UNC SCHOOL OF PUBLIC HEALTH
DEPARTMENT OF EPIDEMIOLOGY

5/31/2013

Dr. Peter Daszak
President
EcoHealth Alliance
460 W 34th St. 17th Floor
New York, NY 10001
USA

Dear Dr. Daszak,

I am writing in response to a request for collaboration on an upcoming NIAID R01 grant entitled "Understanding the risk of bat coronavirus emergence." I agree that studies are definitely needed to identify the key risk factors and develop strategies that prevent the transmission of bat coronaviruses to human populations. Understanding and preventing exposure and transmission of zoonotic diseases from wildlife to humans remains a high priority for prevention of pandemics.

Our laboratory has developed a variety of animal models for understanding human coronavirus pathogenesis in vivo. We have developed transgenic mouse models in the C57BL/6 mice, expressing hACE2 in ciliated cells from the FOXJ1 promoter. Unlike other epithelial cell promoters (e.g., K18, hACE2 expression from FOXJ1 should be specific to the airway epithelium. FOXJ1 (hepatocyte nuclear factor-3/forkhead homologue 4; HFH-4) is a member of the forkhead/winged helix family of transcription factors whose expression is tightly restricted to cells possessing motile cilia or flagella. Inoculation of these mice with wild type SARS-CoV resulted in lethal respiratory tract infections characterized by high virus titers (>10^8 PFU/day 4), hemorrhage, severe pneumonia and acute respiratory distress syndrome between days 2-7 post infection (Fig 1). We also have aged and immunosenescent models that are highly vulnerable to synthetically reconstructed strains of SARS-CoV from early in the epidemic. This letter states my willingness to collaborate with your group to evaluate the in vivo pathogenesis of interesting bat and animal SARS-like coronaviruses.

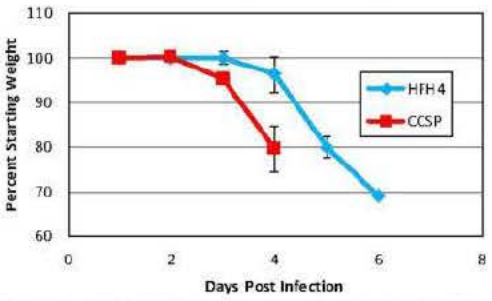

Figure 1. FOXJ1 ACE2 Transgenic Mice are Highly Susceptible to wildtype SARS-CoV Infection. Two different lines were infected with wildtype SARS-virus and clinical disease evaluated at different times postinfection.

It was a pleasure talking with you the other day. I believe your proposal asks fundamentally important questions in the evolution of new human coronaviruses from bats, contributes

dramatically to our understanding of coronavirus variation in natural populations, and provides key insights into the ecology of new emerging infectious diseases. Let me know if I can be of any additional assistance.

Sincerely,

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