

Tropism of an H5N1 virus for bovine cells is determined by the HA2 subunit regulating membrane fusion

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In 2024, H5N1 highly pathogenic avian influenza (HPAI) viruses were first detected in dairy cows in Texas, USA. Unlike typical influenza infections, the virus replicated predominantly in mammary gland tissue, causing a mastitis-like disease associated with high virus titers in milk.

To identify viral determinants of bovine cell tropism, we compared the bovine H5N1Tex/24, with the avian H5N1Yam/04 and H5N1Hok/04 viruses in bovine macrophage (BoMac), bovine kidney (MDBK), canine kidney (MDCK), and human lung epithelial (Calu-3) cells. The polybasic HA cleavage sites of H5N1Tex/24 and H5N1Yam/04 were mutated into monobasic motifs, and reassortant viruses were generated by reverse genetics.

H5N1Tex/24 and H5N1Yam/04 replicated efficiently in BoMac and MDBK cells, whereas H5N1Hok/04 did not. However, all three viruses reached high titers in MDCK and Calu-3 cells. Replacement of genome segments 1, 2, 3, 5, and 8 of H5N1Hok/04 with those of H5N1Tex/24 failed to enhance replication in bovine cells. In contrast, replacement of segment 4 significantly increased viral replication, identifying HA as a major determinant of bovine cell tropism.

Serial passaging of H5N1Hok/04 in BoMac cells increased replication capacity and selected mutations in the HA2 subunit. These mutations enhanced HA-mediated membrane fusion, indicating that HA fusion activity is a key factor influencing influenza virus cell tropism.

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Junior scientist status

No, I am not a junior scientist.

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