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DEVELOPMENT OF AN INNOVATIVE ADENOVIRUS-INPIRED SELF-ASSEMBLING VACCINE PLATFORM RAPIDLY ADAPTABLE TO CORONAVIRUSES AND OTHER EMERGENT VIRUSES

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The COVID-19 pandemic clearly shows how emergent diseases can cause severe global health and economic problems. We must be prepared to react swiftly against new pathogenic agents and this requires the development of vaccines that are safe, efficient in the long-term and easily adaptable with a short revision time. To this end, the COVID-19 mRNA and adenoviral vector vaccines have been spectacular successes, permitting rapid vaccination across the world in an unprecedented manner. Here we report the design of a new adenovirus-derived vaccine technology based on non-infectious pseudo-viral nanoparticles from the serotype 3 human adenovirus. Each nanoparticle comprises sixty identical proteins that assemble to form a 30 nm diameter spherical particle. A sequence has been engineered into the surface of this protein that enables the display of a covalently-bound target antigens. To demonstrate the efficiency of this approach, we added the SARS-CoV 2 spike protein receptor binding domain (RBD), that interacts with host cell ACE2 receptors, to the surface of the nanoparticles. We first showed that the glycosylated RBD retained its ACE2-binding function when displayed on nanoparticles. We then measured the in vivo humoral response of our vaccine candidate in mice and observed a strong antibody response after the prime injection; further levels were achieved following a second booster injection. In mice preimmunized with underivatized adenoviral nanoparticles, we tested if adenovirus seroprevalence, as frequently observed in humans, was detrimental to the RBD-mediated protection provided by our vaccine candidate. Interestingly, a strong anti-coronaviral response was still observed suggesting that existing circulating anti-adenovirus antibodies are not deleterious to our vaccine platform. We then performed pseudo-CoV 2 neutralization assays and obtained higher IDso values than observed with COVID-19 convalescent sera, thus showing the high potential efficacy of our vaccine platform. This new vaccine technology is a tool that is easily adaptable to future SARS-CoV 2 variants and, more generally, to future emergent viruses and pathogens.