

# Universal Flu Vaccine: Light at the end of the tunnel?

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August 7, 2023

## Abstract

Every year, influenza virus infections cause significant morbidity and mortality worldwide. They pose a substantial burden of disease, not only in terms of health but also economic-wise. Owing to the ability of influenza viruses to continuously evolve, annual seasonal influenza vaccines are necessary as a prophylaxis. However, current influenza vaccines against seasonal strains have limited effectiveness and require yearly reformulation due to the virus undergoing antigenic drift or shift. Vaccine mismatches are common, conferring suboptimal protection against seasonal outbreaks, and the threat of the next pandemic continues to loom. Therefore, there is a great need to develop a universal influenza vaccine (UIV) capable of providing broad and durable protection against all influenza virus strains. In the quest to develop a UIV that would obviate the need for annual vaccination and formulation, a multitude of strategies are currently underway. Promising approaches include targeting the highly conserved epitopes of hemagglutinin (HA), neuraminidase (NA), M2 extracellular domain (M2e), and internal proteins of the influenza virus. The identification and characterisation of broadly neutralising antibodies (bnAbs) targeting conserved regions of the viral HA protein, in particular, have provided important insight into novel vaccine designs and platforms. This review discusses universal vaccine approaches presently under development, with an emphasis on those targeting the highly conserved stalk of the HA protein, recent technological advancements used, and the future prospects of a UIV in terms of its advantages, developmental obstacles and potential shortcomings.

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