

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

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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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Junior scientist status

No, I am not a junior scientist.

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