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Bat lung epithelial cells show variable species-specific resistance to human and avian influenza viruses

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Bats (order Chiroptera) are natural reservoirs for zoonotic viruses that cause some of the deadliest diseases in humans, including filoviruses (such as Ebola and Marburg viruses), lyssaviruses, severe acute respiratory syndrome (SARS)-related corona viruses and henipa viruses (e.g. Hendra and Nipah viruses). Recently, two novel influenza viruses, H17N10 and H18N11, were also identified in bats through deep sequencing analyses. Despite being hosts to such an array of pathogens, bats generally show no or mild clinical symptoms to their presence, a phenomenon that is largely a mystery and a potential medical treasure trove that offers new insights into dealing with such pathogens in humans and affected animals. The lack of illness does not mean that bat cells are not infected by such viruses. Bat cells are susceptible to virus infections such as paramyxoviruses, filoviruses and influenza viruses, and show varying degree of permissiveness/resistance to virus replication, a pre-requisite for the hosts to acquire carrier status. Murine encephalomyocarditis virus causes severe cytopathic damage to batlung epithelial cells (TB1 Lu) of Tadarida brasiliensis, and Ebola virus shows persistent infection in such cells. TB1 Lu cells also display resistance to reovirus infection; infected cells show no cytopathic effects and rapid decline in virus production, however, low virus release is maintained for at least 2 months. Insights into bat immune resistance could lead to novel therapeutic developments targeting such viruses. Although bats are not known to act as natural hosts for human and avian influenza viruses, chimeric virus housing the 6 core genes from bat H17N10 replicates well in human primary airway epithelial cells and mice,but poorly in avian cells and chicken embryos without further adaptation. Furthermore, viral ribonucleopolymerase complex (vRNP) from bat H17N10 virus is able to drive with high efficiency the non-coding region of human H1N1 virus (A/WSN/1933) in vRNP mini genome reporter assays, suggesting the potential for viable reassortment between bat and conventional influenza A viruses in non-bat hosts. Likewise, bat TB1 Lu cells appear to be more resistant than other bat cells to avian (H7N7 and H9N2) and porcine (H1N1) influenza viruses based on the extent of viral nucleoprotein (NP) detection at 24 h of infection (2). Additionally, infected bat (Pteroptus alecto) kidney cells show virus reassortment between human H1N1 virus (A/WSN/1933) and highly pathogenic avian influenza (HPAI) H5N1 virus. We hypothesise that bat cells possess novel innate immune ability to resist conventional influenza virus infection. To this end, we aim to examine the innate response of lung epithelial cells of T. brasiliensis (a medium insectivorous bat), Eidolon helvum (a large fruit bat) and Carollia perspicillata (a small fruit and insect eating bat) to influenza A virus infection to understand how the virus is inhibited by the host. We found clear evidence of host innate resistance to permissive virus replication in epithelial cells of the three bat species which appears to be independent of type I and III interferons. There were, however, clear differences between bat species inthe distribution of sialic acid virus receptors, and in relative resistance to avian and human influenza viruses.

Biography

Kin-Chow Chang is Professor of Veterinary Molecular Medicine at the University of Nottingham. One strategic approach adopted is to compare host response to virulent influenza virus infection (such as avian H5N1 virus) between resistant (e.g. pig, duck and bat) and susceptible (human and chicken) host species to identify targets for the development of intervention therapy to reduce disease severity.

Tessa Slater is a second year PhD student at the University of Nottingham working under the supervision of Professor Kin-Chow Chang, Dr. Suresh Kuchipudi and Professor Richard Emes. Her project focuses on the innate host response to influenza A virus infection with a focus on the antiviral resistance found in bats.

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