Notice of Award from NIAID indicating the suspension of these research activities and funding restrictions as a specific condition of award.

Please note that this action does not preclude NIH from taking additional corrective or enforcement actions pursuant to 45 CFR Part 75, including, but not limited to, terminating the grant award. NIH may also take other remedies that may be legally available if NIH discovers other violations of terms and conditions of award on the part of EcoHealth Alliance or WIV.

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Sincerely,

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Email: (b) (6)

cc: Dr. Erik Stemmy
Ms. Emily Linde

The Lab-Leak Hypothesis

Nicholson Baker Jan. 4, 2021

For decades, scientists have been hot-wiring viruses in hopes of preventing a pandemic, not causing one. But what if ...?

By

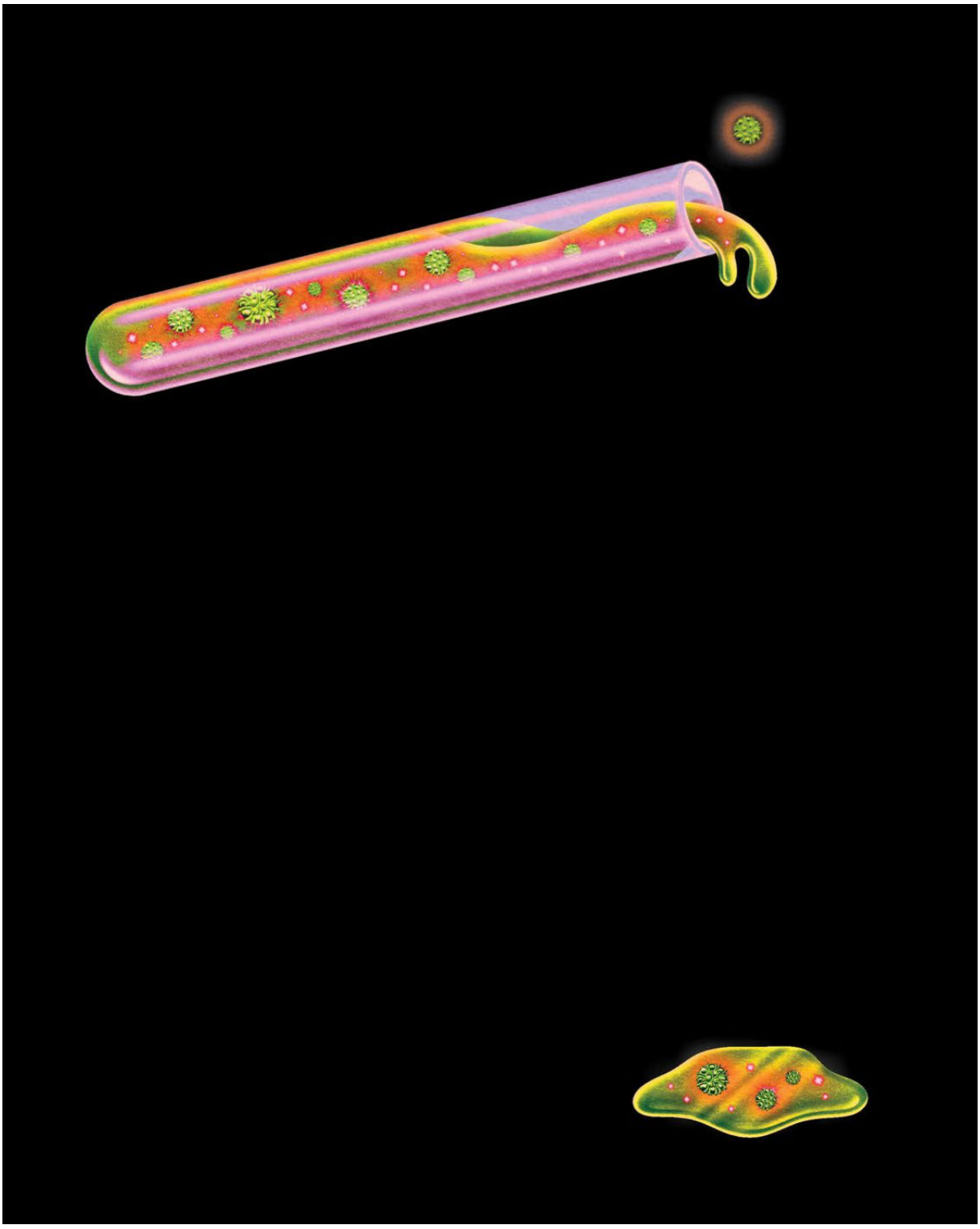

Illustration: Illustration by Robert Beatty for New York Magazine

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I.

Flask Monsters

What happened was fairly simple, I've come to believe. It was an accident. A virus spent some time in a laboratory, and eventually it got out. SARS-CoV-2, the virus that causes COVID-19, began its existence inside a bat, then it learned how to infect people in a claustrophobic mine shaft, and then it was made more infectious in one or more laboratories, perhaps as part of a scientist's well-intentioned but risky effort to create a broad-spectrum vaccine. SARS-2 was not designed as a biological weapon. But it was, I think, designed. Many thoughtful people dismiss this notion, and they may be right. They sincerely believe that the coronavirus arose naturally, "zoonotically," from animals, without having been previously studied, or hybridized, or sluiced through cell cultures, or otherwise worked on by trained professionals. They hold that a bat, carrying a coronavirus, infected some other creature, perhaps a pangolin, and that the pangolin may have already been sick with a different coronavirus disease, and out of the conjunction and commingling of those two diseases within the pangolin, a new disease, highly infectious to humans, evolved. Or they hypothesize that two coronaviruses recombined in a bat, and this new virus spread to other bats, and then the bats infected a person directly — in a rural setting, perhaps — and that this person caused a simmering undetected outbreak of respiratory disease, which over a period of months or years evolved to become virulent and highly transmissible but was not noticed until it appeared in Wuhan.

There is no direct evidence for these zoonotic possibilities, just as there is no direct evidence for an experimental mishap — no written confession, no incriminating notebook, no official accident report. Certainty craves detail, and detail requires an investigation. It has been a full year, 80 million people

have been infected, and, surprisingly, no public investigation has taken place. We still know very little about the origins of this disease.

Nevertheless, I think it's worth offering some historical context for our yearlong medical nightmare. We need to hear from the people who for years have contended that certain types of virus experimentation might lead to a disastrous pandemic like this one. And we need to stop hunting for new exotic diseases in the wild, shipping them back to laboratories, and hot-wiring their genomes to prove how dangerous to human life they might become.

Over the past few decades, scientists have developed ingenious methods of evolutionary acceleration and recombination, and they've learned how to trick viruses, coronaviruses in particular, those spiky hairballs of protein we now know so well, into moving quickly from one species of animal to another or from one type of cell culture to another. They've made machines that mix and mingle the viral code for bat diseases with the code for human diseases — diseases like SARS, severe acute respiratory syndrome, for example, which arose in China in 2003, and MERS, Middle East respiratory syndrome, which broke out a decade later and has to do with bats and camels. Some of the experiments — "gain of function" experiments — aimed to create new, more virulent, or more infectious strains of diseases in an effort to predict and therefore defend against threats that might conceivably arise in nature. The term *gain of function* is itself a euphemism; the Obama White House more accurately described this work as "experiments that may be reasonably anticipated to confer attributes to influenza, MERS, or SARS viruses such that the virus would have enhanced pathogenicity and/or transmissibility in mammals via the respiratory route." The virologists who carried out these experiments have accomplished amazing feats of genetic transmutation, no question, and there have been very few publicized accidents over the years. But there have been some.

And we were warned, repeatedly. The intentional creation of new microbes that combine virulence with heightened transmissibility "poses extraordinary risks to the public," wrote infectious-disease experts Marc Lipsitch and Thomas Inglesby in 2014. "A rigorous and transparent risk-assessment process for this work has not yet been established." That's still true today. In 2012, in *Bulletin of the Atomic Scientists*, Lynn Klotz warned that there was an 80 percent chance, given how many laboratories were then handling virulent viro-varietals, that a leak of a potential pandemic pathogen would occur sometime in the next 12 years.

A lab accident — a dropped flask, a needle prick, a mouse bite, an illegibly labeled bottle — is apolitical. Proposing that something unfortunate happened during a scientific experiment in Wuhan — where COVID-19 was first diagnosed and where there are three high-security virology labs, one of which held in its freezers the most comprehensive inventory of sampled bat viruses in the world — isn't a conspiracy theory. It's just a theory. It merits attention, I believe, alongside other reasoned attempts to explain the source of our current catastrophe.

II.

"A Reasonable Chance"

Seeking Ebola strains in Sierra Leone's wild-animal population for USAID's Predict project in 2018. Photo: Simon Townsley

From early 2020, the world was brooding over the origins of COVID-19. People were reading research papers, talking about what kinds of live animals were or were not sold at the Wuhan seafood market — wondering where the new virus had come from.

Meanwhile, things got strange all over the world. The Chinese government shut down transportation and built hospitals at high speed. There were video clips of people who'd suddenly dropped unconscious in the street. A doctor on YouTube told us how we were supposed to scrub down our produce when we got back from the supermarket. A scientist named Shi Zhengli of the Wuhan Institute of Virology published a paper saying that the novel coronavirus was 96 percent identical to a bat virus, RaTG13, found in

Yunnan province in southern China. On March 13, I wrote in my journal that there seemed to be something oddly artificial about the disease: "It's too airborne — too catching — it's something that has been selected for infectivity. That's what I suspect. No way to know so no reason to waste time thinking about it."

This was just a note to self — at the time, I hadn't interviewed scientists about SARS-2 or read their research papers. But I did know something about pathogens and laboratory accidents; I published a book last year, *Baseless*, that talks about some of them. The book is named after a Pentagon program, Project Baseless, whose goal, as of 1951, was to achieve "an Air Force–wide combat capability in biological and chemical warfare at the earliest possible date."

A vast treasure was spent by the U.S. on the amplification and aerial delivery of diseases — some well known, others obscure and stealthy. America's biological-weapons program in the '50s had A1-priority status, as high as nuclear weapons. In preparation for a total war with a numerically superior communist foe, scientists bred germs to be resistant to antibiotics and other drug therapies, and they infected lab animals with them, using a technique called "serial passaging," in order to make the germs more virulent and more catching.

And along the way, there were laboratory accidents. By 1960, hundreds of American scientists and technicians had been hospitalized, victims of the diseases they were trying to weaponize. Charles Armstrong, of the National Institutes of Health, one of the consulting founders of the American germ-warfare program, investigated Q fever three times, and all three times, scientists and staffers got sick. In the anthrax pilot plant at Camp Detrick, Maryland, in 1951, a microbiologist, attempting to perfect the "foaming process" of high-volume production, developed a fever and died. In 1964,

veterinary worker Albert Nickel fell ill after being bitten by a lab animal. His wife wasn't told that he had Machupo virus, or Bolivian hemorrhagic fever. "I watched him die through a little window to his quarantine room at the Detrick infirmary," she said.

In 1977, a worldwide epidemic of influenza A began in Russia and China; it was eventually traced to a sample of an American strain of flu preserved in a laboratory freezer since 1950. In 1978, a hybrid strain of smallpox killed a medical photographer at a lab in Birmingham, England; in 2007, live foot-and-mouth disease leaked from a faulty drainpipe at the Institute for Animal Health in Surrey. In the U.S., "more than 1,100 laboratory incidents involving bacteria, viruses and toxins that pose significant or bioterror risks to people and agriculture were reported to federal regulators during 2008 through 2012," reported *USA Today* in an exposé published in 2014.
In 2015, the Department of Defense discovered that workers at a germ-warfare testing center in Utah had mistakenly sent close to 200 shipments of live anthrax to laboratories throughout the United States and also to Australia, Germany, Japan, South Korea, and several other countries over the past 12 years. In 2019, laboratories at Fort Detrick — where "defensive" research involves the creation of potential pathogens to defend against — were shut down for several months by the Centers for Disease Control and Prevention for "breaches of containment." They reopened in December 2019.

High-containment laboratories have a whispered history of near misses. Scientists are people, and people have clumsy moments and poke themselves and get bitten by the enraged animals they are trying to nasally inoculate. Machines can create invisible aerosols, and cell solutions can become contaminated. Waste systems don't always work properly. Things can go wrong in a hundred different ways.

Hold that human fallibility in your mind. And then consider the cautious words of Alina Chan, a scientist who works at the Broad Institute of MIT and Harvard. "There is a reasonable chance that what we are dealing with is the result of a lab accident," Chan told me in July of last year. There was also, she added, a reasonable chance that the disease had evolved naturally — both were scientific possibilities. "I don't know if we will ever find a smoking gun, especially if it was a lab accident. The stakes are so high now. It would be terrifying to be blamed for millions of cases of COVID-19 and possibly up to a million deaths by year end, if the pandemic continues to grow out of control. The Chinese government has also restricted their own scholars and scientists from looking into the origins of SARS-CoV-2. At this rate, the origin of SARS-CoV-2 may just be buried by the passage of time."

I asked Jonathan A. King, a molecular biologist and biosafety advocate from MIT, whether he'd thought *lab accident* when he first heard about the epidemic. "Absolutely, absolutely," King answered. Other scientists he knew were concerned as well. But scientists, he said, in general were cautious about speaking out. There were "very intense, very subtle pressures" on them not to push on issues of laboratory biohazards. Collecting lots of bat viruses, and passaging those viruses repeatedly through cell cultures, and making bat-human viral hybrids, King believes, "generates new threats and desperately needs to be reined in."

"All possibilities should be on the table, including a lab leak," a scientist from the NIH, Philip Murphy — chief of the Laboratory of Molecular Immunology — wrote me recently. Nikolai Petrovsky, a professor of endocrinology at Flinders University College of Medicine in Adelaide, Australia, said in an email, "There are indeed many unexplained features of this virus that are hard if not impossible to explain based on a completely natural origin." Richard Ebright, a molecular biologist at Rutgers University, wrote that he'd been concerned for some years about the Wuhan laboratory and about the

work being done there to create "chimeric" (i.e., hybrid) SARS-related bat coronaviruses "with enhanced human infectivity." Ebright said, "In this context, the news of a novel coronavirus in Wuhan ***screamed*** lab release."

III.

"No Credible Evidence"

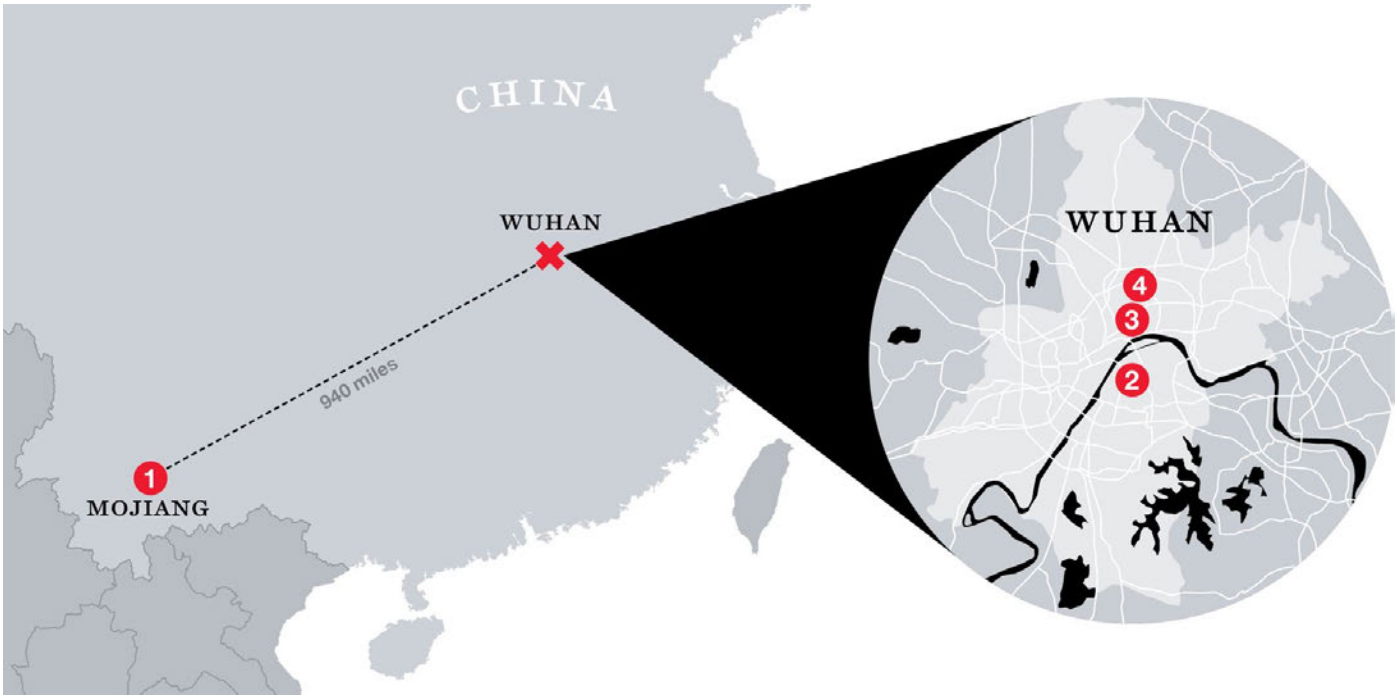
The new disease, as soon as it appeared, was intercepted — stolen and politicized by people with ulterior motives. The basic and extremely interesting scientific question of what happened was sucked up into an ideological sharknado.

Some Americans boycotted Chinese restaurants; others bullied and harassed Asian Americans. Steve Bannon, broadcasting from his living room, in a YouTube series called *War Room*, said that the Chinese Communist Party had made a biological weapon and intentionally released it. He called it the "CCP virus." And his billionaire friend and backer, Miles Guo, a devoted Trump supporter, told a right-wing website that the communists' goal was to "use the virus to infect selective people in Hong Kong, so that the Chinese Communist Party could use it as an excuse to impose martial law there and ultimately crush the Hong Kong pro-democracy movement. But it backfired terribly."

In *The Lancet*, in February, a powerful counterstatement appeared, signed by 27 scientists. "We stand together to strongly condemn conspiracy theories suggesting that COVID-19 does not have a natural origin," the statement said. "Scientists from multiple countries have published and analyzed genomes of the causative agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and they overwhelmingly conclude

that this coronavirus originated in wildlife, as have so many other emerging pathogens."

The behind-the-scenes organizer of this *Lancet* statement, Peter Daszak, is a zoologist and bat-virus sample collector and the head of a New York nonprofit called EcoHealth Alliance — a group that (as veteran science journalist Fred Guterl explained later in *Newsweek*) has channeled money from the National Institutes of Health to Shi Zhengli's laboratory in Wuhan, allowing the lab to carry on recombinant research into diseases of bats and humans. "We have a choice whether to stand up and support colleagues who are being attacked and threatened daily by conspiracy theorists or to just turn a blind eye," Daszak said in February in *Science* magazine.



How Did It Get Out? 1. The Tongguan Mine Shaft in Mojiang, Yunnan, where, in 2013, fragments of RaTG13, the closest known relative of SARSCoV-2, were recovered and transported to the Wuhan Institute of Virology; **2. The Wuhan Institute of Virology,** where Shi Zhengli's team brought the RaTG13 sample, sequenced its genome, then took it out of the freezer several times in recent years; **3. The Wuhan Center for Disease Control and Prevention,** which first reported signs of the novel coronavirus in hospital patients; **4. The Huanan Seafood Wholesale Market,** an early suspected origin of the pandemic, where the first major outbreak occurred. Illustration: Map by Jason Lee

Vincent Racaniello, a professor at Columbia and a co-host of a podcast called *This Week in Virology*, said on February 9 that the idea of an accident in Wuhan was "complete bunk." The coronavirus was 96 percent similar to a bat virus found in 2013, Racaniello said. "It's not a man-made virus. It wasn't released from a lab."

Racaniello's dismissal was seconded by a group of scientists from Ohio State, the University of Pennsylvania, and the University of North Carolina, who put out a paper in *Emerging Microbes and Infections* to quiet the "speculations, rumors, and conspiracy theories that SARS-CoV-2 is of laboratory origin." There was "currently no credible evidence" that SARS-2 leaked from a lab, these scientists said, using a somewhat different argument from Racaniello's. "Some people have alleged that the human SARS-CoV-2 was leaked directly from a laboratory in Wuhan where a bat CoV (RaTG13) was recently reported," they said. But RaTG13 could not be the source because it differed from the human SARS-2 virus by more than a thousand nucleotides. One of the paper's authors, Susan Weiss, told the Raleigh *News & Observer*, "The conspiracy theory is ridiculous."

The most influential natural-origin paper, "The Proximal Origin of SARS-CoV-2," by a group of biologists that included Kristian Andersen of Scripps Research, appeared online in a preliminary version in mid-February. "We do not believe any type of laboratory-based scenario is plausible," the scientists said. Why? Because molecular-modeling software predicted that if you wanted to optimize an existing bat virus so that it would replicate well in human cells, you would arrange things a different way than how the SARS-2 virus actually does it — even though the SARS-2 virus does an extraordinarily good job of replicating in human cells. The laboratory-based scenario was implausible, the paper said, because, although it was true that the virus could conceivably have developed its unusual genetic features in a laboratory, a stronger and "more parsimonious" explanation was that the

features came about through some kind of natural mutation or recombination. "What we think," explained one of the authors, Robert F. Garry of Tulane University, on YouTube, "is that this virus is a recombinant. It probably came from a bat virus, plus perhaps one of these viruses from the pangolin." Journalists, for the most part, echoed the authoritative pronouncements of Daszak, Racaniello, Weiss, Andersen, and other prominent natural-originists. "The balance of the scientific evidence strongly supports the conclusion that the new coronavirus emerged from nature — be it the Wuhan market or somewhere else," said the Washington *Post*'s "Fact Checker" column. "Dr. Fauci Again Dismisses Wuhan Lab As Source of Coronavirus," said CBS News, posting a video interview of Anthony Fauci by *National Geographic*. "If you look at the evolution of the virus in bats, and what's out there now," Fauci said, "it's very, very strongly leaning toward 'This could not have been artificially or deliberately manipulated' — the way the mutations have naturally evolved."

Everyone took sides; everyone thought of the new disease as one more episode in an ongoing partisan struggle. Think of Mike Pompeo, that landmass of Cold War truculence; think of Donald Trump himself. They stood at their microphones saying, in a winking, I-know-something-you-don't-know sort of way, that this disease escaped from a Chinese laboratory. Whatever they were saying must be wrong. It became impermissible, almost taboo, to admit that, of course, SARS-2 could have come from a lab accident. "The administration's claim that the virus spread from a Wuhan lab has made the notion politically toxic, even among scientists who say it could have happened," wrote science journalist Mara Hvistendahl in the Intercept.

IV.

"Is It a Complete Coincidence?"

Even so, in January and February of 2020, there were thoughtful people who were speaking up, formulating their perplexities.

One person was Sam Husseini, an independent journalist. He went to a CDC press conference at the National Press Club on February 11, 2020. By then, 42,000 people had gotten sick in China and more than a thousand had died. But there were only 13 confirmed cases in the U.S. Halfway through the Q&A period, Husseini went to the microphone and asked the CDC's representative, Anne Schuchat, where the virus had come from. His head was spinning, he told me later.

"Obviously the main concern is how to stop the virus," Husseini said; nonetheless, he wanted to know more about its source. "Is it the CDC's contention," he asked, "that there's absolutely no relation to the BSL-4 lab in Wuhan? It's my understanding that this is the only place in China with a BSL-4 lab. We in the United States have, I think, two dozen or so, and there have been problems and incidents." (A BSL-4 laboratory is a maximum-security biosafety-level-four facility, used to house research on the most dangerous known pathogens. *New York* has confirmed there are at least 11 BSL-4 facilities currently operating in the U.S.) Husseini hastened to say that he wasn't implying that what happened in Wuhan was in any way intentional. "I'm just asking, Is it a complete coincidence that this outbreak happened in the one city in China with a BSL-4 lab?"

Schuchat thanked Husseini for his questions and comments. Everything she'd seen was quite consistent with a natural, zoonotic origin for the disease, she said.

That same month, a group of French scientists from Aix-Marseille University posted a paper describing their investigation of a small insertion in the genome of the new SARS-2 virus. The virus's spike protein contained a

sequence of amino acids that formed what Etienne Decroly and colleagues called a "peculiar furin-like cleavage site" — a chemically sensitive region on the lobster claw of the spike protein that would react in the presence of an enzyme called furin, which is a type of protein found everywhere within the human body, but especially in the lungs. When the spike senses human furin, it shudders, chemically speaking, and the enzyme opens the protein, commencing the tiny morbid ballet whereby the virus burns a hole in a host cell's outer membrane and finds its way inside.

The code for this particular molecular feature — not found in SARS or any SARS-like bat viruses, but present in a slightly different form in the more lethal MERS virus — is easy to remember because it's a roar: "R-R-A-R." The letter code stands for amino acids: arginine, arginine, alanine, and arginine. Its presence, so Decroly and his colleagues observed, may heighten the "pathogenicity" — that is, the god-awfulness — of a disease.

Botao Xiao, a professor at the South China University of Technology, posted a short paper on a preprint server titled "The Possible Origins of 2019-nCoV Coronavirus." Two laboratories, the Wuhan Center for Disease Control and Prevention (WHCDC) and the Wuhan Institute of Virology, were not far from the seafood market, which was where the disease was said to have originated, Xiao wrote — in fact, the WHCDC was only a few hundred yards away from the market — whereas the horseshoe bats that hosted the disease were hundreds of miles to the south. (No bats were sold in the market, he pointed out.) It was unlikely, he wrote, that a bat would have flown to a densely populated metropolitan area of 15 million people. "The killer coronavirus probably originated from a laboratory in Wuhan," Xiao believed. He urged the relocation of "biohazardous laboratories" away from densely populated places. His article disappeared from the server.

And late in the month, a professor at National Taiwan University, Fang Chi-

tai, gave a lecture on the coronavirus in which he described the anomalous R-R-A-R furin cleavage site. The virus was "unlikely to have four amino acids added all at once," Fang said — natural mutations were smaller and more haphazard, he argued. "From an academic point of view, it is indeed possible that the amino acids were added to COVID-19 in the lab by humans." When the Taiwan *News* published an article about Fang's talk, Fang disavowed his own comments, and the video copy of the talk disappeared from the website of the Taiwan Public Health Association. "It has been taken down for a certain reason," the association explained. "Thank you for your understanding."

V.

"A Serious Shortage of Appropriately Trained Technicians"

In the spring, I did some reading on coronavirus history. Beginning in the 1970s, dogs, cows, and pigs were diagnosed with coronavirus infections; dog shows were canceled in 1978 after 25 collies died in Louisville, Kentucky. New varieties of coronaviruses didn't start killing humans, though, until 2003 — that's when restaurant chefs, food handlers, and people who lived near a live-animal market got sick in Guangzhou, in southern China, where the shredded meat of a short-legged raccoonlike creature, the palm civet, was served in a regional dish called "dragon-tiger-phoenix soup." The new disease, SARS, spread alarmingly in hospitals, and it reached 30 countries and territories. More than 800 people died; the civet-borne virus was eventually traced to horseshoe bats.

Later, smaller outbreaks of SARS in Taiwan, Singapore, and China's National Institute of Virology in Beijing were all caused by laboratory accidents. Of the Beijing Virology Institute, the World Health Organization's safety

investigators wrote, in May 2004, that they had "serious concerns about biosafety procedures." By one account, a SARS storage room in the Beijing lab was so crowded that the refrigerator holding live virus was moved out to the hallway. "Scientists still do not fully understand exactly where or how SARS emerged 18 months ago," wrote Washington *Post* reporter David Brown in June 2004. "But it is clear now that the most threatening source of the deadly virus today may be places they know intimately — their own laboratories."

I'm just asking, Is it a complete coincidence that this outbreak happened in the one city in China with a BSL-4 lab?

MERS arose in 2012, possibly spread by camels that had contracted the disease from bats or bat guano, then passed it to human drinkers of raw camel milk and butchers of camel meat. It was an acute sickness, with a high fatality rate, mostly confined to Saudi Arabia. Like SARS, MERS ebbed quickly — it all but disappeared outside the Middle East, except for an outbreak in 2015 at the Samsung Medical Center in South Korea, where a single case of MERS led to more than 180 infections, many involving hospital workers.

In January 2015, the brand-new BSL-4 lab in Wuhan, built by a French contractor, celebrated its opening, but full safety certification came slowly. According to State Department cables from 2018 leaked to the Washington *Post*, the new BSL-4 lab had some start-up problems, including "a serious shortage of appropriately trained technicians and investigators needed to safely operate this high-containment laboratory." The staff had gotten some training at a BSL-4 lab in Galveston, Texas, but they were doing potentially dangerous work with SARS-like viruses, the memo said, and they needed more help from the U.S.

In November or December of 2019, the novel coronavirus began to spread. Chinese scientists initially named it "Wuhan seafood market pneumonia virus," but soon that idea went away. The market, closed and decontaminated by Chinese officials on January 1, 2020, was an amplifying hub, not the source of the outbreak, according to several studies by Chinese scientists. Forty-five percent of the earliest SARS-2 patients had no link with the market.

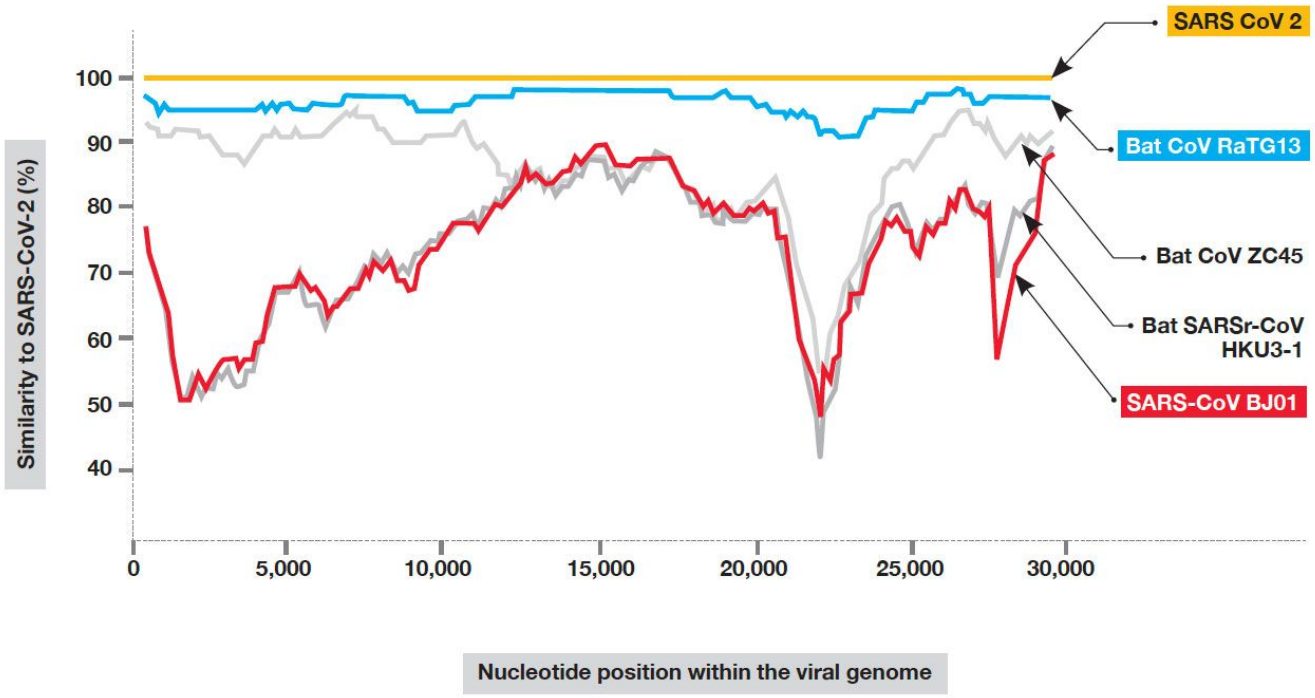
VI.

Emergence

Now let's take a step back. AIDS, fatal and terrifying and politically charged, brought on a new era in government-guided vaccine research, under the guidance of Anthony Fauci. A virologist at Rockefeller University, Stephen S. Morse, began giving talks on "emerging viruses" — other plagues that might be in the process of coming out of nature's woodwork. In 1992, Richard Preston wrote a horrific account of one emergent virus, Ebola, in *The New Yorker*, which became a best-selling book in 1994; Laurie Garrett's *The Coming Plague: Newly Emerging Diseases in a World Out of Balance* appeared that same year and was also a best seller. The idea seemed to be everywhere: We were on the verge of a wave of zoonotic, emergent plagues.

This new, useful term, *emerging*, began to glow in the research papers of some coronavirologists, who were out of the spotlight, working on common colds and livestock diseases. The term was useful because it was fluid. An emerging disease could be real and terrifying, as AIDS was — something that had just arrived on the medical scene and was confounding our efforts to combat it — or it could be a disease that hadn't arrived, and might never arrive, but could be shown in a laboratory to be waiting in the wings, just a

few mutations away from a human epidemic. It was real and unreal at the same time — a quality that was helpful when applying for research grants.



Where Did It Come From? This chart measures the genetic similarity of known viruses to the novel coronavirus (which appears in yellow). By far the closest is the bat virus RaTG13, which appears in blue, and which was recovered in 2013 and brought to the Wuhan Institute of Virology. The first SARS, marked in red, is a much more distant relative. Graphic: Zhou, P., Yang, XL., Wang, XG. et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579, 270–273 (2020)

Take, for instance, this paper from 1995: "High Recombination and Mutation Rates in Mouse Hepatitis Viruses Suggest That Coronaviruses May Be Potentially Important Emerging Viruses." It was written by Dr. Ralph Baric and his bench scientist, Boyd Yount, at the University of North Carolina. Baric, a gravelly voiced former swim champion, described in this early paper how his lab was able to train a coronavirus, MHV, which causes hepatitis in mice, to jump species, so that it could reliably infect BHK (baby-hamster kidney) cell cultures. They did it using serial passaging: repeatedly dosing a mixed solution of mouse cells and hamster cells with mouse-hepatitis virus,

while each time decreasing the number of mouse cells and upping the concentration of hamster cells. At first, predictably, the mouse-hepatitis virus couldn't do much with the hamster cells, which were left almost free of infection, floating in their world of fetal-calf serum. But by the end of the experiment, after dozens of passages through cell cultures, the virus had mutated: It had mastered the trick of parasitizing an unfamiliar rodent. A scourge of mice was transformed into a scourge of hamsters. And there was more: "It is clear that MHV can rapidly alter its species specificity and infect rats and primates," Baric said. "The resulting virus variants are associated with demyelinating diseases in these alternative species." (A demyelinating disease is a disease that damages nerve sheaths.) With steady prodding from laboratory science, along with some rhetorical exaggeration, a lowly mouse ailment was morphed into an emergent threat that might potentially cause nerve damage in primates. That is, nerve damage in us.

A few years later, in a further round of "interspecies transfer" experimentation, Baric's scientists introduced their mouse coronavirus into flasks that held a suspension of African-green-monkey cells, human cells, and pig-testicle cells. Then, in 2002, they announced something even more impressive: They'd found a way to create a full-length infectious clone of the entire mouse-hepatitis genome. Their "infectious construct" replicated itself just like the real thing, they wrote.

Not only that, but they'd figured out how to perform their assembly seamlessly, without any signs of human handiwork. Nobody would know if the virus had been fabricated in a laboratory or grown in nature. Baric called this the "no-see'm method," and he asserted that it had "broad and largely unappreciated molecular biology applications." The method was named, he wrote, after a "very small biting insect that is occasionally found on North Carolina beaches."

In 2006, Baric, Yount, and two other scientists were granted a patent for their invisible method of fabricating a full-length infectious clone using the seamless, no-see'm method. But this time, it wasn't a clone of the mouse-hepatitis virus — it was a clone of the entire deadly human SARS virus, the one that had emerged from Chinese bats, via civets, in 2002. The Baric Lab came to be known by some scientists as "the Wild Wild West." In 2007, Baric said that we had entered "the golden age of coronavirus genetics."

"I would be afraid to look in their freezers," one virologist told me.

Baric and Shi Zhengli of the Wuhan Institute of Virology, the two top experts on the genetic interplay between bat and human coronaviruses, began collaborating in 2015.

VII.

"I Had Not Slept a Wink"

Virologist Shi Zhengli at the Wuhan Institute of Virology in 2017. Photo: Feature China / Barcroft Studios / Future Publishing / Getty Images

Early in the pandemic, *Scientific American* profiled Shi Zhengli, known in China as the "bat woman." Shi trapped hundreds of bats in nets at the mouths of caves in southern China, sampled their saliva and their blood, swabbed their anuses, and gathered up their fecal pellets. Several times, she visited and sampled bats in a mine in Mojiang, in southern China, where, in 2012, six men set to work shoveling bat guano were sickened by a severe lung disease, three of them fatally. Shi's team took the samples back to Wuhan and analyzed whatever fragments of bat virus she could find. In some cases, when she found a sequence that seemed particularly significant, she experimented with it in order to understand how it might potentially infect humans. Some of her work was funded by the National Institutes of Health and some of it by the U.S. Defense Threat Reduction

Agency of the Department of Defense via Peter Daszak's EcoHealth Alliance.

As Shi explained to *Scientific American*, late in December 2019, she heard from the director of the Wuhan Institute that there was an outbreak of a new disease in the city. Medical samples taken from hospital patients arrived at her lab for analysis. Shi determined that the new virus was related to SARS but even more closely related to a bat disease that her own team had found on a virus-hunting trip: the now-famous RaTG13. Shi was surprised that the outbreak was local, she said: "I had never expected this kind of thing to happen in Wuhan, in central China." The bat hiding places that she'd been visiting were, after all, as far away as Orlando, Florida, is from New York City. Could this new virus, she wondered, have come from her own laboratory? She checked her records and found no exact matches. "That really took a load off my mind," she said. "I had not slept a wink for days."

If one of the first thoughts that goes through the head of a lab director at the Wuhan Institute of Virology is that the new coronavirus could have come from her lab, then we are obliged to entertain the scientific possibility that it could indeed have come from her lab. Right then, there should have been a comprehensive, pockets-inside-out, fully public investigation of the Virology Institute, along with the other important virus labs in Wuhan, including the one close by the seafood market, headquarters of the Wuhan CDC. There should have been interviews with scientists, interviews with biosafety teams, close parsings of laboratory notebooks, freezer and plumbing and decontamination systems checks — everything. It didn't happen. The Wuhan Institute of Virology closed down its databases of viral genomes, and the Chinese Ministry of Education sent out a directive: "Any paper that traces the origin of the virus must be strictly and tightly managed."

Shi made some WeChat posts early in 2020. "The novel 2019 coronavirus is nature punishing the human race for keeping uncivilized living habits," she wrote. "I, Shi Zhengli, swear on my life that it has nothing to do with our laboratory." She advised those who believed rumors, and gave credence to unreliable scientific papers, to "shut their stinking mouths."

VIII.

" 'Bug to Drug' in 24 Hours"

It wasn't only AIDS that changed the way the NIH funded research. The War on Terror also influenced which diseases got the most attention. In the late '90s, under Bill Clinton and then George W. Bush, biodefense specialists became interested — again — in anthrax. The Defense Threat Reduction Agency built a small anthrax factory in Nevada, using simulants, to demonstrate how easy it would be for a terrorist to build a small anthrax factory. And in the first year of the Bush presidency, the Defense Intelligence Agency wrote up plans to create a vaccine-resistant form of anthrax using state-of-the-art gene-splicery. A front-page article describing these initiatives, "U.S. Germ Warfare Research Pushes Treaty Limits," appeared in the New York *Times* on September 4, 2001, one week before 9/11. "Pentagon Says Projects Are Defense, Is Pressing Ahead," was the subtitle.

After the 9/11 attacks, and the mysterious anthrax mailings that began a week later (which said, "TAKE PENACILIN [*sic*] NOW / DEATH TO AMERICA / DEATH TO ISRAEL / ALLAH IS GREAT"), the desire for biopreparedness became all consuming. Now there were emerging biothreats from humans as well as from the evolving natural world. Fauci's anti-terror budget went from $53 million in 2001 to $1.7 billion in 2003. Setting aside his work toward an AIDS vaccine, which was taking longer than he'd foreseen, Fauci

said he would be going all out to defend against a suite of known Cold War agents, all of which had been bred and perfected in American weapons programs many years before — brucellosis, anthrax, tularemia, and plague, for instance. "We are making this the highest priority," Fauci said. "We are really marshaling all available resources."

> *I would be afraid to look in their freezers.*

Vaccine development had to progress much faster, Fauci believed; he wanted to set up "vaccine systems" and "vaccine platforms," which could be quickly tailored to defend against a particular emergent strain some terrorist with an advanced biochemistry degree might have thrown together in a laboratory. "Our goal within the next 20 years is 'bug to drug' in 24 hours," Fauci said. "This would specifically meet the challenge of genetically engineered bioagents." The first Project BioShield contract Fauci awarded was to VaxGen, a California pharmaceutical company, for $878 million worth of shots of anthrax vaccine.

By 2005, so much money was going toward biothreat reduction and preparedness that more than 750 scientists sent a protest letter to the NIH. Their claim was that grants to study canonical biowar diseases — anthrax, plague, brucellosis, and tularemia, all exceptionally rare in the U.S. — had increased by a factor of 15 since 2001, whereas funds for the study of widespread "normal" diseases, of high public-health importance, had decreased.

Fauci was firm in his reply: "The United States through its leaders made the decision that this money was going to be spent on biodefense," he said. "We disagree with the notion that biodefense concerns are of 'low public-health significance.' "

In 2010, by one count, there were 249 BSL-3 laboratories and seven BSL-4 laboratories in the U.S., and more than 11,000 scientists and staffers were authorized to handle the ultralethal germs on the government's select pathogen list. And yet the sole bioterrorist in living memory who actually killed American citizens, according to the FBI — the man who sent the anthrax letters — turned out to be one of the government's own researchers. Bruce Ivins, an eccentric, suicidal laboratory scientist from Ohio who worked in vaccine development at Fort Detrick, allegedly wanted to boost the fear level so as to persuade the government to buy more of the patented, genetically engineered anthrax VaxGen vaccine, of which he was a co-inventor. (See David Willman's fascinating biography of Ivins, *Mirage Man*.) Fauci's staff at NIH funded Ivins's vaccine laboratory and gave $100 million to VaxGen to accelerate vaccine production. (The NIH's $878 million contract with VaxGen, however, was quietly canceled in 2006; Ivins, who was never charged, killed himself in 2008.)

"The whole incident amounted to a snake eating its own tail," wrote Wendy Orent in an August 2008 piece titled "Our Own Worst Bioenemy" in the Los Angeles *Times*. "No ingenious biowarrior from Al Qaeda sent the lethal envelopes through the U.S. postal system. An American scientist did." What confirmed Ivins's guilt, according to the FBI, was that there was a genetic match between the anthrax used in the killings and the strain held at Fort Detrick.

IX.

"Weapons of Mass Disruption"

After SARS appeared in 2003, Ralph Baric's laboratory moved up the NIH funding ladder. SARS was a "dual use" organism — a security threat and a zoonotic threat at the same time. In 2006, Baric wrote a long, fairly creepy

paper on the threat of "weaponizable" viruses. Synthetic biology had made possible new kinds of viral "weapons of mass disruption," he wrote, involving, for example, "rapid production of numerous candidate bioweapons that can be simultaneously released," a scattershot terror tactic Baric called the " 'survival of the fittest' approach."

Baric hoped to find a SARS vaccine, but he couldn't; he kept looking for it, year after year, supported by the NIH, long after the disease itself had been contained. It wasn't really gone, Baric believed. Like other epidemics that pop up and then disappear, as he told a university audience some years later, "they don't go extinct. They are waiting to return." What do you do if you run a well-funded laboratory, an NIH "center of excellence," and your emergent virus is no longer actually making people sick? You start squeezing it and twisting it into different shapes. Making it stand on its hind legs and quack like a duck, or a bat. Or breathe like a person.

Baric's safety record is good — although there was a minor mouse-bite incident in 2016, uncovered by ProPublica — and his motives are beyond reproach: "Safe, universal, vaccine platforms are needed that can be tailored to new pathogens as they emerge, quickly tested for safety, and then strategically used to control new disease outbreaks in human populations," he wrote in a paper on public health. But the pioneering work he did over the past 15 years — generating tiny eager single-stranded flask monsters and pitting them against human cells, or bat cells, or gene-spliced somewhat-human cells, or monkey cells, or humanized mice — was not without risk, and it may have led others astray.

In 2006, for instance, Baric and his colleagues, hoping to come up with a "vaccine strategy" for SARS, produced noninfectious virus replicon particles (or VRPs) using the Venezuelan-equine-encephalitis virus (another American germ-warfare agent), which they fitted with various SARS spike

proteins. Then, wearing Tyvek suits and two pairs of gloves each, and working in a biological safety cabinet in a BSL-3-certified laboratory, they cloned and grew recombinant versions of the original SARS virus in an incubator in a medium that held African-green-monkey cells. When they had grown enough virus, the scientists swapped out one kind of spike protein for a carefully chosen mutant, and they challenged their prototype vaccine with it in mice.

The scientists also tried their infectious SARS clones in something called an air-liquid interface, using a relatively new type of cell culture developed by Raymond Pickles of the University of North Carolina's Cystic Fibrosis Center. Pickles had perfected a method of emulating the traits of human airway tissue by cultivating cells taken from lung-disease patients — nurturing the culture over four to six weeks in such a way that the cells differentiated and developed a crop of tiny moving hairs, or cilia, on top and goblet cells within that produced real human mucus. In fact, before infecting these HAE (human airway epithelial) cells with a virus, the lab worker must sometimes rinse off some of the accumulated mucus, as if helping the lab-grown tissue to clear its throat. So Baric was exposing and adapting his engineered viruses to an extraordinarily true-to-life environment — the juicy, sticky, hairy inner surface of our breathing apparatus.

SARS-2 seems almost perfectly calibrated to grab and ransack our breathing cells and choke the life out of them. "By the time SARS-CoV-2 was first detected in late 2019, it was already pre-adapted to human transmission," Alina Chan and her co-authors have written, whereas SARS, when it first appeared in 2003, underwent "numerous adaptive mutations" before settling down. Perhaps viral nature hit a bull's-eye of airborne infectivity, with almost no mutational drift, no period of accommodation and adjustment, or perhaps some lab worker somewhere, inspired by Baric's

work with human airway tissue, took a spike protein that was specially groomed to colonize and thrive deep in the ciliated, mucosal tunnels of our inner core and cloned it onto some existing viral bat backbone. It could have happened in Wuhan, but — because anyone can now "print out" a fully infectious clone of any sequenced disease — it could also have happened at Fort Detrick, or in Texas, or in Italy, or in Rotterdam, or in Wisconsin, or in some other citadel of coronaviral inquiry. No conspiracy — just scientific ambition, and the urge to take exciting risks and make new things, and the fear of terrorism, and the fear of getting sick. Plus a whole lot of government money.

X.

"Risky Areas for Spillover"

Project Bioshield began to fade by the end of the Bush administration, although the expensive high-containment laboratories, controversial preservers and incubators of past and future epidemics, remain. By 2010, some BioShield projects had dissolved into Obama's Predict program, which paid for laboratories and staff in 60 "risky areas for spillover" around the world. Jonna Mazet, a veterinary scientist from the University of California, Davis, was in charge of Predict, which was a component of USAID's "Emerging Pandemic Threats" program. Her far-flung teams collected samples from 164,000 animals and humans and claimed to have found "almost 1,200 potentially zoonotic viruses, among them 160 novel coronaviruses, including multiple SARS- and MERS-like coronaviruses." The fruits of Predict's exotic harvest were studied and circulated in laboratories worldwide, and their genetic sequences became part of GenBank, the NIH's genome database, where any curious RNA wrangler anywhere could quickly synthesize snippets of code and test out a new disease on human cells.

Baric, Jonna Mazet, and Peter Daszak of EcoHealth worked together for years — and Daszak also routed Predict money to Shi Zhengli's bat-surveillance team in Wuhan through his nonprofit, mingling it with NIH money and money from the U.S. Defense Threat Reduction Agency. In 2013, Mazet announced that Shi Zhengli's virus hunters, with Predict's support, had, for the first time, isolated and cultured a live SARS-like virus from bats and demonstrated that this virus could bind to the human ACE2, or "angiotensin-converting enzyme 2," receptor, which Baric's laboratory had determined to be the sine qua non of human infectivity. "This work shows that these viruses can directly infect humans and validates our assumption that we should be searching for viruses of pandemic potential before they spill over to people," Mazet said.

Daszak, for his part, seems to have viewed his bat quests as part of an epic, quasi-religious death match. In a paper from 2008, Daszak and a co-author described Bruegel's painting *The Fall of the Rebel Angels* and compared it to the contemporary human biological condition. The fallen angels could be seen as pathogenic organisms that had descended "through an evolutionary (not spiritual) pathway that takes them to a netherworld where they can feed only on our genes, our cells, our flesh," Daszak wrote. "Will we succumb to the multitudinous horde? Are we to be cast downward into chthonic chaos represented here by the heaped up gibbering phantasmagory against which we rail and struggle?"

XI.

"Lab-Made?"

There are, in fact, some helpful points of agreement between zoonoticists — those who believe in a natural origin of the SARS-2 virus — and those who believe that it probably came from a laboratory. Both sides agree, when

pressed, that a lab origin can't be conclusively ruled out and a natural origin can't be ruled out either — because nature, after all, is capable of improbable, teleological-seeming achievements. Both sides also agree, for the most part, that the spillover event that began the human outbreak probably happened only once, or a few times, quite recently, and not many times over a longer period. They agree that bat virus RaTG13 (named for the *Rinolophus affinus* bat, from Tongguan, in 2013) is the closest match to the human virus that has yet been found, and that although the two viruses are very similar, the spike protein of the bat virus lacks the features the human spike protein possesses that enable it to work efficiently with human tissue.

Zoonoticists hold that SARS-2's crucial features — the furin cleavage site and the ACE2 receptor — are the result of a recombinant event involving a bat coronavirus (perhaps RaTG13 or a virus closely related to it) and another, unknown virus. Early on, researchers proposed that it could be a snake sold at the seafood market — a Chinese cobra or a banded krait — but no: Snakes don't typically carry coronaviruses. Then there was a thought that the disease came from sick smuggled pangolins, because there existed a certain pangolin coronavirus that was, inexplicably, almost identical in its spike protein to the human coronavirus — but then, no: There turned out to be questions about the reliability of the genetic information in that diseased-pangolin data set, on top of which there were no pangolins for sale at the Wuhan market. Then a group from China's government veterinary laboratory at Harbin tried infecting beagles, pigs, chickens, ducks, ferrets, and cats with SARS-2 to see if they could be carriers. (Cats and ferrets got sick; pigs, ducks, and most dogs did not.)

In September, some scientists at the University of Michigan, led by Yang Zhang, reported that they had created a "computational pipeline" to screen nearly a hundred possible intermediate hosts, including the Sumatran orangutan, the Western gorilla, the Olive baboon, the crab-eating macaque,

and the bonobo. All these primates were “permissive” to the SARS-2 coronavirus and should undergo “further experimentational investigation,” the scientists proposed.

Despite this wide-ranging effort, there is at the moment no animal host that zoonoticists can point to as the missing link. There’s also no single, agreed-upon hypothesis to explain how the disease may have traveled from the bat reservoirs of Yunnan all the way to Wuhan, seven hours by train, without leaving any sick people behind and without infecting anyone along the way.

The zoonoticists say that we shouldn’t find it troubling that virologists have been inserting and deleting furin cleavage sites and ACE2-receptor-binding domains in experimental viral spike proteins for years: The fact that virologists have been doing these things in laboratories, in advance of the pandemic, is to be taken as a sign of their prescience, not of their folly. But I keep returning to the basic, puzzling fact: This patchwork pathogen, which allegedly has evolved without human meddling, first came to notice in the only city in the world with a laboratory that was paid for years by the U.S. government to perform experiments on certain obscure and heretofore unpublicized strains of bat viruses — which bat viruses then turned out to be, out of all the organisms on the planet, the ones that are most closely related to the disease. What are the odds?

In July, I discovered a number of volunteer analysts who were doing a new kind of forensic, samizdat science, hunched over the letter code of the SARS-2 genome like scholars deciphering the cuneiform impressions in Linear B tablets. There were the anonymous authors of Project Evidence, on GitHub, who “disavow all racism and violent attacks, including those which are aimed at Asian or Chinese people,” and there was Yuri Deigin, a biotech entrepreneur from Canada, who wrote a massive, lucid paper on Medium, “Lab-Made?,” which illumined the mysteries of the spike protein. Jonathan

Latham of the Bioscience Resource Project, with his co-author Allison Wilson, wrote two important papers: one a calm, unsparing overview of laboratory accidents and rash research and the other a close look at the small outbreak of an unexplained viral pneumonia in a bat-infested copper mine in 2012. I corresponded with Alina Chan (now the subject of a nicely turned piece in *Boston* magazine by Rowan Jacobsen) and with the pseudonymous Billy Bostickson, a tireless researcher whose Twitter photo is a cartoon of an injured experimental monkey, and Monali Rahalkar, of the Agharkar Research Institute in Pune, India, who wrote a paper with her husband, Rahul Bahulikar, that also sheds light on the story of the bat-guano-shoveling men whose virus was remarkably like SARS-2, except that it was not nearly as catching. I talked to Rossana Segreto, a molecular biologist at the University of Innsbruck, whose paper, "Is Considering a Genetic-Manipulation Origin for SARS-CoV-2 a Conspiracy Theory That Must Be Censored?," co-authored with Yuri Deigin, was finally published in November under a milder title; it argued that SARS-2's most notable features, the furin site and the human ACE2-binding domain, were unlikely to have arisen simultaneously and "might be the result of lab manipulation techniques such as site directed mutagenesis." Segreto is also the person who first established that a bat-virus fragment named BtCoV/4991, identified in 2013, was 100 percent identical to the closest known cousin to SARS-CoV-2, the bat virus RaTG13, thereby proving that the virus closest to the SARS-2-pandemic virus was linked back not to a bat cave but to a mine shaft, and that this same virus had been stored and worked on in the Wuhan Institute for years. This made possible the first big investigative piece on SARS-2's origins, in the *Times* of London, in July: "Nobody can deny the bravery of scientists who risked their lives harvesting the highly infectious virus," the *Times* authors write. "But did their courageous detective work lead inadvertently to a global disaster?"

XII.

"A New, Non-Natural Risk"

In 2011, a tall, confident Dutch scientist, Ron Fouchier, using grant money from Fauci's group at NIH, created a mutant form of highly pathogenic avian influenza, H5N1, and passaged it ten times through ferrets in order to prove that he could "force" (his word) this potentially fatal disease to infect mammals, including humans, "via aerosols or respiratory droplets." Fouchier said his findings indicated that these avian influenza viruses, thus forced, "pose a risk of becoming pandemic in humans."

This experiment was too much for some scientists: Why, out of a desire to prove that something extremely infectious could happen, would you make it happen? And why would the U.S. government feel compelled to pay for it to happen? Late in 2011, Marc Lipsitch of the Harvard School of Public Health got together with several other dismayed onlookers to ring the gong for caution. On January 8, 2012, the New York *Times* published a scorcher of an editorial, "An Engineered Doomsday." "We cannot say there would be no benefits at all from studying the virus," the *Times* said. "But the consequences, should the virus escape, are too devastating to risk."

These gain-of-function experiments were an important part of the NIH's approach to vaccine development, and Anthony Fauci was reluctant to stop funding them. He and Francis Collins, director of the National Institutes of Health, along with Gary Nabel, NIAID director of vaccine research, published an opinion piece in the Washington *Post* in which they contended that the ferret flu experiments, and others like them, were "a risk worth taking." "Important information and insights can come from generating a potentially dangerous virus in the laboratory," they wrote; the work can "help delineate the principles of virus transmission between species." The

work was safe because the viruses were stored in a high-security lab, they believed, and the work was necessary because nature was always coming up with new threats. “Nature is the worst bioterrorist,” Fauci told a reporter. “We know that through history.”

Soon afterward, there followed some distressing screwups in secure federal laboratories involving live anthrax, live smallpox, and live avian influenza. These got attention in the science press. Then Lipsitch’s activists (calling themselves the Cambridge Working Group) sent around a strong statement on the perils of research with “Potential Pandemic Pathogens,” signed by more than a hundred scientists. The work might “trigger outbreaks that would be difficult or impossible to control,” the signers said. Fauci reconsidered, and the White House in 2014 announced that there would be a “pause” in the funding of new influenza, SARS, and MERS gain-of-function research.

Baric, in North Carolina, was not happy. He had a number of gain-of-function experiments with pathogenic viruses in progress. “It took me ten seconds to realize that most of them were going to be affected,” he told NPR. Baric and a former colleague from Vanderbilt University wrote a long letter to an NIH review board expressing their “profound concerns.” “This decision will significantly inhibit our capacity to respond quickly and effectively to future outbreaks of SARS-like or MERS-like coronaviruses, which continue to circulate in bat populations and camels,” they wrote. The funding ban was itself dangerous, they argued. “Emerging coronaviruses in nature do not observe a mandated pause.”

Hoping to smooth over controversy by showing due diligence, the National Science Advisory Board for Biosecurity, founded in the BioShield era under President Bush, paid a consulting firm, Gryphon Scientific, to write a report on gain-of-function research, which by now was simply referred to as GoF.

In chapter six of this thousand-page dissertation, published in April 2016, the consultants take up the question of coronaviruses. “Increasing the transmissibility of the coronaviruses could significantly increase the chance of a global pandemic due to a laboratory accident,” they wrote.

The Cambridge Working Group continued to write letters of protest and plead for restraint and sanity. Steven Salzberg, a professor of biomedical engineering at Johns Hopkins, said, “We have enough problems simply keeping up with the current flu outbreaks — and now with Ebola — without scientists creating incredibly deadly new viruses that might accidentally escape their labs.” David Relman of Stanford Medical School said, “It is unethical to place so many members of the public at risk and then consult only scientists — or, even worse, just a small subset of scientists — and exclude others from the decision-making and oversight process.” Richard Ebright wrote that creating and evaluating new threats very seldom increases security: “Doing so in biology — where the number of potential threats is nearly infinite, and where the asymmetry between the ease of creating threats and the difficulty of addressing threats is nearly absolute — is especially counterproductive.” Lynn Klotz wrote, “Awful as a pandemic brought on by the escape of a variant H5N1 virus might be, it is SARS that now presents the greatest risk. The worry is less about recurrence of a natural SARS outbreak than of yet another escape from a laboratory researching it to help protect against a natural outbreak.” Marc Lipsitch argued that gain-of-function experiments can mislead, “resulting in worse not better decisions,” and that the entire gain-of-function debate as overseen by the NIH was heavily weighted in favor of scientific insiders and “distinctly unwelcoming of public participation.”

Nariyoshi Shinomiya, a professor of physiology and nano-medicine at the National Defense Medical College in Japan, offered this warning: “Similar to nuclear or chemical weapons there is no going back once we get a thing in

our hands."

But in the end, Baric was allowed to proceed with his experiments, and the research papers that resulted, showered with money, became a sort of *Anarchist's Cookbook* for the rest of the scientific world. In November 2015, Baric and colleagues published a collaboration paper with Shi Zhengli titled "A SARS-like Cluster of Circulating Bat Coronaviruses Shows Potential for Human Emergence." Into a human SARS virus that they had adapted so that it would work in mice, Baric and Shi et al. inserted the spike protein of a bat virus, SHC014, discovered by Shi in southern China. They dabbed the mice nasally with virus and waited, looking for signs of sickness: "hunching, ruffled fur." They also infected human airway cells with the mouse-adapted bat-spike-in-a-human-virus backbone. In both mice and human airway cells, the chimeric virus caused a "robust infection."

This proved, Baric and Shi believed, that you did not need civets or other intermediate hosts in order for bats to cause an epidemic in humans and that therefore all the SARS-like viruses circulating in bat populations "may pose a future threat." Peter Daszak, who had used Predict funds to pay Shi for her work on the paper, was impressed by this conclusion; the findings, he said, "move this virus from a candidate emerging pathogen to a clear and present danger."

Richard Ebright was trenchantly unenthusiastic. "The only impact of this work," he said, "is the creation, in a lab, of a new, non-natural risk."

Early in 2016, Baric and Shi again collaborated. Shi sent Baric a fresh bat virus spike protein, and Baric inserted it into the backbone of a human SARS virus and then used that infectious clone to attack human airway cells. "The virus readily and efficiently replicated in cultured human airway tissues, suggesting an ability to potentially jump directly to humans,"

reported the UNC's website. This time, they also used the bat-human hybrid virus to infect transgenic humanized mice that grew human ACE2 protein. The mice, young and old, lost weight and died, proving, again, that this particular bat virus was potentially "poised to emerge in human populations." It was "an ongoing threat," Baric wrote. But was it? Civets and camels that are exposed to a lot of bat-guano dust may be an ongoing threat and a manageable one. But the bats themselves just want to hang in their caves and not be bothered by frowning sightseers in spacesuits who want to poke Q-tips in their bottoms. This 2016 "poised for human emergence" paper was supported by eight different NIH grants. In 2015, Baric's lab received $8.3 million from the NIH; in 2016, it received $10.5 million.

Gain-of-function research came roaring back under Trump and Fauci. "The National Institutes of Health will again fund research that makes viruses more dangerous," said an article in *Nature* in December 2017. Carrie Wolinetz of the NIH's office of science policy defended the decision. "These experiments will help us get ahead of viruses that are already out there and pose a real and present danger to human health," she told *The Lancet*. The NIH, Wolinetz said, was committed to a leadership role with gain-of-function research internationally. "If we are pursuing this research in an active way, we will be much better positioned to develop protection and countermeasures should something bad happen in another country."

A reporter asked Marc Lipsitch what he thought of the resumption of NIH funding. Gain-of-function experiments "have done almost nothing to improve our preparedness for pandemics," he said, "yet they risked creating an accidental pandemic."

XIII.

"Proximity Is a Problem"

In April, four months into the coronavirus emergency, a deputy director at the NIH wrote an email to EcoHealth Alliance. "You are instructed to cease providing any funds to Wuhan Institute of Virology," it said. In response, Daszak and the chief scientific officer of New England Biolabs (a company that sells seamless gene-splicing products to laboratories, among other things) got 77 Nobel Prize winners to sign a statement saying that the cancellation deprived the "nation and the world of highly regarded science that could help control one of the greatest health crises in modern history and those that may arise in the future." Later, as a condition of further funding, the NIH wrote to say it wanted Daszak to arrange an outside inspection of the Wuhan lab and to procure from Wuhan's scientists a sample of whatever they'd used to sequence the SARS-2 virus. Daszak was outraged ("I am not trained as a private detective"), and again he fought back. He was reluctant to give up his own secrets, too. "Conspiracy-theory outlets and politically motivated organizations have made Freedom of Information Act requests on our grants and all of our letters and emails to the NIH," he told *Nature.* "We don't think it's fair that we should have to reveal everything we do."

But Daszak has survived — even prospered. Recently, *The Lancet* made him the lead investigator in its inquiry into the origins of the pandemic, and the World Health Organization named him to its ten-person origins investigation. ("We're still close enough to the origin to really find out more details about where it has come from," Daszak told *Nature*.)

The NIH has also set up an ambitious new international program, called CREID, which stands for Centers for Research in Emerging Infectious Diseases, and it has put Daszak's EcoHealth in charge of trapping animals and looking for obscure bat viruses in Singapore, Malaysia, and Thailand.

Baric is one of Daszak's partners in CREID. The virus hunting and collecting, which Richard Ebright likens to "looking for a gas leak with a lighted match," will continue and widen with U.S. funding. "We're going to work in remote parts of Malaysia and Thailand to get to the front line of where the next pandemic is going to start," Daszak told NPR.

In May, an interviewer from the People's Pharmacy website asked Baric if he had any thoughts on whether the coronavirus began with a natural bat-to-human transfer. "Or was there something a little bit more, perhaps, insidious involved?"

"Well, of course the answers to those questions are in China," Baric replied. "Exactly how they work in that facility is something that would be very difficult for a Westerner to know," he said. "The main problems that the Institute of Virology has is that the outbreak occurred in close proximity to that Institute. That Institute has in essence the best collection of virologists in the world that have gone out and sought out, and isolated, and sampled bat species throughout Southeast Asia. So they have a very large collection of viruses in their laboratory. And so it's — you know — proximity is a problem. It's a problem."

Over the course of the fall, and especially after the election muffled Donald Trump's influence over the country's public-health apparatus, that proximity problem — and the uncomfortable questions of origins it raised — began to grow somewhat more discussable. The BBC, *Le Monde*, and Italy's RAI have all recently taken seriously the scientific possibility of a lab leak. In late October, the World Health Organization convened the first meeting of its second inquiry into the origins of the disease. The WHO's effort is perhaps the world's best chance to satisfy its curiosity about goings-on at the Wuhan Institute of Virology and at the Wuhan CDC's virus lab near the Wuhan seafood market. But, as the New York *Times* has reported, the

WHO's information gathering has been hindered by Chinese secretiveness since February, when an initial investigative team sent to Beijing was told its members' access to scientists would be restricted and that it couldn't visit the seafood market, then considered a hub of the pandemic.

When a BBC video team tried to inspect the Yunnan mine shaft, they found the road to the mine blocked by a strategically parked truck that had "broken down" shortly before they arrived. Reporter John Sudworth asked Daszak, one of the ten members of the second WHO investigative team, whether he would push for access to the Wuhan Institute of Virology. "That's not my job to do that," Daszak replied.

In November, David Relman, the Stanford microbiologist, one of the most thoughtful of the voices warning against gain-of-function research, published a paper in *Proceedings of the National Academy of Sciences* on the urgent need to unravel the origins of COVID-19. "If SARS-CoV-2 escaped from a lab to cause the pandemic," he wrote, "it will become critical to understand the chain of events and prevent this from happening again." Conflicts of interest by researchers and administrators will need to be addressed, Relman wrote; to reach the truth, the investigation must be transparent, international, and, as much as possible, unpolitical. "A more complete understanding of the origins of COVID-19 clearly serves the interests of every person in every country on this planet."

"The world is sitting on a precedent-setting decision right now," wrote Alina Chan on December 8. "It is unclear if SARS2 is 100 percent natural or emerged due to lab/research activities. If we walk away from this, demonstrating that we cannot effectively investigate its origins, it will pave the way for future COVIDS."

Just before this issue of *New York* went to press, I reached Ralph Baric by

phone and asked him where he now believed SARS-2 came from. (Anthony Fauci, Shi Zhengli, and Peter Daszak didn't respond to emails, and Kristian Andersen said he was busy with other things.) Baric said he still thought the virus came from bats in southern China, perhaps directly, or possibly via an intermediate host, although the smuggled pangolins, in his view, were a red herring. The disease evolved in humans over time without being noticed, he suspected, becoming gradually more infectious, and eventually a person carried it to Wuhan "and the pandemic took off." Then he said, "Can you rule out a laboratory escape? The answer in this case is probably not."

XIV.

Transmission

So how did we actually get this disease?

Here's what I think happened. In April 2012, in a copper mine in Mojiang, China, three men were given an awful job — they were told to shovel bat guano out of a mine shaft. They went to work and shoveled guano for seven hours a day in the confined, insufficiently ventilated space of the mine shaft, and by the end of the week, they were sick with a viral pneumonia of unknown etiology. Three more, younger shovelers were hired to replace the ones who were out sick.

The viral load in their lungs was so huge, because of all the guano dust, that their lungs became a kind of accelerated laboratory passaging experiment, as Jonathan Latham and Allison Wilson have written, forcing the virus to switch its allegiance from bats to humans. SARS experts were consulted, and the disease was judged to be SARS-like but not SARS. It was something new. (Shi Zhengli told *Scientific American* that the guano shovelers had died of a fungal disease, but, as Monali Rahalkar pointed out,

they were treated with antivirals, and their symptoms were consistent with viral pneumonia with attendant secondary fungal infections.)

Although it was a severe disease, and in the end three of the shovelers died, there was no resultant epidemic. It was actually a case of industrial overexposure to an infectious substance — what we might call a massive OSHA violation. The bat disease that the men encountered wasn't necessarily all that dangerous except in an environment of immunosuppressive overload.

Peter Daszak and Shi Zhengli were interested, of course, because this unidentified coronavirus disease involved bats and people. Of the fragmentary bits of virus Shi retrieved from the mine shaft, one was SARS-like, and Shi sequenced it and called it BtCoV/4991 and published a paper about it. Several times — in 2016 and 2018 and 2019 — this most interesting sample, a portion of what we now know as RaTG13, was taken out of the freezers in Shi's lab and worked on in undisclosed ways. (Peter Daszak claims that these samples have disintegrated and can't be validated or studied.) Samples of the nameless human disease also traveled back to the Wuhan Institute of Virology — few specifics about these valuable specimens have been released by Chinese sources, however.

This is the period in the story that demands a very close investigation, when chimeric assemblages may have been created and serially passaged, using BtCoV/4991, a.k.a. RaTG13, and other bat viruses, perhaps along with forms of the human virus. It's when Shi and Baric both published papers that were about what happened when you hot-swapped mutant spike proteins between bat viruses and human viruses.

The link, via the renamed sample BtCoV/4991, to the copper mine is of exceptional importance because of the one huge difference between the

unnamed guano shovelers' virus and the SARS-2 virus that is now ravaging, for example, California: transmissibility. Airborne human-to-human transmissibility — the kind of thing that gain-of-functioneers like Ron Fouchier and Ralph Baric were aiming at, in order to demonstrate what Baric called "lurking threats" — is COVID-19's crucial distinguishing feature. If six men had gotten extremely sick with COVID-19 back in 2012 in southern China, doctors and nurses in the hospital where they lay dying would likely have gotten sick as well. There might have been hundreds or thousands of cases. Instead, only the shovelers themselves, who had breathed a heavy concentration of guano dust for days, got it.

The existence of bat virus RaTG13 is therefore not necessarily evidence of a natural bat origin. In fact, it seems to me to imply the opposite: New functional components may have been overlaid onto or inserted into the RaTG13 genome, new Tinkertoy intermolecular manipulations, especially to its spike protein, which have the effect of making it unprecedentedly infectious in human airways.

This is where the uniquely peculiar furin insert and/or the human-tuned ACE2-receptor-binding domain may come in — although it's also possible that either of these elements could have evolved as part of some multistep zoonotic process. But in the climate of gonzo laboratory experimentation, at a time when all sorts of tweaked variants and amped-up substitutions were being tested on cell cultures and in the lungs of humanized mice and other experimental animals, isn't it possible that somebody in Wuhan took the virus that had been isolated from human samples, or the RaTG13 bat virus sequence, or both (or other viruses from that same mine shaft that Shi Zhengli has recently mentioned in passing), and used them to create a challenge disease for vaccine research — a chopped-and-channeled version of RaTG13 or the miners' virus that included elements that would make it thrive and even rampage in people? And then what if, during an

experiment one afternoon, this new, virulent, human-infecting, furin-ready virus got out?

For more than 15 years, coronavirologists strove to prove that the threat of SARS was ever present and must be defended against, and they proved it by showing how they could doctor the viruses they stored in order to force them to jump species and go directly from bats to humans. More and more bat viruses came in from the field teams, and they were sequenced and synthesized and "rewired," to use a term that Baric likes. In this international potluck supper of genetic cookery, hundreds of new variant diseases were invented and stored. And then one day, perhaps, somebody messed up. It's at least a reasonable, "parsimonious" explanation of what might have happened.

This may be the great scientific meta-experiment of the 21st century. Could a world full of scientists do all kinds of reckless recombinant things with viral diseases for many years and successfully avoid a serious outbreak? The hypothesis was that, yes, it was doable. The risk was worth taking. There would be no pandemic.

I hope the vaccine works.

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LIFE & ARTS | IDEAS | ESSAY

The World Needs a Real Investigation Into the Origins of Covid-19

A team of WHO researchers has arrived in China but won't investigate the possibility that the coronavirus originated in a lab.

Dr. Shi Zhingli, whose lab at the Wuhan Institute of Virology has been a suspected source of the coronavirus, in 2017.
PHOTO: JOHANNES EISELE/AFP/GETTY IMAGES

By Alina Chan and Matt Ridley
Jan. 15, 2021 11:31 am ET

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In the first week of January, scientists representing the World Health Organization (WHO) were due to arrive in China to trace the origins of Covid-19. The team membership and terms of reference were preapproved by the Chinese government, yet at the last minute Beijing denied entry to the investigators. This prompted WHO to take the rare step of criticizing China, which relented and allowed the group to enter the country this week.

The brief standoff highlights a more serious problem: the inadequacy of WHO's current investigative framework for exploring all plausible origins of Covid-19. The world needs an inquiry that considers not just natural origins but the possibility that SARS-CoV-2, the virus that causes Covid-19, escaped from a laboratory. The WHO team, however, plans to build on reports by Chinese scientists rather than mount an independent investigation. Given that Chinese authorities have been slow to release information, penalized scientists and doctors who shared clinical and genomic details of the novel coronavirus, and have since demonstrated a keen interest in controlling the narrative of how the virus emerged, this is not a promising foundation for WHO's investigation.

The WHO team includes experts who traced the origins of Ebola and MERS outbreaks, but critics are concerned that it doesn't have the expertise for an investigation that would examine possible lab origins. Dr. David Relman of Stanford University, who raised the possibility early on that the virus might have leaked from a lab, told us: "Based on the scant information that has been shared publicly about the WHO investigation, it doesn't appear that WHO has adequately represented the range of views and perspectives of key stakeholders or incorporated all needed forms of expertise." Responding to whether the

Critics are concerned that the WHO team doesn't have the expertise for an investigation that would examine possible lab origins of the coronavirus.

WHO team will investigate lab origins, Dr. Peter Ben Embarek, the leader of the team, told us, "If our studies point to a possible lab accident, then other international mechanisms would be involved to document such an event. It would take time and additional types of expertise."

Tedros Adhanom Ghebreyesus, director-general of the World Health Organization, at a press conference in March 2020.

PHOTO: SALVATORE DI NOLFI/ASSOCIATED PRESS

Could the virus have escaped from a laboratory? Then-deputy U.S. national security adviser Matthew Pottinger told international leaders late last year that the latest intelligence points to SARS-CoV-2 having originated from the Wuhan Institute of Virology (WIV). This intelligence has not been made public, and China has denied that the virus came from a lab. Dr. Shi Zhengli, whose lab at WIV has been a suspected source of the virus, told Scientific American last March that "none of the [early SARS-CoV-2] sequences matched those of the viruses her team had sampled from bat caves."

The hypothesis that SARS-CoV-2 originated in a lab remains controversial. Last March, in the journal Nature Medicine, Dr. Kristian Andersen of the Scripps Research Institute and colleagues asserted that "SARS-CoV-2 is not a laboratory construct or a purposefully manipulated virus." They said there was no evidence to support lab-based origins and that the available data was consistent with natural evolution. Dr. David Robertson of the University of Glasgow told us that "SARS-CoV-2 is just too different to the [viruses] we were aware of prior to its emergence."

The ability to build coronavirus genomes without leaving traces of manipulation has existed for years.

In November, however, in the journal PNAS, Dr. Relman wrote that Dr. Andersen's argument didn't acknowledge that unpublished viruses closely related to SARS-CoV-2 could have been studied in a laboratory. For more than a decade, Dr. Shi has been publishing experiments on "chimera" coronaviruses, built by inserting parts of newly found viruses into better known viruses to understand how novel viruses could infect human cells. These were used to assess the risk that such viruses could spill over

into humans.

The ability to build coronavirus genomes without leaving traces of manipulation has existed for years. Dr. Ralph Baric of the University of North Carolina at Chapel Hill, a world-leading coronavirus expert and collaborator of Dr. Shi, told an Italian television documentary last June, "In sequence databases there were sequences for a large number of bat coronaviruses that were SARS-like, reported out of China." He added that "whether the virus existed beforehand, it would only be within the records of the Institute of Virology in Wuhan."

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For some scientists, the location of the first detected outbreak is enough to raise suspicions. In the words of Dr. Richard Ebright of Rutgers University, "the outbreak occurred on the doorstep of laboratories that conduct the world's largest research project on horseshoe-bat viruses, that have the world's largest collection of horseshoe-bat viruses, and that possessed and worked with the world's closest sequenced relative of the outbreak virus. The laboratories actively searched for new horseshoe-bat viruses in horseshoe-bat colonies in caves in remote rural areas in Yunnan province, brought those new horseshoe-bat viruses to Wuhan, and then mass-produced and studied those new horseshoe-bat viruses, year-round, inside Wuhan."

Such concerns have gained prominence over the past year and were recently explored in a much-discussed article in New York magazine, "The Lab-Leak Hypothesis" by Nicholson Baker.

In January 2020, a police officer stands guard outside the seafood market in Wuhan, China, where the coronavirus was first detected.
PHOTO: HECTOR RETAMAL/AFP/GETTY IMAGES

SARS viruses are known to have escaped previously from laboratories in Singapore, Taiwan and twice in Beijing. Dr. Maciej Boni of Pennsylvania State University told us that if the virus escaped from the Wuhan lab (though he thinks this is unlikely), he would expect that "some of the early December cases should be traceable to WIV employees, family members of WIV employees or frequent social contacts of WIV employees. If this evidence is presented, it will be the first 'positive evidence' that SARS-CoV-2 may have a lab origin."

What would it take to properly investigate possible lab origins? Dr. Relman said that "it will be critical to obtain independently verified, time-stamped records of sample

inventories, data, lab notebooks and records, internal and external communications, personnel health records and serum samples, and access to personnel so that they can be interviewed in private without fear of repercussions." Yet the path to such a credible investigation seems nearly impossible in the current geopolitical climate.

Several scientists also told us they were troubled by the presence on the WHO team of Dr. Peter Daszak of the New York-based EcoHealth Alliance. Dr. Daszak has been a longtime collaborator of Dr. Shi since they worked together to trace SARS viruses to bats after the 2003 epidemic. His organization has administered more than $100 million in U.S. federal grants to fund overseas fieldwork and laboratory experiments, including those performed by WIV, to find and characterize new viruses in order to predict the next pandemic, according to the EcoHealth Alliance.

Last February, Dr. Peter Daszak organized a statement in The Lancet, a prominent medical journal, to 'condemn conspiracy theories suggesting that Covid-19 doesn't have a natural origin.'

Last February, Dr. Daszak organized a statement in The Lancet, a prominent medical journal, to "condemn conspiracy theories suggesting that Covid-19 doesn't have a natural origin." The statement was drafted when little was yet known about the virus. Dr. Daszak declined to comment for this piece, but a spokesman for Dr. Daszak told us: "The Lancet letter was written during a time in which Chinese scientists were receiving death threats and the letter was intended as a showing of support for them as they were caught between important work trying to stop an outbreak and the crush of online harassment." Yet, in June, Dr. Daszak wrote an opinion piece for the Guardian headlined, "Ignore the conspiracy theories: scientists know Covid-19 wasn't created in a lab."

The spokesman for Dr. Daszak told us that any questions about his potential conflict of interest should be referred to WHO. Dr. Ben Embarek said that he sees no problem in having Dr. Daszak on his investigative team: "Of course the WHO team will have discussion with the scientists and researchers in Wuhan. And therefore it is good to have on the team someone who knows the area well."

Miles Pomper, a co-author of an expert guide to investigating outbreak origins published in October by the Middlebury Institute of International Studies at Monterey, said that "The independence of the WHO investigation may be seriously compromised by the process used to choose investigators.... In particular, the choice of Dr. Daszak, who has a personal stake in ensuring current Chinese practices continue and who is a longtime collaborator of a scientist at the center of the investigation, is likely to taint its results."

Another co-author of the guide, Dr. Filippa Lentzos, said, "We also need to take a hard look in the mirror. It is our own virologists, funders and publishers who are driving and endorsing the practice of actively hunting for viruses and the high-risk research of deliberately making viruses more dangerous to humans. We need to be more open about the heavily vested interests of some of the scientists given prominent platforms to make claims about the pandemic's origins."

As a scientist and a science writer, we believe that both natural and lab-based scenarios of Covid-19's origins must be rigorously investigated, not only to avert future pandemics but for the sake of science's reputation. The formal investigation launched by WHO is only

taking steps to look into natural origins. That needs to change.

—Dr. Chan is a researcher at the Broad Institute of MIT and Harvard. Mr. Ridley is a member of the House of Lords and the author, most recently, of "How Innovation Works: And Why It Flourishes in Freedom."

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OPINION

To stop the next pandemic, we need to unravel the origins of COVID-19

David A. Relman[a,b,c,d,1]

We find ourselves ten months into one of the most catastrophic global health events of our lifetime and, disturbingly, we still do not know how it began. What's even more troubling is that despite the critical importance of this question, efforts to investigate the origins of the severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) virus and of the associated disease, coronavirus disease 2019 (COVID 19), have become mired in politics, poorly supported assumptions and assertions, and incomplete information.

SARS CoV 2 is a betacoronavirus whose apparent closest relatives, RaTG13 and RmYN02, are reported to have been collected from bats in 2013 and 2019, respectively, in Yunnan Province, China (1). COVID 19 was first reported in December 2019 more than 1,000 miles away in Wuhan City, Hubei Province, China. Beyond these facts, the "origin story" is missing many key details, including a plausible and suitably detailed recent evolutionary history of the virus, the identity and provenance of its most recent ancestors, and surprisingly, the place, time, and mechanism of transmission of the first human infection. Even though a definitive answer may not be forthcoming, and even though an objective analysis requires addressing

To avoid or mitigate the dire consequences of this and future pandemics (here, people in PPE bury a victim in Delhi, India in June), unraveling the origins of SARS-CoV-2 and COVID-19 will be essential—even though a definitive answer may be elusive, and an objective analysis means broaching some uncomfortable possibilities. Image credit: Shutterstock/PradeepGaurs.

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some uncomfortable possibilities, it is crucial that we pursue this question. Preventing the next pandemic depends on understanding the origins of this one.

There are several potential origin scenarios. First, SARS CoV 2 may have evolved in bats, which are known reservoirs of immense coronavirus diversity (2), and then spread directly, or indirectly via an intermediate host, to humans through natural mechanisms. The degree of anticipated but undiscovered natural diversity clearly lends support to this scenario, as well as support to other scenarios. Second, SARS CoV 2 or a recent ancestor virus may have been collected by humans from a bat or other animal and then brought to a laboratory where it was stored knowingly or unknowingly, propagated and perhaps manipulated genetically to understand its biological properties, and then released accidentally.

Some have argued that a deliberate engineering scenario is unlikely because one would not have had the insight *a priori* to design the current pandemic virus (3). This argument fails to acknowledge the possibility that two or more as yet undisclosed ancestors (i.e., more proximal ancestors than RaTG13 and RmYN02) had already been discovered and were being studied in a laboratory for example, one with the SARS CoV 2 backbone and spike protein receptor binding domain, and the other with the SARS CoV 2 polybasic furin cleavage site. It would have been a logical next step to wonder about the properties of a recombinant virus and then create it in the laboratory. Alternatively, the complete SARS CoV 2 sequence could have been recovered from a bat sample and viable virus resurrected from a synthetic genome to study it, before that virus accidentally escaped from the laboratory. The third scenario, seemingly much less l kely, involves laboratory manipulation or release, with the clear intention of causing harm.

Even though strong opinions abound, none of these scenarios can be confidently ruled in or ruled out with currently available facts. Just because there are no public reports of more immediate, proximal ancestors in natural hosts, doesn't mean that these ancestors don't exist in natural hosts or that COVID 19 didn't began as a spillover event. Nor does it mean that they have not been recovered and studied, or deliberately recombined in a laboratory.

Why do these distinctions matter? If we find more concrete evidence of a "spill over" event with SARS CoV 2 passing directly from bat to human, then efforts to understand and manage the bat human interface need to be significantly strengthened. But if SARS CoV 2 escaped from a lab to cause the pandemic, it will become critical to understand the chain of events and prevent this from happening again. Rather than resorting to hunches or finger pointing, each scenario must be systematically and objectively analyzed using the best available science based approaches. There is a path to greater clarity. It requires scientific rigor, forensic approaches, deliberate methods, transparency, and cooperation.

In an effort to reveal the origins of the pandemic, researchers so far have focused on the SARS CoV 2 genome sequence. However, the sequence of the pandemic virus tells us only so much. First, the closest known relatives, RaTG13 and RmYN02, are not that close (4). Second, there is probably more than one recent ancestral lineage that contributes to SARS CoV 2 because its genome shows evidence of recombination between different parental viruses. In nature, recombination is common among coronaviruses. But it's also common in some research laboratories where recombinant engineering is used to study those viruses. The bottom line is simple: We need to identify the immediate parent(s) of SARS CoV 2, and they're missing.

To find its parents and understand its recent history, we need 1) additional genome sequences of coronaviruses from relevant bats and other suspect hosts some of these likely exist already in laboratories, given the efforts so far undertaken to survey bats in particular (2, 5); 2) measurements of SARS CoV 2 evolution under a variety of defined conditions so that differences between viral genomes can be understood better as differences in time on an evolutionary clock; and 3) data from antibody surveys of humans at high risk of coronavirus exposure and from past cases of similar disease, so that previously unrecognized encounters can be revealed. In addition, we need to address whether there is information about host or environmental samples that contain recent ancestors of SARS CoV 2, data perhaps not yet publicly available. More generally, are there relevant scientific data, including from coronavirus engineering work in laboratories, that have not been shared widely? Who knew what about relevant viruses and cases of disease before December 2019, and when? This information will go a long way toward clarifying the origins of this pandemic, even if certainty continues to elude us.

A deliberative process for investigating the origins of this pandemic must be representative of all relevant disciplines, expertise, and stakeholders; must achieve political neutrality, scientific balance, and access to all relevant information and samples; and must operate with transparency and independent oversight. Without these features, it will not be credible, trustworthy, or effective.

The means are just as important as the goals. An investigative process should be transparent, collaborative, international, and, to the extent possible, devoid of political interest. Recent, productive scientific collaborations between the United States and China, for example, provide hope that such a process can be achieved. But the kind of effort required will need to expand far beyond what's taken place so far, and nations other than the United States and China will need to be involved. Conflicts of interest by researchers, administrators, and policymakers on all sides must be revealed and addressed, and all relevant global

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constituencies must be included. Both the World Health Organization and *The Lancet* COVID 19 Commission (6) have hinted that they have taken some first steps, but their efforts so far have been cloaked in secrecy (7, 8). A deliberative process for investigating the origins of this pandemic must be representative of all relevant disciplines, expertise, and stakeholders; must achieve political neutrality, scientific balance, and access to all relevant information and samples; and must operate with transparency and independent oversight. Without these features, it will not be credible, trustworthy, or effective.

A more complete understanding of the origins of COVID 19 clearly serves the interests of every person in every country on this planet. It will limit further recriminations and diminish the likelihood of conflict; it will lead to more effective responses to this pandemic, as well as efforts to anticipate and prevent the next one. It will also advance our discussions about risky science. And it will do something else: Delineating COVID 19's origin story will help elucidate the nature of our very precarious coexistence within the biosphere.

1 Y.-Z. Zhang, E. C. Holmes, A genomic perspective on the origin and emergence of SARS-CoV-2. *Cell* **181**, 223–227 (2020).
2 A. Latinne *et al.*, Origin and cross-species transmission of bat coronaviruses in China. *Nat. Commun.* **11**, 4235 (2020).
3 K. G. Andersen, A. Rambaut, W. I. Lipkin, E. C. Holmes, R. F. Garry, The proximal origin of SARS-CoV-2. *Nat. Med.* **26**, 450–452 (2020).
4 M. F. Boni *et al.*, Evolutionary origins of the SARS-CoV-2 sarbecovirus lineage responsible for the COVID-19 pandemic. *Nat. Microbiol.* (2020).
5 Z. Wu *et al.*, Deciphering the bat virome catalog to better understand the ecological diversity of bat viruses and the bat origin of emerging infectious diseases. *ISME J.* **10**, 609–620 (2016).
6 J. D. Sachs *et al.*; The Lancet COVID-19 Commission. *Lancet* **396**, 454–455 (2020).
7 World Health Organization, WHO experts to travel to China. https://www.who.int/news-room/detail/07-07-2020-who-experts-to-travel-to-china/. Accessed 20 September 2020.
8 P. Nuki, S. Newey, Scientists to examine possibility Covid leaked from lab as part of investigation into virus origins. *The Telegraph*, 15 September 2020. https://www.telegraph.co.uk/global-health/science-and-disease/scientists-examine-possibility-covid-leaked-lab-part-investigation/. Accessed 27 September 2020.

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