

# SARS-CoV-2 ferritin nanoparticle vaccines elicit broad SARS coronavirus immunogenicity

M Joyce<sup>1</sup>

<sup>1</sup>Henry M. Jackson Foundation / Walter Reed Army Institute of Research  
joycegordo@gmail.com

The need for next-generation SARS-CoV-2 vaccines has been highlighted by the rapid emergence of variants of concern (VoC), while the long-term threat of other coronaviruses further highlights the need for pan-coronavirus vaccines that can provide broad protection. Using structure-based vaccine design, we designed and characterized four categories of engineered nanoparticle CoV immunogens that recapitulate the structural and antigenic properties of prefusion Spike (S), S1 and RBD. These encompass the major antigenic regions of the S ectodomain. These immunogens were assessed in multiple animal models including mice, hamsters, and non-human primates and in all cases induced robust S-binding, ACE2-inhibition, and authentic and pseudovirus neutralizing antibodies against SARS-CoV-2.

A Spike-ferritin nanoparticle (SpFN) vaccine elicited neutralizing titers more than 20-fold higher than convalescent donor serum, following a single immunization, while RBD-Ferritin nanoparticle (RFN) immunogens elicited similar responses after two immunizations in mice. Passive transfer of IgG purified from SpFN- or RFN-immunized mice protected K18-hACE2 transgenic mice from a lethal SARS-CoV-2 virus challenge. Immunization of non-human primates, and hamsters, produced high neutralizing antibody titers, and provided robust protection against SARS-CoV-2 and VoC viral challenge in these animal models. Furthermore, SpFN- and RFN-immunization elicited ACE2 blocking activity and neutralizing ID50 antibody titers >2,000 against SARS-CoV-1, in mice, non-human primates, and hamsters, along with high magnitude neutralizing titers against the major SARS-CoV-2 VoC.

Structure-based design parameters from these SARS-CoV-2 immunogens have been translated to other coronavirus nanoparticle immunogens that are currently being tested in animal studies. Overall, these results provide a design blueprint for pan-coronavirus vaccine development.

