Dissecting immunological mechanisms underlying influenza viralnucleoprotein-induced mucosal immunity against diverse viral strains

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Presenter: Yi-Chen Tsai **Date/Time:**2025/03/27,15:00-16:00

Commentator: **Location:** Room 601 , Med College Building

Background:

The nucleoprotein (NP) of type A influenza virus (IAV), highly conserved across all strains, is a promising target for universal influenza vaccines. Influenza A causes significant global morbidity and mortality, highlighting the urgent need for effective vaccines. While intramuscular (IM) delivery is standard, intranasal (IN) administration offers potential advantages by inducing robust mucosal immunity critical for combating respiratory pathogens. IN delivery targets the respiratory tract, the primary site of infection, and promotes strong local immune memory. Understanding the comparative effectiveness of IM and IN delivery is essential to optimize vaccine strategies and advance the development of universal influenza vaccines targeting conserved antigens like NP.

Objective:

To compare systemic and mucosal immune responses of IM and IN delivery of a recombinant adenovirus vaccine expressing NP-CD40 ligand.

Results:

Intramuscular (IM) vaccination effectively induced robust systemic immune responses, including antibody-dependent cellular cytotoxicity (ADCC). However, intranasal (IN) vaccination demonstrated distinct advantages by eliciting stronger mucosal immunity, critical for defending against respiratory pathogens. IN vaccination enhanced antigen-specific recall responses in the nasal-associated lymphoid tissue (NALT) of the upper respiratory tract and significantly boosted pulmonary CD8 T cell responses in the lower respiratory tract.

A key distinction between the two routes was the role of immune memory. Blocking lymphocyte circulation abolished the protective effect of IM vaccination but did not affect IN-induced immunity, emphasizing the importance of localized immune memory with IN delivery. Additionally, IN vaccination provided broader protection against diverse influenza A virus (IAV) strains, including effective defense against a highly pathogenic H5N1 strain.

These findings highlight the superiority of IN vaccination in reducing viral loads, limiting disease severity, and promoting robust mucosal and systemic immunity, offering a promising approach for developing universal influenza vaccines.

Conclusion:

Intranasal vaccination offers distinct advantages over intramuscular delivery by promoting localized mucosal immunity and broader protection. These findings support the potential of IN delivery in the development of universal mucosal vaccines, particularly for respiratory pathogens like influenza viruses.