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# Correlation in the sequential evolutionary pattern of influenza hemagglutinin reveals its immunogenic and structural characters

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— The immune system recognizes the hemagglutinin (HA) protein on the surface of the influenza virus. It is this protein that evolves to escape immune recognition. Correlation analysis is performed for all pairs of positions in the alignment of HA sequences collected in history. Spectral decomposition of the resulting matrix yields several independent eigenvectors that clusters those positions into several sectors, each of which corresponds to a subset of the positions and follows a relatively independent evolutionary pattern. Some of the obtained sectors match well with the five experimentally and statistically (using Shannon entropy) determined epitopes that are the sites of antibody binding. This result implies that different immunogenic epitopes of HA have characteristic patterns of escape mutation, arguably due to the distinct structures of the epitopes and properties of corresponding antibodies. In the three dimensional structure of HA, each sector is located in a compact surface region, thus the correlations in the evolution pattern occur locally in the tertiary structure. Novel sectors found, beyond the five known HA epitopes, may also possess certain biophysical functions.

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