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Dissecting the evolutionary pathway of a shared antibody response targeting the H1N1 subtype of influenza A virus

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Introduction: Although infection or vaccination with a virus induces antibodies that can protect individuals from reinfection, some viruses like influenza virus can evade pre-existing immunity by acquiring mutations in antibody epitopes within viral glycoproteins. This process is known as antigenic drift and erodes population immunity, allowing the virus to continue circulating. The project at hand focuses on characterizing an antibody response to the H1N1 subtype that is shared among individuals born during the 1970s-1980s to understand how this antibody response developed and how these antibodies evolved to bind different influenza viruses.

Methods: The researchers used enzyme-linked immunosorbent assays (ELISA) to characterize the binding ability of antibodies to different influenza variants and X-ray crystallography to obtain the structure for antibodies that bound with high affinity. To further clarify the role of different mutations in the binding ability of the antibodies, the researchers introduced point mutations into unmutated versions of the antibodies using site-directed mutagenesis.

Results: Most antibodies bound tightly to their eliciting strain, which circulated in the early 1980s, consistent with the established phenomenon of immune imprinting. Based on structural data, the researchers selected additional mutations to introduce to the unmutated antibodies. Most point mutants bound better when compared to their unmutated precursors, and in some cases, a single mutation appeared to be sufficient to restore binding to the levels of the wild-type antibody.

Conclusions: The elucidation of these key residues and their role in mediating cross-reactivity of these antibodies to different influenza A strains provides a molecular explanation for how this shared antibody response evolved. Given that some individuals made a highly focused immune response that was predominantly composed of this shared antibody response, understanding this phenomenon can contribute to comprehending how prior exposure history shaped population immunity, viral evolution, and vaccine effectiveness.