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VIRAL EVOLUTION

Flu host evasion

> Seasonal antigenic alterations are … more restricted than previously thought

To evade immune detection, the influenza virus undergoes mutations, such that its immune-reactive antigens are no longer recognized by host antibodies. Knowing how these antigens evolve — in a process known as antigenic drift — is crucial for vaccination strategies. A new study finds that, surprisingly, in strains that evolved both between 1968 and 2003, and more recently, key alterations occurred at only seven amino acid positions of the virus.

Flu vaccines primarily target the haemagglutinin viral surface glycoprotein. Previous work has identified 131 amino acid positions in five antigenic sites that may be targeted by antibodies, which suggested that antigenic drift involves many positions.

In this study, the authors used a ferret model and mutant viruses to examine the changes that occurred between the 11 antigenic clusters of viruses that evolved between 1968 and 2003. They found that mutations at only seven positions were involved, all of which flanked the receptor-binding site (RBS).

The authors suggest that, given the high mutation rate of influenza virus and the slow emergence of novel antigenic clusters, antigenic change has a fitness cost. Indeed, they found that several mutations near the RBS were detrimental to the virus. Thus, slow antigenic emergence could be explained by the requirement for co-mutations at other amino acid positions — some of which were identified by the authors.

Seasonal antigenic alterations are thus more restricted than previously thought — a finding that has far-reaching implications for the evolution of viruses in response to host immune responses.

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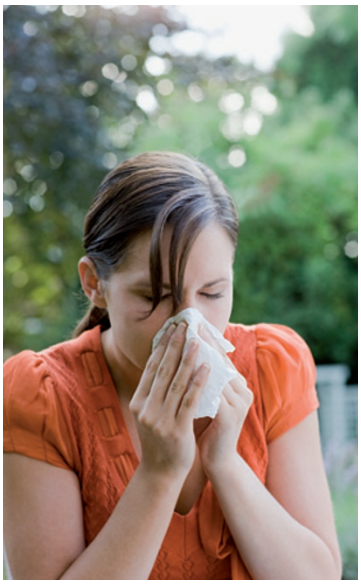
ORIGINAL RESEARCH PAPER Koel, B. F. *et al.* Substitutions near the receptor binding site determine major antigenic change during influenza virus evolution. *Science* **342**, 976–979 (2013)



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