

A Long-Lasting Ebola Vaccine that is Gone Without a Trace: How Pharmaceutical Science Can Influence Global Medicine

Maria A. Croyle, R.Ph., Ph.D.

In response to the severity and scale of the 2014 Ebola outbreak in West Africa, several experimental vaccines were granted fast-track status for clinical testing. Although each of them may provide long-lasting protection from Ebola, they had been developed as refrigerated, injectable platforms to be stored and distributed by highly trained medical personnel, limited in number in the areas where vaccines are needed the most. During our effort to develop an effective adenovirus-based Ebola vaccine suitable for use in Africa, an area in which prior exposure to the adenovirus serotype we selected for our vaccine platform was quite high, we found that pre-existing immunity to adenovirus significantly compromised the number of poly-functional T cells and Th2-type antibodies generated against the Ebola glycoprotein transgene. Both of these components of the immune response were critical for protection from Ebola. Formulation candidates were then evaluated for their ability to improve transduction efficiency of adenovirus in the presence of physiological concentrations of neutralizing antibodies (NAB) with respect to unformulated virus *in vitro*. Successful candidates were further evaluated for their ability to improve multi-functional CD8⁺ T cell and Th2 type antibody responses with respect to unformulated virus in mice. They also improved survival in other rodent models after lethal challenge with respect to unformulated vaccine. The most successful formulation candidate was used to immunize non-human primates against Ebola. This formulation protected all of the primates treated with the vaccine one year after immunization from a lethal dose of Ebola Zaire. *This was summarized in the first report detailing the durability of a single dose Ebola vaccine evaluated in large animal models of Ebola virus disease.* Other considerations that impacted design of our vaccine were the limited resources and inability to maintain cold chain requirements in developing countries. As a result, a very novel method for stabilization of the recombinant adenovirus-based vaccine in a thin film for transport was discovered that could significantly impact the way vaccines and other biologicals are stored and administered in the future. This technology will also be discussed throughout the presentation.