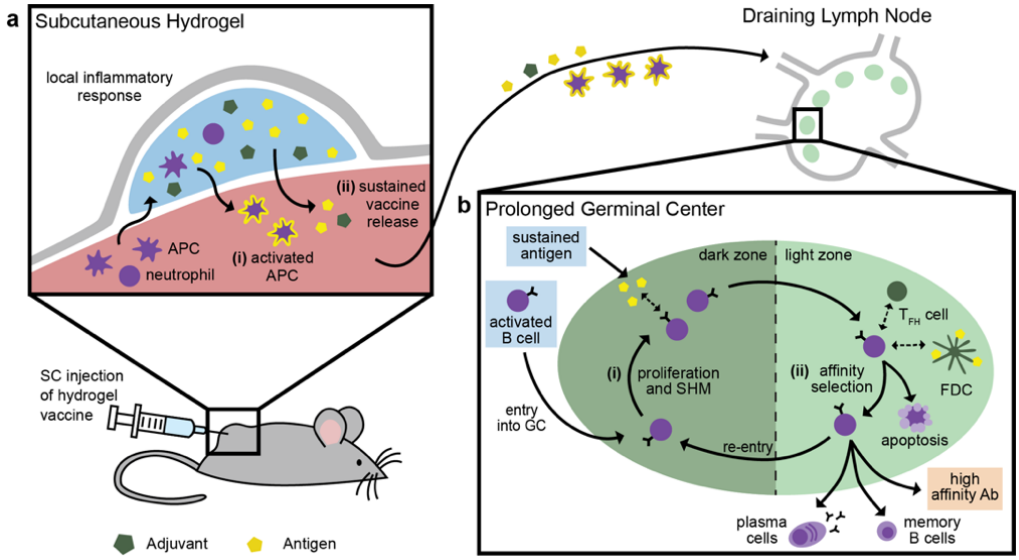
Docket #: S18-354

Nanoparticle hydrogels for sustained release of multiple agents in vaccines or cancer immunotherapy

Researchers in Prof. Eric Appel and Mark Davis' laboratories have developed a versatile, single-injection vaccine formulation platform that can enhance immune response by providing tunable, prolonged release of multiple immunomodulatory agents over time scales similar to natural infections. Specifically, this technology replaces PBS with an injectable hydrogel as a delivery vehicle to appropriately activate the immune system with biological cargo that can be dramatically different in size or chemical composition (e.g., antigens, cytokines, adjuvants). These shear-thinning and self-healing hydrogels can encapsulate essentially any immunomodulatory molecule using simple mixing for scalable manufacturing. A single injection of the cargo-loaded hydrogels creates a new local stimulatory microenvironment within the body to activate a strong and lasting targeted immune response. This hydrogel technology could provide a simple and effective platform to deliver vaccines or cancer immunotherapy. In particular, it could: improve the potency of subunit vaccines by controlling the timing and presentation of antigens and adjuvants; enable single injection of vaccines that currently require multiple shots; or improve administration of multi-agent immunotherapies.



Schematic illustration of response to vaccine delivered with hydrogel: *After injection, immune cells (e.g., neutrophils and APCs) are activated. APCs may migrate to the lymph nodes, prolonging the germinal center response. This promotes higher affinity antibodies and a strong humoral immune response.*

Stage of Research

Proof of concept results in vivo (mice):

-hydrogels enhanced the magnitude and duration of the humoral immune response to a model vaccine compared to a standard bolus administration

-hydrogel formulation can release two different size cargos (OVA and Poly(I:C)) at similar rates, demonstrating potential for co-presentation of antigen and adjuvant over prolonged time frames

-material does not cause fibrotic response

Ongoing studies:

-testing antigens for **HIV, influenza and malaria.**

-preliminary results in mouse model of **melanoma** indicates a single administration significantly reduces tumor growth and increases survival

Applications

- **Formulation for injectable drug delivery in:**
  - **vaccines** - particularly subunit vaccines, as well as vaccines for HIV, influenza and pathogens without current vaccines

    - **cancer immunotherapy** - particularly combination therapies, including those with immunomodulatory agents of dramatically different sizes and chemical compositions

Advantages

- **Robust immune response:**
    - hydrogel formulation enhances both the magnitude and duration of the humoral immune response compared to standard bolus
    - prolonged antigen presentation mimics typical natural infection and results in prolonged germinal centers
    - may allow for single administration of vaccines that currently use multiple doses
- **Sustained, tunable release of multiple agents:**
    - dynamic network rearrangement enables co-release, even with molecules that are dramatically different in size or chemical makeup
    - tunable release from days to weeks to appropriately harness the immune system
    - high loading capacity, well-suited for encapsulation and delivery of combination immunotherapies
    - shear thinning and self-healing properties enable easy administration
- **Scalable, versatile manufacturing**
    - simple mixing of hydrogel and nanoparticles in aqueous solution to load biologic cargo
    - can replace PBS as vehicle to be used with any vaccine or immunotherapy
- **Stable storage** - hydrogel stabilizes immunomodulatory cargo during storage

Patents

- Published Application: WO2020072495

Innovators

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