



# Investigating the Potential for Broadly Neutralizing Antibody Induction through Multi-Strain Influenza Vaccination

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## Description

Seasonal influenza viruses pose a continuous threat to public health, causing significant morbidity and mortality worldwide [1]. Current influenza vaccines are typically trivalent or quadrivalent, containing inactivated strains of influenza A (H1N1 and H3N2) and influenza B viruses predicted to circulate in the upcoming season [2]. While these vaccines are generally effective in inducing strain-specific neutralizing antibodies that protect against matched or closely related viruses, their efficacy can be limited when circulating strains antigenically drift or shift significantly [3]. The development of broadly neutralizing antibodies (bnAbs) that target conserved epitopes across different influenza subtypes and strains has emerged as a major goal in influenza vaccine research [4]. Such bnAbs could provide more durable and universal protection against both seasonal and pandemic influenza threats. Several conserved epitopes on the hemagglutinin (HA) and neuraminidase (NA) proteins of influenza viruses have been identified as targets for bnAbs [5, 6]. One potential strategy to elicit bnAbs is through vaccination regimens that expose the immune system to a diverse array of influenza antigens. Multi-strain influenza vaccines, containing antigens from multiple subtypes and strains, could theoretically broaden the antibody response and potentially drive the maturation of B cells that recognize conserved epitopes shared across different viruses [7].

This short communication describes a preclinical study investigating the potential of a multi-strain inactivated influenza vaccine to induce broadly neutralizing antibodies. We immunized animal models with a combination of inactivated influenza viruses representing distinct seasonal strains and subtypes and assessed the resulting antibody responses for both strain-specific and broadly neutralizing activity. This preclinical study investigated the potential of a multi-strain inactivated influenza vaccine to induce broadly neutralizing antibodies. While the multi-strain vaccine elicited robust strain-specific antibody responses against the vaccine components, the

induction of broadly neutralizing antibodies exhibiting significant cross-reactivity against drifted seasonal strains and, importantly, pandemic-potential avian influenza viruses was limited [8].

The strong HAI responses against the vaccine strains indicate that the multi-strain formulation was immunogenic for each of the included viruses. However, the lack of substantial cross-neutralization suggests that simply combining multiple inactivated seasonal influenza viruses may not be an effective strategy for consistently eliciting potent bnAbs. This could be due to several factors. The immune response to each strain in the multi-strain vaccine might be largely independent, with limited cross-priming of B cells recognizing conserved epitopes. Furthermore, the dominant immunogenic epitopes on the seasonal influenza viruses are often strain-specific, potentially overshadowing the subdominant conserved epitopes that are targets for bnAbs [9].

The minimal neutralizing activity observed against the avian influenza viruses is particularly concerning, as these viruses pose a significant pandemic threat. The lack of cross-reactivity suggests that vaccination with seasonal influenza strains alone is unlikely to provide significant protection against antigenically novel avian influenza viruses [10].

In conclusion, while multi-strain inactivated influenza vaccines can induce robust strain-specific immunity, our preclinical data suggest that they may not be sufficient to consistently elicit potent broadly neutralizing antibodies. Future efforts in universal influenza vaccine development should focus on strategies that specifically target conserved epitopes and promote the development of broadly reactive B cell responses.

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