

Substitutions Near the Receptor Binding Site Determine Major Antigenic Change During Influenza Virus Evolution

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Flu Drift Limited

Five antigenic sites in the virus surface hemagglutinin protein, which together comprise 131 amino acid positions, are thought to determine the full scope of antigenic drift of influenza A virus. **Koel *et al.*** (p. 976) show that major antigenic change can be caused by single amino acid substitutions. These single substitutions substantially skew the way the immune system "sees" the virus. All substitutions of importance are located next to the receptor-binding site in the hemagglutinin. Because there are few positions of importance for antigenic drift, there are strict biophysical limitations to the substitutions at these positions, which restricts the number of new antigenic drift variants at any point in time. Thus, the evolution of influenza virus may be more predictable than previously thought.

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