

The Eye as a Gateway: Ocular Tropism, Host Responses and Transmission of Clade 2.3.4.4b H5 Viruses

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Human infections with U.S. clade 2.3.4.4b H5N1 viruses frequently present with conjunctivitis, suggesting the eye as an important portal of infection. We compared the ocular tropism of U.S. H5N1 (B3.13 and D1.1) and European H5N1/H5N5 viruses in human conjunctival epithelial and corneal endothelial cells. All viruses infected human ocular cells, but the U.S. human H5N1 isolates displayed markedly enhanced replication. European viruses differed substantially in ocular fitness, with one H5N5 isolate exhibiting similarly high replication. Using reverse genetics approach, we identified mutations in PB2, PB1, PA, NA and NS1 that contribute to ocular tropism. Integrated proteomic, cytokine, flow cytometric and imaging analyses revealed distinct host responses induced by human H5N1 B3.13, including differences in innate immune signaling, cytokine production and apoptosis. Following ocular inoculation, U.S. H5N1 viruses established productive infection in ferrets with dissemination to the respiratory tract and brain and efficient direct contact, but not airborne transmission. Viruses recovered from infected ferrets remained genetically stable without reversion of mammalian adaptation-associated signatures. These findings identify viral and host determinants of ocular H5N1 infection and demonstrate that the eye is a functional route of H5N1 infection and direct transmission, with implications for zoonotic risk assessment and infection control.

Keywords

H5N1 clade 2.3.4.4b, Ocular tropism, Zoonotic transmission, Host response, Ferret model

Professional status of the speaker

Senior Scientist

Junior scientist status

No, I am not a junior scientist.

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