

Beyond H5N1: Influenza A virus infection in bovine udder organoids

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Influenza A viruses (IAVs) have recently expanded their host range to cattle, raising critical questions about tissue tropism, replication capacity, and consequences for dairy production and zoonotic risk. The detection of highly pathogenic avian influenza H5N1 in bovine milk highlights the mammary gland as a previously underappreciated site of infection and viral shedding.

To study mammary-specific influenza biology, we established bovine mammary gland organoids (MGOs) derived from primary epithelial cells and maintained in chemically defined media. This scalable ex vivo model recapitulates key features of the bovine udder, including luminal–basal polarity, lineage-specific cytokeratin expression, and lactation-associated differentiation, enabling physiologically relevant infection studies.

Using this system, we compared infection dynamics of avian, swine, and human IAVs. Viruses from diverse host origins productively infected MGOs, largely independent of culture conditions. Mammalian-adapted H1N1 strains replicated with efficiencies comparable to bovine H5N1, whereas low pathogenic avian H9N2 showed restricted replication, indicating subtype-specific constraints in mammary tropism.

Together, this work establishes bovine mammary organoids as a platform to investigate influenza virus–host interactions in the udder and provides insight into determinants of mammary infection with implications for animal health, dairy safety, and zoonotic risk assessment.

Keywords

Influenza A virus, H5N1, bovine mammary gland, organoids, udder, lactation

Professional status of the speaker

Postdoc

Junior scientist status

No, I am not a junior scientist.

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