An AAV-based Single Dose, Thermostable Vaccine Platform that Provides Durable Immunogenicity

Nerea Zabaleta, PhD
Principal Investigator, Grousbeck Gene Therapy Center, Mass Eye and Ear; Instructor in Ophthalmology, HMS
nerea_zabaletalasarte@meei.harvard.edu

Dr. Zabaleta is focused on improving AAV-based gene therapies for infectious diseases. She is currently working on a novel, gene-based COVID-19 vaccine that leverages a unique AAV platform. This approach was highly effective at eliciting neutralizing antibody responses and cellular immunity from a single dose.

The SARS-CoV-2 pandemic has had a disastrous impact on health and economy globally. Although several vaccine candidates have shown to be effective in combating SARS-CoV-2, logistical, economical and sociological aspects limit vaccine access and effectiveness globally. Additionally, mRNA vaccines present limitations that include the need for several doses to induce high immunogenicity, limited durability of responses, and cold-chain requirements. In the light of these limitations highlight the need for improved vaccine platforms, for the current, as well as future, pandemics.

We have developed and characterized an adeno-associated virus (AAV)-based genetic vaccine for COVID-19 and validated this across different SARS antigens. After a single, low dose administration in non-human primates (NHP), our vaccines induce high humoral and cellular immune responses to the antigen, conferring near-complete protection against a live SARS-CoV-2 viral challenge. Additionally, neutralizing antibody responses remain at peak levels for at least 20 months after single dose vaccination, with no signs of waning immunity. Cellular responses to the antigen were also found to be high, polyfunctional and durable. We further demonstrated a rapid and robust programmability of our vaccine platform to express different SARS antigens, which elicit potent and protective immunogenicity against several variants of concern. Finally, we demonstrated that AAV-based vaccines can be manufactured at scale and are stable for 1 month at room temperature and for at least 3 months refrigerated, considerably reducing cold chain requirements.

In conclusion, AAV-based vaccines present ideal features for the development of vaccines: a single and low dose that elicits high and durable immunogenicity, and room temperature stability. High circulating antibody responses and protection from SARS-CoV-2 challenge suggest that our platform has the potential to confer protective immunity against respiratory infection as well as other mucosal or systemic viruses.

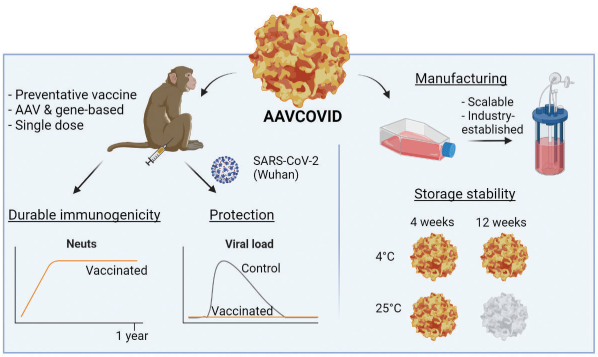

Figure 1. Graphical abstract that summarizes some important attributes of AAV-based vaccines.