ID der Kurzfassung : **165**

Clade 2.3.4.4b H5N1 influenza A virus exhibits high infectivity in human respiratory tract models

Inhalt

Introduction: Bovine-transmitted clade 2.3.4.4b H5N1 viruses have raised concerns about mammalian adaptation and pandemic potential. Primary human respiratory models enable direct assessment of viral replication and host responses. **Goal**: To characterize replication, tropism and pathogenicity of a bovine clade 2.3.4.4b H5N1 virus in human respiratory models. **Materials & Methods**: Primary nasal air-liquid interface cultures (nALI), organoid-derived bronchial epithelium and ex vivo human lung tissue (aHuLu) were infected with H5N1bov/2024 and compared with H5N1/2004, H3N2/1999 and H5N8/2016. Viral replication, tropism, epithelial injury and host responses were analysed. **Results**: H5N1bov/2024 replicated efficiently in all models, comparable to H5N1/2004. Bronchial cultures produced viral titres ~2 $\log_{10}$ higher than nasal and alveolar tissues. In ex vivo lung tissue, infection predominantly targeted alveolar type II cells. At 72 h post infection, infected ATII cells detached, accompanied by loss of occludin and increased caspase-3 activation. RNA sequencing demonstrated a transcriptional response resembling H5N1/2004, with strong induction of interferons, ISGs and inflammatory chemokines. **Summary**: H5N1bov/2024 efficiently infects human respiratory tissues, induces robust innate immune responses and causes epithelial injury. These findings support the use of complementary human respiratory models for influenza pathogenesis studies and pandemic risk assessment.

Keywords

H5N1; human 3D models; pandemic potential.

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Junior scientist status

No, I am not a junior scientist.

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