SUSTAINED RELEASE VACCINE PLATFORMS FOR ENHANCED HUMORAL IMMUNITY

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Vaccines aim to modulate the immune system to elicit a sufficiently robust, yet targeted, immune response with specifiable immune cell phenotypes.[1,2] Failure of a single vaccine administration to elicit such a response likely arises from inappropriate temporal control over antigen/adjuvant presentation and immune cell activation.[2] Recent work demonstrates the potential for sustained, low-level presentation of antigens and adjuvants for just over a week to yield more potent and long-lasting immunity.[3] However, an incomplete understanding of the enormously complex and dynamic immune system dramatically limits the ability to rationally design true, single-administration vaccines.[3] Our lab has developed injectable and self-healing polymer-nanoparticle (PNP) hydrogels with the ability to deliver multiple cargo of differing compositions.[4] Due to the supramolecular interactions between the HPMC-C_{12} polymer and PEG-PLA nanoparticles, these materials are prepared by simply mixing the components. This ability to streamline material preparation mitigates common challenges observed with manufacturing typical biomaterials at scale, thereby significantly enhancing translatability.[5] We have expanded this PNP hydrogel platform to allow for prolonged controlled release of an encapsulated model subunit vaccine composed of an antigen (ovalbumin) and adjuvant (poly(I:C)) (Figure 1A). The studies with this vaccine platform have yielded a deeper understanding of the effect of the kinetics of antigen/adjuvant presentation on immune activation. With a single injection of the vaccine, hydrogel formulations can elicit 10-fold higher antibody concentrations by day 35 compared to the same vaccine delivered in a typical bolus administration in PBS and had detectable antibodies past 120 days (Figure 1B). Upon an immune challenge, mice immunized with hydrogel-based vaccine formulations induced upwards of 3-fold higher antibody concentrations and higher affinity antibodies systemically. Cell phenotyping experiments indicate an increase in germinal center B cells in hydrogel formulations. These data, along with the boost in the humoral immune response, suggest that prolonged vaccine exposure from the PNP hydrogels leads to an increase in vaccine interaction with immune cells, allowing for somatic hypermutation and clonal selection of B cells. The unique properties of PNP hydrogels make this system ideally suited for controlling release of antigen and adjuvants to elucidate what molecular levers must be pulled, how hard, and when, to produce robust long-term immunity.

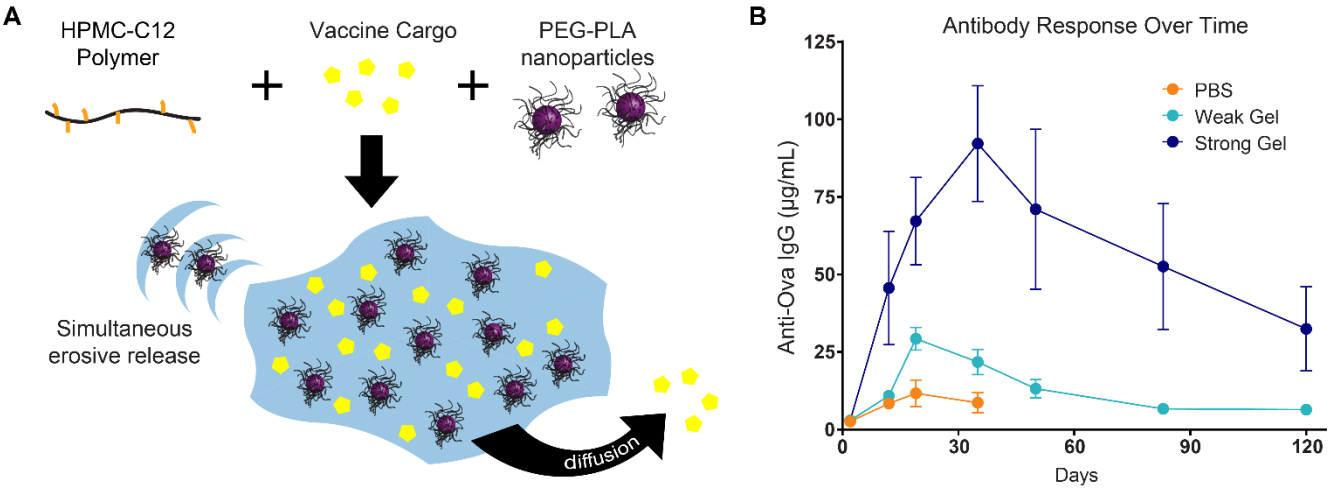

Figure 1 – (A) Schematic of the polymer-nanoparticle hydrogel with vaccine cargo. (B) Serum concentrations of anti-ovalbumin antibodies after single administration of vaccine.

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