Histology Clinical Isolate SV068 Hematoxilin Eosin 60 days

Conclusion: Our preliminary findings suggest that the host defense can vary accordingly to the type of clinical isolation, leading to a correlation between the virulence and the source of infection.

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73.007
Evaluation of the ferret as a model for influenza A/Brisbane/10/07 H3N2
J. Garver 1, K. Van Zandt 2, J. Rhone 2, G. Stark 2, J. Bigger 2
1 Battelle Memorial Institute, Columbus, OH, USA
2 Battelle, Columbus, OH, USA

Background: During the 2008-2009 influenza season, an outbreak of the H3N2 A/Brisbane/10/07 strain occurred in several European countries. Great Britain experienced its worst influenza outbreak in eight years. Further, the World Health Organization (WHO) reports that influenza seasons in which H3N2 strains are predominate have been associated with a greater risk of severe illness and mortality rates. Thus, the need for effective vaccines and therapeutics against interpandemic influenza strains remains a high priority. To provide an appropriate animal model for these novel products, the ferret was evaluated as a possible efficacy model for Influenza A/Brisbane/10/07 H3N2.

Methods: Forty-eight male ferrets were divided among 8 groups. Four groups of 8 ferrets were infected with approximately 1x10^6 TCID50/mL of A/Brisbane/10/07 in the nasal cavity. Sham control groups of 3 ferrets each were inoculated with allantoic fluid produced in embryonated chicken eggs and CMF-PBS. The ferrets were monitored for signs of infection by clinical observation, changes in weight and temperature, detection of viral shedding in nasal washes, and seroconversion as determined by microneutralization assay.

Results: All animals survived infection with only mild signs of illness. Weight loss was generally not observed after infection. Instances of fever (defined as greater than two standard deviations from the baseline temperature) were present in some animals and persisted through the end of the study. Viral load in the nasal wash was present at 16 hours post-challenge. Nasal washes collected 24 to 72 hours post-challenge demonstrated an increased titer of 1 to 2 logs from the previous time-points, while samples collected 96 to 120 hours post-challenge exhibited a decrease in titer. Pre-challenge sera tested by the microneutralization assay (MN) lacked detectable neutralizing antibodies against A/Brisbane/10/07, however sera collected at the study end-point displayed a discernible increase in neutralizing antibody titer.

Conclusion: The most reliable indications of infection for an individual animal were viral recovery from nasal washes and observation of sneezing or coughing.

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73.008
Natural history study of a low dose HPAI (A/Vietnam/1203/04) infection in ferrets
J. Long 1, J. Edwards 1∗, A. Wasko 1, M. Gainey 1, P. Herr-Calomeni 1, G. Stark 2, J. Bigger 2
1 Battelle, Columbus, OH, USA
2 Battelle, Columbus, OH, USA

Background: The objective of this study was to refine a low dose ferret therapeutic model of A/Vietnam/1203/04 influenza infection.

Methods: Forty-four male ferrets (Mustela putorius furo), 8–15 weeks in age, were divided into 4 groups of 8 ferrets (groups A, C, E and G; experimental) and 4 groups of 3 ferrets (groups B, D, F and H; controls). Animals in groups A, C, E and G were challenged with 5 x 10^3 TCID50 of A/Vietnam/1203/04 via the intranasal route. Data collection was staggered by group pairs (groups A+B, C+D, E+F, G+H) so that clinical observations, blood (clinical hematology and clinical chemistry), nasal wash specimens (qPCR and TCID50), and temperature data were collected at approximately 8 hour intervals from 16-48 hours and at 24 hour intervals between 72 and 120 hours. After 120 hours, temperatures and clinical observations were recorded 2 times daily until the end of the study (Day 14) or death of the animal. Tissues were collected from any infected animal found dead or euthanized prior to day 14, for determination of viral load by a combination of qPCR and TCID50.

Results: All animals challenged with A/Vietnam/1203/04 succumbed. Observations for infected animals included: 1) significant decreases in body weight on all study days, 2) significant increases in body temperature as early as 1 day post-challenge, and 3) significant changes in clinical activity beginning at 40 hours. Analysis of clinical hematology data for peripheral blood specimens revealed significant differences between control and infected animals as early as 32–48 hours post-challenge for lymphocytes, white blood cells, and platelets. Significant persistent clinical chemistry parameter changes were limited to serum glucose, albumin, calcium and phosphorous. Results of TCID50 assays and qPCR demonstrated virus shedding in nasal wash specimens as well as high viral titers in a number of tissues (brain, olfactory bulb, liver, lung, and nasal turbinates).

Conclusion: This study identified a combination of clinical parameters that can be used to characterize early onset of disease following a low dose A/Vietnam/1203/04 challenge.

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