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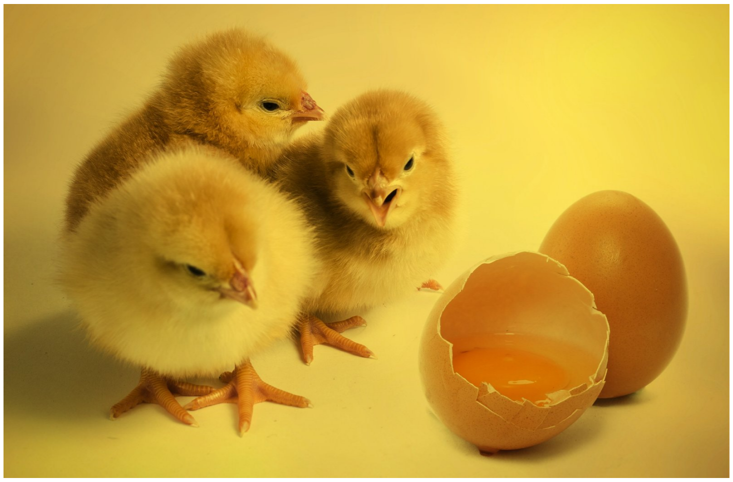
UK study uncovers genetic drivers of vaccine escape in H5 avian influenza

28 May 2026 | News

Research integrates antigenic mapping and structural modelling to track mutations affecting immune protection in poultry



Research integrates antigenic mapping and structural modelling to track mutations affecting immune protection in poultry

The UKâ??s The Pirbright Institute has identified key genetic mutations in the haemagglutinin (HA) protein of H5 avian influenza viruses that significantly influence vaccine effectiveness in poultry, offering new insights into how viral evolution may undermine existing disease control strategies.

The findings, published in the *Journal of Virology*, stem from a multidisciplinary study combining phylogenetic analysis, antigenic cartography, structural modelling, and experimental validation. Together, these approaches enabled researchers to map the molecular drivers behind antigenic drift in highly pathogenic avian influenza viruses.

Since its emergence in 1996, the H5 avian influenza lineage A/Goose/Guangdong/1/1996 (Gs/GD) has diversified into more than 30 genetically and antigenically distinct clades. Among them, clade 2.3.4.4b has become globally dominant in recent outbreaks, affecting domestic poultry, wild birds, and an expanding range of mammalian hosts.

While vaccination remains a cornerstone of avian influenza control in poultry and a critical tool in reducing zoonotic spillover risks, the rapid evolution of the virus continues to challenge vaccine efficacy. Frequent mismatches between vaccine strains and circulating field viruses can reduce immune protection and allow continued viral spread.

In the study, researchers used reverse genetics to generate recombinant viruses representing multiple H5 clades, enabling detailed analysis of their antigenic relationships through haemagglutination inhibition assays and antigenic cartography. This allowed the team to visualize immunological distances between viral strains and assess how they evolve over time.

The analysis identified 48 candidate amino acid positions in the HA protein associated with antigenic variation. Experimental validation further confirmed four mutationsâ??R82K, A83T, T204I, and F229Yâ??as having significant effects on antigenicity, with three of them (R82K, T204I, and F229Y) newly recognized as important determinants of immune escape.

Researchers noted that some of these mutations have already been detected sporadically in recent outbreaks, including the ongoing H5N1 epizootic in North American cattle, suggesting their potential role in shaping future viral evolution and vaccine performance.

The study also found that clade 2.3.4.4 viruses are not only genetically distinct but also antigenically separated from other H5 lineages, with substantial diversity even within the clade itself. This complexity presents ongoing challenges for vaccine seed strain selection and underscores the need for more precise antigenic matching in poultry vaccine development.

In addition, variations in glycosylation sites on the HA protein were identified as another mechanism contributing to immune evasion, as these modifications can shield viral epitopes from antibody recognition and enhance vaccine escape potential.

According to lead author Professor Munir Iqbal, head of the Avian Influenza and Newcastle Disease group at The Pirbright Institute, the findings provide a practical framework for improving vaccine design and selection strategies, with implications for both animal health and zoonotic disease prevention.

Overall, the study offers a comprehensive model for tracking antigenic drift and anticipating viral changes, potentially supporting more effective surveillance systems and more resilient poultry vaccination programs in the face of rapidly evolving avian influenza threats.