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Cross-linking of Antigens to Overcome Sub-type Bias and Broaden Vaccine Efficacy

Stanford scientists have discovered that cross-linking antigens can overcome sub-type bias in response to multi-strain vaccines and induce patients to have a complete, broad immune response to all included antigens. Cross-linking antigens can be a transformative method and eliminate sub-type bias in vaccines against rapidly evolving pathogens, such as in influenza and SARS-CoV-2.

Sub-type bias is a phenomenon where patients only have a robust immune response against a single antigen in vaccines that contain multiple antigens. Sub-type bias leaves patients vulnerable to infection by strains containing the other antigens and is a major limitation of vaccination against rapidly evolving viruses. Low vaccine efficacy in recent years (between 19% and 60%) necessitates novel methods to broaden patient immune responses to vaccines. Sub-type bias occurs in ~65% of vaccinated patients which suggests that eliminating it may be a valid pathway to increased vaccine efficacy.

Cross-linking antigens in a vaccine formulation resulted in a broad, complete response to multiple strains of influenza in an *in vitro* system, which suggests cross-linking antigens is robust to heterogeneity in host genetics. Consequently, antigen cross-linking has the potential to drastically improve vaccine efficacy and transform the vaccine medical field by eliminating sub-type bias in patients.

Stage of Development
Preclinical – *in vitro* data

Applications

- Development of vaccines against influenza and SARS-CoV-2

- Elimination of sub-type bias in multi-antigen vaccines
- Increasing vaccine efficacy against rapidly evolving pathogens

Advantages

- Broadens the immune response in patients vaccinated with multiple antigens
- Robust against heterogeneity in host genetics
- Versatile cross-linking method that can be used to enhance most vaccine formulations

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