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Sarbecovirus Ferritin Nanoparticle Vaccines as Protein or mRNA-LNP Elicit Broad Immunogenicity

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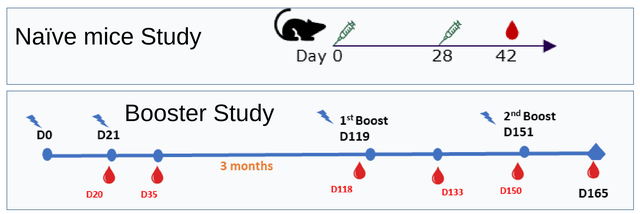
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Background

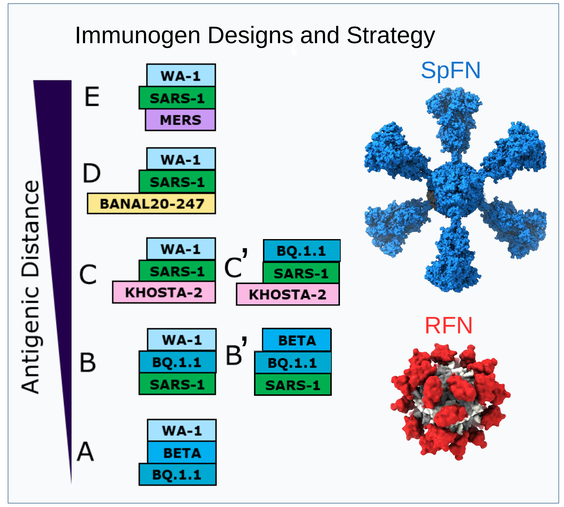
The need for SARS-CoV-2 next-generation vaccines is clear. Early in the COVID-19 pandemic, we designed and characterized engineered ferritin nanoparticle immunogens based on the WA-1 sequence that recapitulate the structural and antigenic properties of prefusion SARS-CoV-2 Spike. A lead candidate, Spike-Ferritin nanoparticle (SpFN) adjuvanted with a liposomal-saponin adjuvant (ALFQ) was subsequently assessed in a Phase I study in humans and showed broad immunogenicity to VoCs (see Poster 673). Building on that work, we have developed novel immunogen designs that have increased antigenic diversity and are delivered as mRNA-LNP immunogens. This study aims to understand the breadth of sarbecovirus immune response that can be elicited using either adjuvanted protein or mRNA platforms.

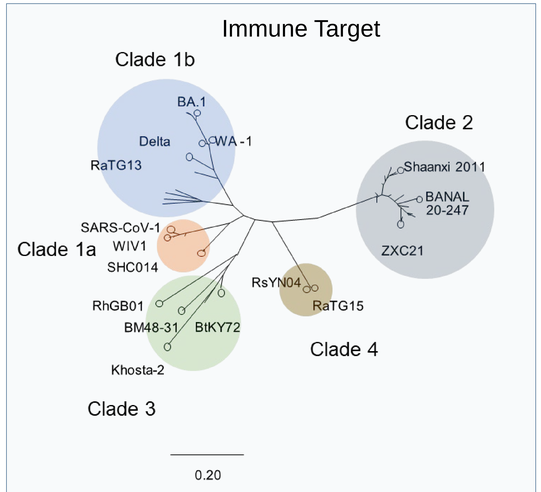
Methods

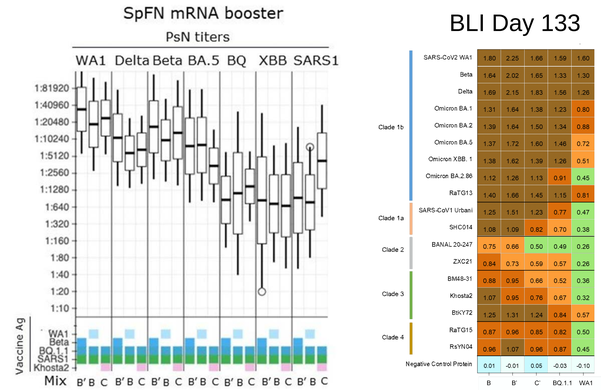
Designs based on Spike and RBD proteins contain antigenic matter from multiple sarbecovirus strains. To further increase the vaccine immunogen diversity, formulations including two or more of these antigen designs were combined as cocktail or mosaic immunogens. These immunogens were either produced as proteins in mammalian cells or expressed in vivo as mRNA encapsulated in LNP. Groups of naïve male and female C57BL/6 mice were immunized 2-3 times. A second immunization study was carried out – "Booster Study" – where pre-immune mice were boosted either once or twice with single immunogens or cocktails of immunogens. Immune responses were assessed by serum sarbecovirus RBD-binding and pseudovirus neutralization assays.

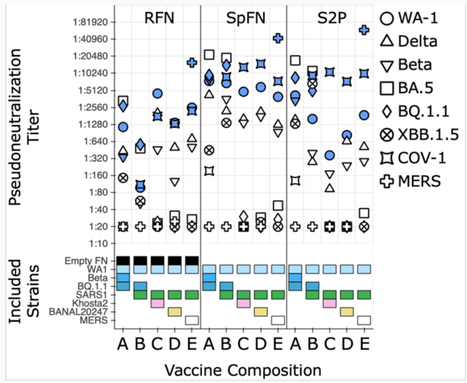


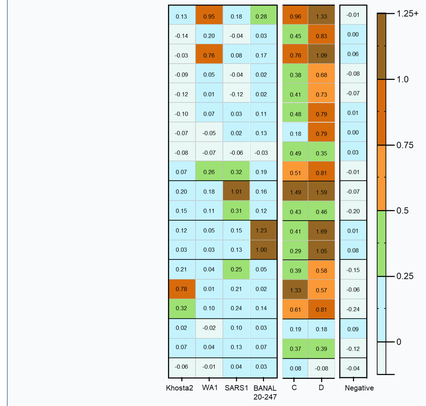
The ferritin nanoparticle platform either as a protein or mRNA format provides a potent platform for elicitation of pan-sarbecovirus immune responses.











Results

Immunogens in both protein-ALFQ or mRNA format elicited broad and robust neutralizing responses in C57BL/6 mice. The mRNA formulations containing BQ.1.1 immunogens (either singly or in combinations) elicited potent neutralizing responses against all Omicron virus strains assessed. Vaccine candidates combining antigens from three sarbecovirus strains elicited high ID50 GMT titers against all sarbecovirus strains tested, including heterologous pseudoviruses not included in the vaccine. Of further note, following two immunizations, ID50 GMT titers of 19,200 and 1,400 against heterologous Omicron BA.5 and XBB.1.5 respectively were observed in mice immunized with this trivalent combination. In pre-immune Balb/c mice, neutralization titers were lower but followed a similar trend to the naïve mice.

Conclusion

Both BLI binding and neutralization results indicate the ability of multivalent vaccines to generate broader immune responses. Antigenic Distance B shows the highest level of neutralization titers against non-homologous strains. The ferritin platform either as a protein or mRNA format provides a potent platform for pan-sarbecovirus vaccine development.

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