



H9N2 avian influenza virus: Emergence of immune Escape Mutant with No Haemagglutination Activity

Thusitha K. Karunaratna^{1,2}, Jean-Remy Sadeyen¹, Sushant Bhat¹, Pengxiang Chang¹, Jiayun Yang¹, Mehnaz Qurashi^{1,3}, Joshua Sealy¹, Rebecca Daines¹ and Munir Iqbal¹

¹Avian Influenza and Newcastle Disease Group, The Pirbright Institute, Pirbright, Woking, GU24 0NF, UK.

² Royal Veterinary College, University of London, Hertfordshire, AL9 7TA, UK.

³ Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, Liverpool, L3 3RF, UK.

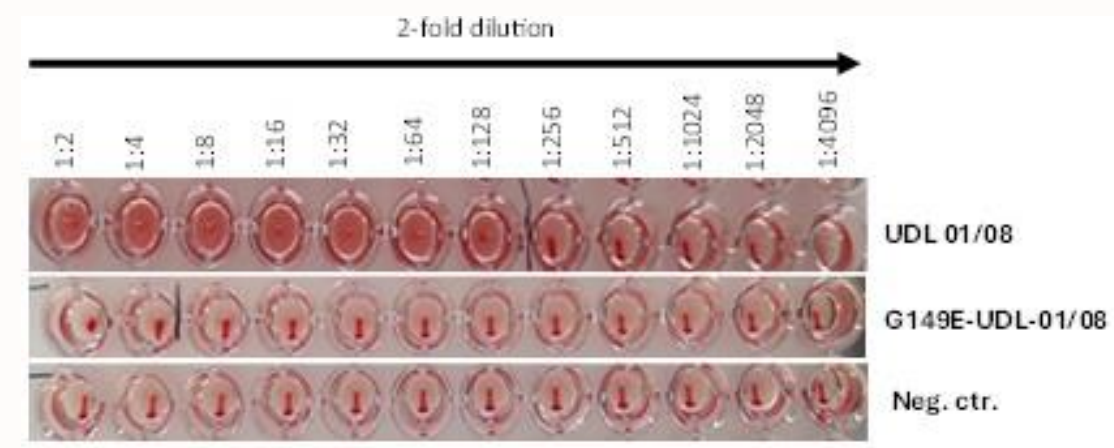
Background

H9N2 avian influenza viruses (AIVs) pose a global threat to animal and human health carrying potential pandemic risk. Vaccination and surveillance collaborate closely for the successful control and prevention of AIVs. The emergence of immune-escape variants impedes vaccines' effectiveness. In this study, we identified an immune-escape (G149E) variant that also contributes to the loss of agglutination of chicken erythrocytes.

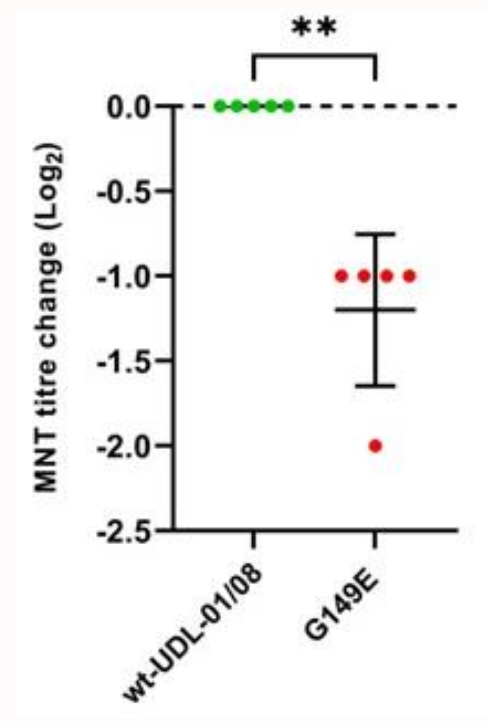


Results

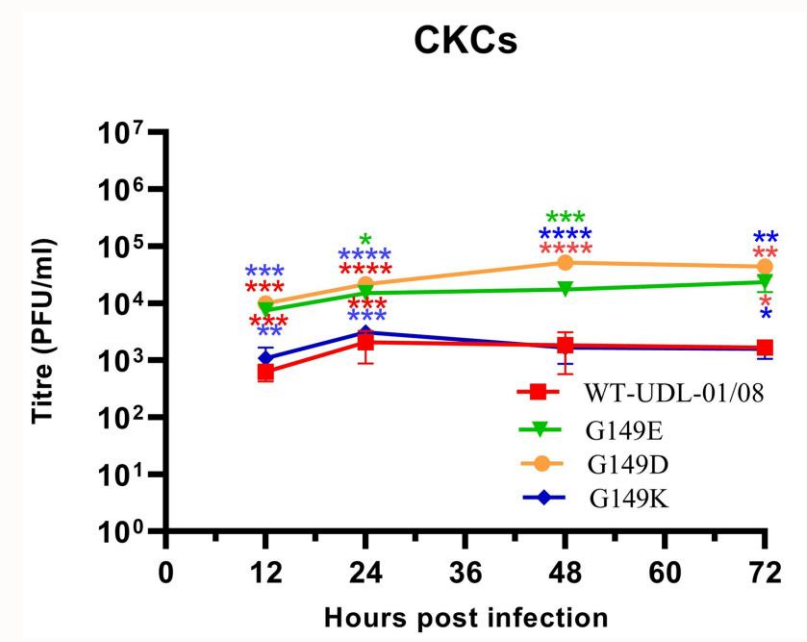
Loss of haemagglutination



Reduced antigenic cross-reactivity



Retained replicative fitness



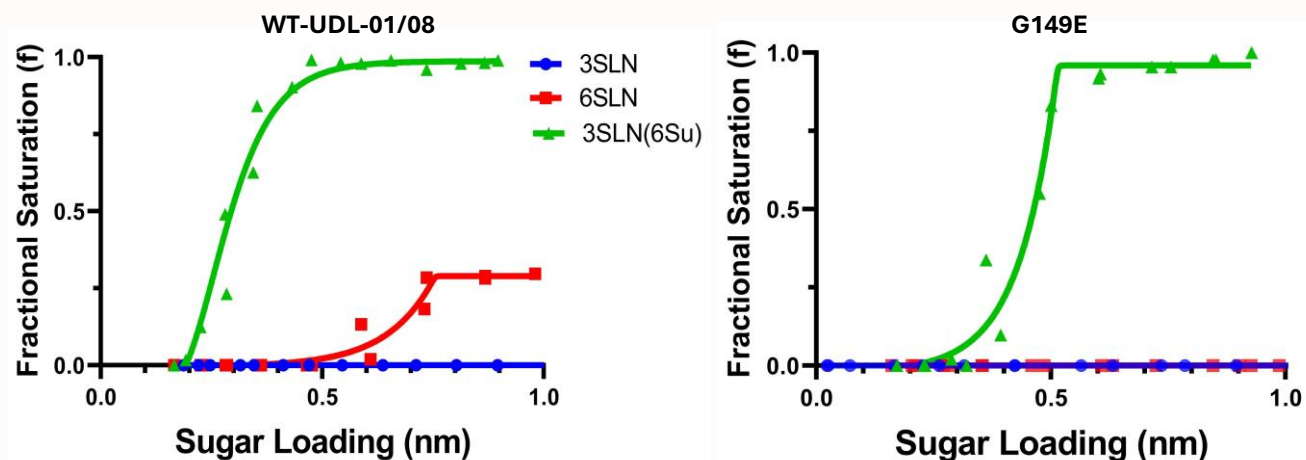
The G149E mutation in the HA of H9N2 virus caused:

- Loss of haemagglutination activity.
- Reduction in antigenic cross-reactivity compared to the wild-type virus.
- Increase in replication fitness in avian cells.

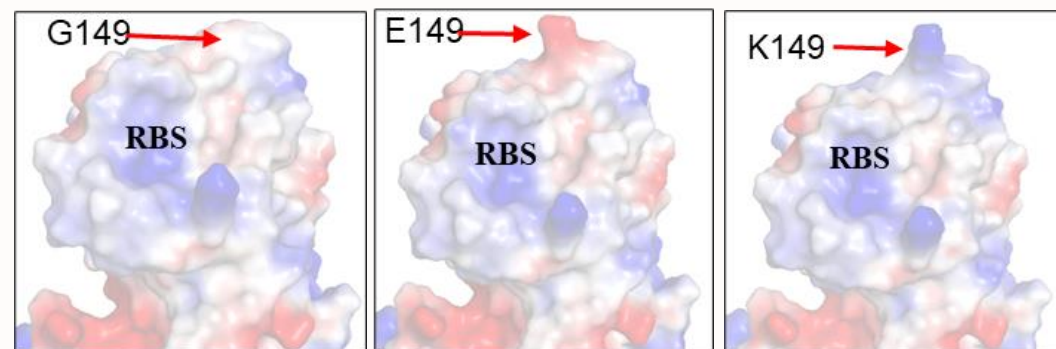


Results Continued

Altered receptor binding avidity to avian cell surface receptors



Increased the negative charge around the receptor binding site



Take home message

- H9N2 avian influenza virus may likely acquire the G149E mutation under immune pressure in nature.
- G149E variant challenges the vaccination and surveillance efforts.
- This immune escape mutant underscores the intricate interplay between antigenic variation and viral traits.