ARMY LIPOSOMAL SPIKE FERRITIN NANOPARTICLE VACCINE INDUCES DURABLE IMMUNE RESPONSES

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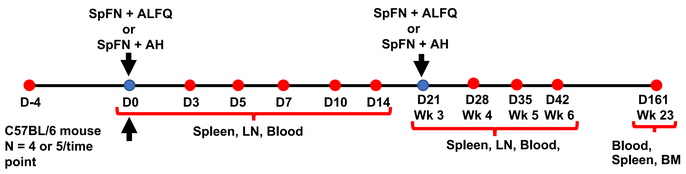
BACKGROUND

Immunization strategies that rapidly modulate appropriate and precise interactions between the innate and adaptive immune responses are essential to generate robust, durable, and protective immunity against pathogens. Here, we describe a novel vaccine platform, Spike Ferritin Protein Nanoparticle (SpFN) mixed with the adjuvant Army Liposome Formulation containing QS-21 (ALFQ) and assessed the vaccine-induced immune signatures.

METHODS

C57BL/6 mice were vaccinated with SpFN formulated with either Alhydrogel (SpFN+AH) or ALFQ (SpFN+ALFQ) and immunological assessment from the vaccine draining lymph nodes (dLNs), lung and spleen was performed to assess cellular engagement and cytokine activation induced by the distinct vaccine-adjuvant combinations using ELISA, flow cytometry, intracellular cytokine staining assay, Biacore, and immunohistochemistry-based methods. Data were displayed as dot plots or bar graphs. AH and ALFQ groups were compared by unpaired Student's t-test or Mann–Whitney U-test using GraphPad Prism v.8.4.0.

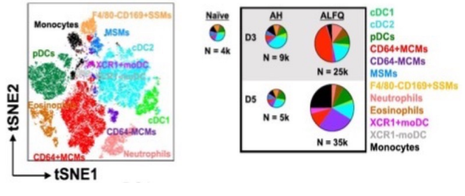
IMMUNIZATION SCHEME



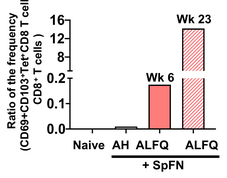
SARS-CoV-2 Spike-Ferritin Nanoparticle Vaccine (SpFN) with Army Liposome Formulation ALFQ induces early recruitment and activation of Antigen Presenting Cells leading to Robust and Durable Humoral and Cellular immune responses

RESULTS

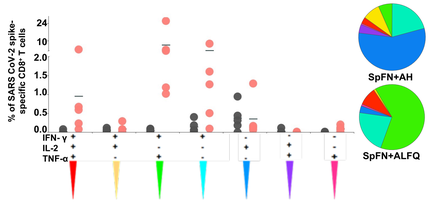
1 ALFQ Enhances APC Recruitment at Early Time Points



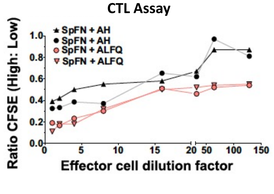
Spike Specific CD8 T cells in Perfused Lungs (Week 6 and 23)



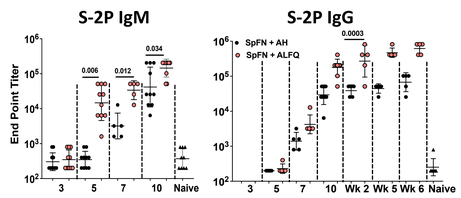
ALFQ increases virus specific CD8 T-cell poly-functional responses



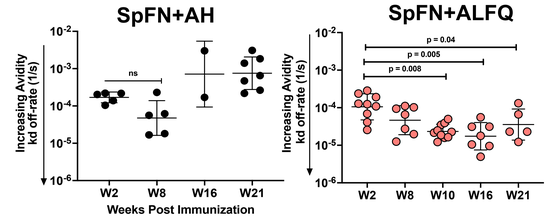
Spike Specific CD8+ T cells from SpFN + ALFQ immunized mice effectively lyse target cells



2 ALFQ Promotes Rapid Development of Antigen-Specific IgM and IgG Responses

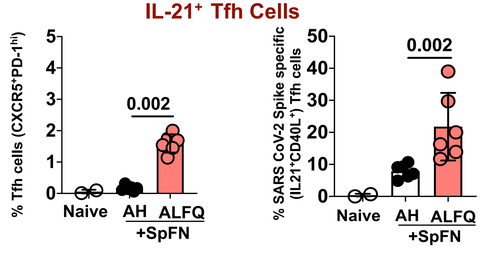


ALFQ Enhances Avidity of Spike Specific Antibodies

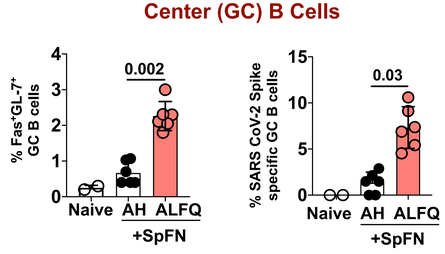


3 Post Priming (Spleen Day 7)

Increased Frequency of Spike-Specific IL-21+ Tfh Cells

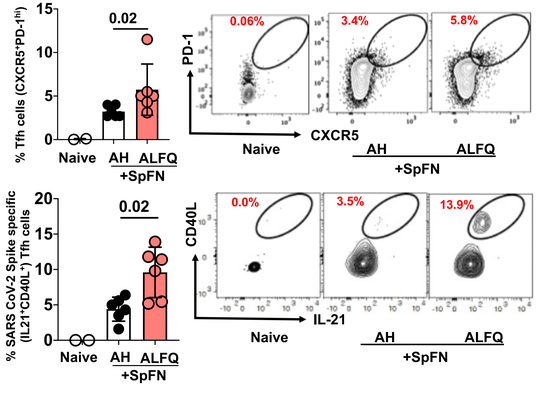


Increased Frequency of Spike-Specific Germinal Center (GC) B Cells

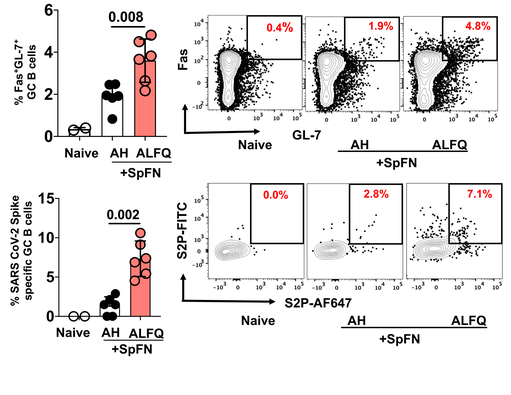


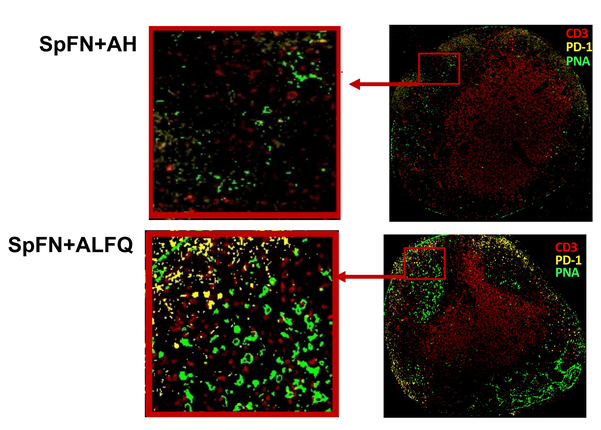
4 Post boosting (Spleen Week 4)

Induction of Higher Spike-Specific IL-21+ Tfh Cells

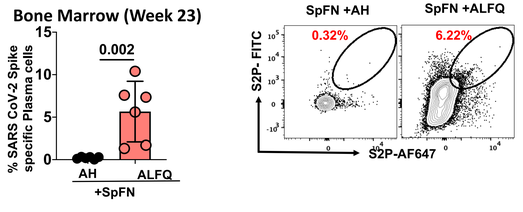


Maintenance of Antigen-Specific GC B Cell Responses





Increased Number of Spike specific Plasma cells in the bone marrow of SpFN + ALFQ immunized mice at week 23



CONCLUSIONS

- The SpFN+ALFQ vaccine formulation effectively recruited highly activated multifaceted APCs driving potent antigen-specific polyfunctional T cell cytokine responses and cytolytic functions.
- Increased and early APC recruitment/activation induced by ALFQ leads to robust downstream responses
- ALFQ induces early antibody production (both IgM and IgG) and ultimately durable immune responses
- ALFQ increases the frequency and maintenance of Spike specific IL-21 producing Tfh cells, GC B cells in lymph node and spleen and durable plasma cells in the bone marrow

5 Higher Frequencies of GC Follicles and Tfh Cells (Lymph Nodes Week 4)

DISCLAIMER

The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army or the Department of Defense.