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A Vector-Based Influenza Vaccine Reveals the HA Stalk as a Dual Humoral and Cellular Immune Target

Inhalt

Universal influenza vaccine strategies predominantly exploit the conserved hemagglutinin (HA) stalk as a target for broadly neutralizing antibodies. Whether the HA stalk also contributes to protective T cell immunity remains poorly understood. We therefore investigated the underappreciated immunological capacity of HA stalk in shaping CD4+ T cell immunity within our Orf virus–based universal influenza vaccine candidate (ORFV-Flu).

Mice were immunized with ORFV-Flu expressing chimeric HA constructs. Overlapping HA stalk peptide libraries of multiple influenza A virus strains were screened by ELISpot and multiparametric flow cytometry to identify HA stalk–specific $CD4^+$ T cell responses.

ORFV-Flu elicited potent HA stalk-specific $CD4^+$ T cell responses, establishing the stalk as a dual humoral and cellular immune target through the discovery of immunogenic regions containing candidate MHC class II epitopes.

These findings expand the immunological concept of chimeric HA–based vaccination beyond antibody induction by identifying the HA stalk as a dual-function antigen capable of eliciting both humoral and $CD4^+$ T cell immunity. Combined with the potent HA stalk–specific antibody responses and conserved antigen-specific $CD8^+$ T cell immunity elicited by ORFV-Flu, these findings complete a coordinated immune framework integrating humoral, helper, and cytotoxic T cell responses for next-generation influenza vaccination.

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No, I am not a junior scientist.

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