Modeling human respiratory viral infections in the cotton rat

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Abstract

Over three decades the cotton rat has been shown to be a preferred model for Respiratory Syncytial Virus (RSV) infection and pathogenesis, and a reliable model for an impressive list of human respiratory pathogens including influenza, adenoviruses, parainfluenza virus, measles, human metapneumovirus. The most significant contribution of the cotton rat to biomedical research has been the development of anti-RSV antibodies for prophylactic use in high-risk infants.

Now we showed that cotton rats are susceptible to avian and swine influenza viruses. Cotton rats express 2-3-linked sialic acid (SA) and 2-6-linked SA residues in the trachea, and 2-6-linked SA residues in the lung parenchyma. Prototypic avian influenza viruses (H3N2, H9N2, and H5N1) and swine-origin 2009 pandemic H1N1 viruses replicated in the respiratory tract of cotton rats without prior adaptation and produced strong lung pathology. This model allowed us to recently demonstrate the efficacy of Eritoran, a TLR4 antagonist, to reduce human influenza-induced lung pathology.

In addition, we have now shown that the cotton rat is permissive to infection with HRV16, a rhinovirus serotype commonly used in human challenge studies. Virus replicates in the upper and lower respiratory tract of cotton rats after intranasal infection, and results in measurable pathology, mucus production, and expression of interferon-activated genes. The importance of this model for advancing vaccines and therapeutics against rhinovirus infections will be presented.

Biography

Dr. Jorge Blanco has completed his Ph.D from the University of Buenos Aires in 1992 his post-doctoral studies at NIH in 1997. He is the President and Scientific Director at Sigmovir Biosystems, Inc., a contract and research organization advocated to study human respiratory viral infection and pathogenesis. Dr. Blanco has published more than 60 papers in reputed journals and spent more that 12 years in the development of the cotton rat model, and has been awarded with several NIH grant that support his research.