Docket #: S21-063

TLR7-agonist-nanoparticle vaccine adjuvant

Stanford researchers have developed a nanoparticle adjuvant with spatiotemporal controlled release of TLR7 agonist for broad protection against influenza or SARS-CoV-2.

Vaccines made from inactivated viruses or protein subunits offer numerous advantages. However, with current aluminum-based adjuvants, these vaccines often require multiple doses or fail to elicit broad antibody responses against constantly mutating viruses such as seasonal influenza virus or SARS-CoV-2 virus. Toll-like receptor (TLR) agonists have shown promise as more potent adjuvants, but progress has been limited by toxic side effects. In response, the researchers have applied well-controlled chemistry to formulate an adjuvant from PEG-PLGA nanoparticles loaded with TLR7 agonist via an ester linkage. This chemistry allows for the programmed release profile of TLR7 agonist in the body - slow release in circulation and faster release in intracellular endosomes, promoting immune responses and reducing systemic serum cytokine expression. This adjuvant platform also improves lymph node accumulation and enhances cellular uptake, which leads to significant improvement of humoral and cellular immune responses, including broad antibodies against different antigenic variants and cytotoxic T cell responses. Notably, it can induce stalk-specific influenza hemagglutinin antibodies (considered an important goal in developing a universal flu vaccine).

Stage of Development
Pre-clinical. When administered with influenza hemagglutinin in mice, the TLR7-agonist nanoparticles induce a cross-reactive antibody response and improve heterosubtypic infection survival. With SARS-CoV-2 spike protein, the adjuvant promotes antibody response in mice and human tonsil organoids.

Applications

- Adjuvant to multiple vaccine platforms including influenza and SARS-CoV-2
- Potential adjuvant to HIV vaccine

Advantages

- Controlled release to minimize toxic side effects
- Induces early cross-reactivity for influenza subtypes and SARS-CoV-2 variants
- Innovative synthesis method allows large-scale, consistent production
- Highly biocompatible nanoparticle polymers (PEG-PLGA)

Publications

- Yin, Q., Luo, W., Mallajosyula, V. et al. A TLR7-nanoparticle adjuvant promotes a broad immune response against heterologous strains of influenza and SARS-CoV-2. Nat. Mater. 22, 380–390 (2023).

Patents

- Published Application: WO2022226035
- Published Application: 20240207394
- Issued: 12,691,173 (USA)

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