NOBLE LIFE SCIENCES

Cotton Rat Model of Influenza Infection

Introduction

Noble Life Sciences, in partnership with IBT Bioservices, has optimized a cotton rat model of influenza virus infection. Although vaccines and antiviral agents are effective in the prophylaxis and treatment of the disease, each year changes in the influenza virus surface proteins require the development of new vaccines and the emergence of drug resistant strains necessitates the search for new antiviral agents. The need for more effective influenza vaccines and antiviral agents is also highlighted by the potential emergence of avian viruses in the human population which would pose an even greater risk to human health than seasonal influenza epidemics. Therefore, animal models are of considerable importance for the development of practical treatment of influenza and vaccines to prevent it.

The cotton rat is a commonly used model of influenza virus infection in humans because:

- Cotton rats can be infected by non-adapted human influenza viruses. Both influenza A and B strains replicate in the upper and the lower respiratory tract of cotton rats. Cotton rats can be infected with and replicate avian influenza H3N2 and H9N2 viruses.
- Virus infection results in histopathological lesions in the lungs that are similar to those seen during natural infection of humans.
- Virus replication in the lung coincides with the induction of cytokines characteristic of the innate immune response, a potentially important factor in understanding early antiviral mechanisms.
- Hetero-subtypic (or cross-protective) immunity has been observed in cotton rats as a result of influenza virus infection making the model a valuable tool for the development of broadly active influenza vaccines.

Applications

- Vaccine and antiviral drug development
- Adenoviral vector gene therapy
- Infectious disease pathogenesis

Model Read-Outs Include

- Viral load in nasal and lung tissue
- Tissue pathology
- Cytokine levels

Methodology

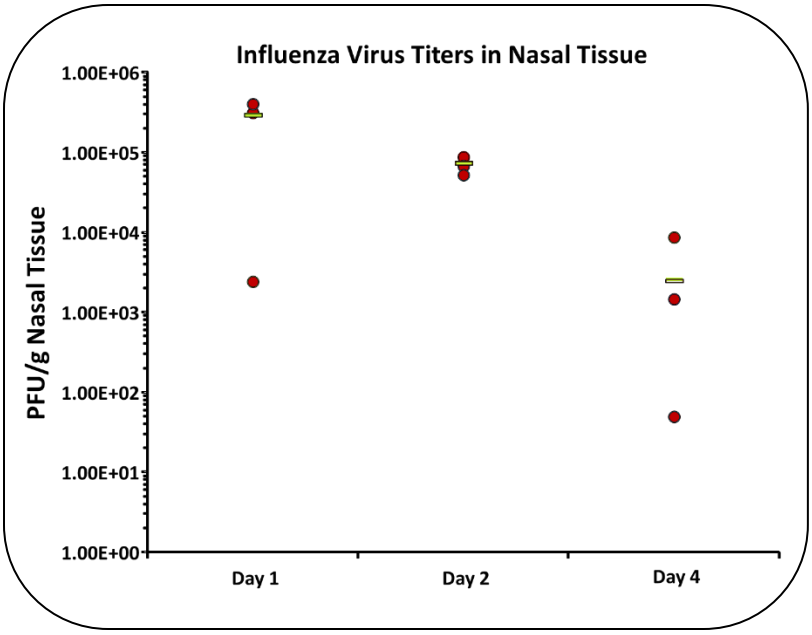
Cotton rats (7-9 weeks of age) were divided into three groups with five animals in Group 1 and four animals each in Groups 2 and 3.

The animals were infected intranasally under light anesthesia (3% isoflurane) with influenza virus A/PR8 (H1N1) at 10^6 TCID50/rat. Animals in Group 1 were euthanized at Day 1, Group 2 at Day 2, and Group 3 at Day 4 post infection.

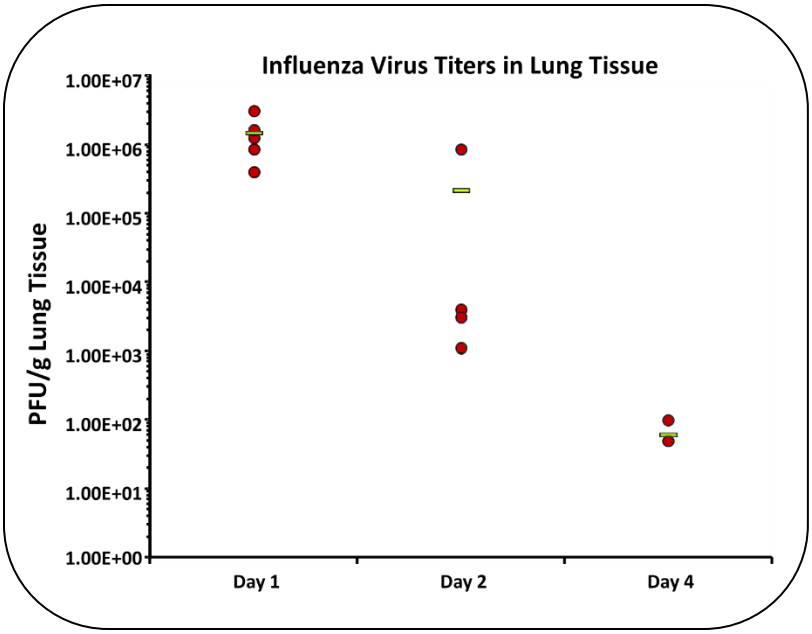
Nasal and lung tissues from euthanized animals were harvested and homogenized; viral titers of tissue homogenates were determined via plaque assay.

Results

Viral titers in nasal tissue homogenates reached more than 10^5 PFU/g of tissue at Day 1 post infection and then declined to about 10^3 PFU/g of tissue by Day 4 post infection (see figure at right).



Viral titers in lung homogenates reached more than 10^6 PFU/g of tissue at Day 1 post infection and then declined to about 10^2 PFU/g of tissue by Day 4 post infection (see figure at right).



In general, viral titers in both lung and nasal tissue homogenates declined from Day 1 to Day 4.