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DNA-based delivery of antiviral antibodies for infectious disease prevention

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The importance of vaccines for public health can hardly be overstated, and yet there are two areas of infectious disease prevention that remain sources of vulnerability for vaccine use and effectiveness: rapid responses to emerging infectious diseases and protection of immunocompromised populations.

Though vaccines are an invaluable tool for the prevention of infectious diseases, there are barriers to their rapid development and deployment in the event of an outbreak of a novel pathogen. The COVID-19 pandemic revealed the possibilities for rapid vaccine development where preexisting research on SARS provided a head start for vaccine design (and previously unproven technologies yielded excellent clinical results), but there will almost certainly be future pathogens for which that scenario doesn't exist. The successful development of a vaccine often takes many years, a timeframe incompatible with quickly halting a novel infectious disease outbreak. In contrast, the identification and characterization of antiviral antibodies, primarily from patient sera, is a field that has made significant advances in recent years, enabling programs like the DARPA-funded Pandemic Prevention Platform to boast multiple groups capable of screening and down selecting to potential clinical candidate molecules in a matter of weeks. The rapid deployment of such antibodies could serve as a firebreak while vaccine development is underway. A mechanism for further improving the speed of such a response could be to deliver such antibodies not as traditional recombinant proteins, but via antibody-encoding DNA. Just as plasmid DNA would typically be used as the starting material for manufacturing antibodies, it can be administered directly to patients using intramuscular electroporation, where an individual's own muscle cells act as a bioreactor, durably delivering the encoded antibody to systemic circulation.

In the case of infectious diseases for which effective vaccines already exist, there remain a substantial number of people whose compromised immune systems prevent them from fully benefitting from vaccine-induced protective immunity. For these patients, the acquisition of passive immunity in the form of antiviral antibodies has the potential to be very beneficial. Indeed, the anti-SARS-CoV-2 antibody cocktail, Evusheld, was authorized by the US FDA for both treatment and prevention of COVID-19. In order to provide the most durable protection, however, the delivery of antiviral antibodies in DNA form has the potential to

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transform months-long protection of recombinant protein into protection for a year or more from a single administration.

Vaccines have been, and undoubtedly will continue to be one of the most valuable tools for protecting public health. There are, however, gaps in their timing and widespread coverage in the settings of rapid responses to novel viral outbreaks and robust protection of immunocompromised populations. In these areas, DNA-based delivery of antiviral antibodies has the potential to be enormously impactful.