

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

Monday, September 14, 2026 1:47 PM (1 minute)

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 $\sim 2 \log_{10}$ 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.

Professional status of the speaker

Professor

Junior scientist status

No, I am not a junior scientist.

Registration ID

INF26-113

Authors: Dr LÖWA, Anna (Department of Infectious Diseases, Respiratory Medicine and Critical Care, Charité - Universitätsmedizin Berlin, Berlin, Germany); Dr BUDT, Matthias (Unit 17 “Influenza and other Respiratory Viruses”, Robert Koch Institute, Berlin, Germany.)

Co-authors: Dr BALÁZS, Anita (Department of Pediatric Respiratory Medicine, Immunology and Critical Care Medicine, Charité –Universitätsmedizin Berlin, Berlin, Germany); SIKORA, Victor (Department of Infectious Diseases, Respiratory Medicine and Critical Care, Charité - Universitätsmedizin Berlin, Berlin, Germany); MELZER, Mark (Department of Infectious Diseases, Respiratory Medicine and Critical Care, Charité - Universitätsmedizin Berlin, Berlin, Germany.); Dr PFEIFFER, Annika E (Unit 17 “Influenza and other Respiratory Viruses”, Robert Koch Institute, Berlin, Germany.); Mrs FISCHER, Mara (Department of Infectious Diseases, Respiratory Medicine and Critical Care, Charité - Universitätsmedizin Berlin, Berlin, Germany); Dr MIETH, Maren (Department of Infectious Diseases, Respiratory Medicine and Critical Care, Charité - Universitätsmedizin Berlin, Berlin, Germany); Mrs HELLOWIG, Katharina (Department of Infectious Diseases, Respiratory Medicine and Critical Care, Charité - Universitätsmedizin Berlin, Berlin, Germany); Dr WYLER, Emanuel (Berlin Institute for Medical Systems Biology (BIMSB), Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC) and IRI Life Sciences,

Institute for Biology, Humboldt Universität zu Berlin, Berlin, Germany); Dr TÖNNIES, Mario (HELIOS Clinic Emil von Behring, Department of Pneumology and Department of Thoracic Surgery, Chest Hospital Heckeshorn, Berlin, Germany); Prof. BAUER, Torsten T (HELIOS Clinic Emil von Behring, Department of Pneumology and Department of Thoracic Surgery, Chest Hospital Heckeshorn, Berlin, Germany); Dr GRAFF, Mareike (Department for Thoracic Surgery, DRK Clinics, Berlin, Germany); Prof. NEUDECKER, Jens (Department of General, Visceral, Vascular and Thoracic Surgery, Charité - Universitätsmedizin Berlin); Prof. RÜCKERT, Jens C (Department of General, Visceral, Vascular and Thoracic Surgery, Charité - Universitätsmedizin Berlin); Prof. GRUBER, Achim D (Institute of Veterinary Pathology, Freie Universität Berlin, Berlin, Germany); Prof. LANDTHALER, Markus (Berlin Institute for Medical Systems Biology (BIMSB), Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC) and IRI Life Sciences, Institute for Biology, Humboldt Universität zu Berlin, Berlin, Germany); Prof. BUCHAUER, Lisa (Department of Infectious Diseases, Respiratory Medicine and Critical Care, Charité - Universitätsmedizin Berlin, Berlin, Germany); HIPPENSTIEL, Stefan (Department Infectious Diseases and Respiratory Medicine; Charite - Universitätsmedizin Berlin, Augustenburger Platz 1, 13353 Berlin, Germany); Dr WOLFF, Thorsten (Unit 17 "Influenza and other Respiratory Viruses", Robert Koch Institute, Berlin, Germany); Prof. HOCKE, Andreas C (Department of Infectious Diseases, Respiratory Medicine and Critical Care, Charité - Universitätsmedizin Berlin, Berlin, Germany)

Presenter: HIPPENSTIEL, Stefan (Department Infectious Diseases and Respiratory Medicine; Charite - Universitätsmedizin Berlin, Augustenburger Platz 1, 13353 Berlin, Germany)

Session Classification: Poster viewing

Track Classification: Virus host cell interaction