Docket #: S21-082

Subunit vaccines with dinucleotide-loaded hydrogel adjuvant

Stanford researchers have developed a platform for sustained delivery of immune stimulating dinucleotides in single-dose viral vaccines and cancer immunotherapies.

Subunit vaccines, such as the SARS-CoV-2 spike protein receptor binding domain (RBD), are easy to manufacture but often show poor immunogenicity. Innate immune research has demonstrated that dinucleotides, including cGAMP and CpG, could be powerful next-generation adjuvants. These compounds, however, have bad pharmacokinetics because of their small size and tendency to be degraded.

Researchers in the Appel and Li Labs researchers have developed an injectable hydrogel vaccine that slowly releases cGAMP or CpG over time frames similar to a natural infection. The polymer/nanoparticle hydrogel self-heals after injection to form a local immune-stimulating depot (see "Stanford Docket S18-354" for hydrogel design). Immunogenicity is greatly increase with either cGAMP (a secondary messenger with extracellular activity) or CpG (a pathogen-associated molecular pattern).

Stage of Development
Preclinical. A SARS-CoV-2 RBD subunit vaccine study in mouse demonstrated that one dose with CpG/cGAMP hydrogel achieved a good antibody response, unlike two doses with typical adjuvants, as measured by titer and pseudotyped neutralization assays.

Applications

- Injectable, sustained delivery of cGAMP or CpG for:
  - Subunit vaccines, e.g., against SARS-CoV-2
  - Cancer immunotherapies

Advantages

- Powerful innate immune stimulus via prolonged release
- Potential for single dose vaccine
- Subcutaneous injection is more practical than intratumoral implantation
- Simple and mild synthesis
- Compatible with a wide array of antigens and adjuvants

Publications

- Gale et al. "Hydrogel-based slow release of a receptor-binding domain subunit vaccine elicits neutralizing antibody responses against SARS-CoV-2" *pre-print* 2021

Patents

- Published Application: WO2022192438

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