

Neurotropism Distinguishes U.S. Human-Origin H5N1 from European Avian-Origin H5N5 Virus Infection in the Ferret Model

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Highly pathogenic avian influenza A viruses (HPAIV) of the clade 2.3.4.4b H5Nx lineage continue to emerge globally, posing a growing threat to animal and human health. The ferret model is one of the most reliable animal models for predicting the pathogenicity and virulence of HPAIV in humans.

This study compared the light microscopic lesions and viral tropism in ferrets infected with U.S. human-origin H5N1 by ocular inoculation or with European avian-origin H5N5 by intranasal inoculation.

H5N1 virus infection was characterized by necrotizing encephalitis accompanied by limited lesions in the respiratory tract. Bone marrow necrosis was also observed, indicating systemic dissemination. In contrast, H5N5 virus infection induced mild lesions in the respiratory tract without evidence of encephalitis and was associated with lymphoid necrosis within the pulmonary lymph nodes. Immunohistochemistry for the influenza A virus matrix protein confirmed viral antigen in affected tissues and closely correlated with the distribution of lesions.

Overall, our findings demonstrate distinct differences in lesion profiles and viral tropism in the ferret model. While the U.S. human-origin H5N1 virus exhibited pronounced neurotropism and systemic spread, the European avian-origin H5N5 virus remained largely restricted to the respiratory tract.

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Yes, I am a junior scientist.

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