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Single-dose, needle-free Ebola vaccine provides long-term protection in macaques

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Scientists have demonstrated for the first time that a single-dose, needleless Ebola vaccine given to primates through their noses and lungs protected them against infection for at least 21 weeks. A vaccine that doesn't require an injection could help prevent passing along infections through unintentional pricks. They report the results of their study on macaques in the ACS journal *Molecular Pharmaceutics*.

Maria A. Croyle and colleagues note that in the current Ebola outbreak, which is expected to involve thousands more infections and deaths before it's over, an effective vaccine could help turn the tide. Even better, taking the needle out of the inoculation process could also help prevent the accidental transmission of Ebola, as well as other diseases, such as HIV, that might otherwise spread from unintentional needle pricks and unsafe handling of medical wastes. Other vaccines are currently under development to fight the virus, but they require an injection. Croyle's team tested an adenovirus-based Ebola vaccine using a respiratory delivery route.

The researchers gave a novel formulation of an Ebola vaccine to several macaques then exposed them to the virus more than four months later. All three of the animals that received the vaccine through the nose and via a catheter into their airways did not fall ill. However, since special equipment and training are required for the current respiratory delivery method, the scientists conclude that further work is needed if this formula, or an under-the-tongue version, is to be used eventually in large-scale immunization campaigns.

More information: "A Single Dose Respiratory Recombinant Adenovirus-Based Vaccine Provides Long-Term Protection for Non-Human Primates from Lethal Ebola Infection" *Mol. Pharmaceutics*, Just Accepted Manuscript, DOI: 10.1021/mp500646d

Abstract

As the Ebola outbreak in West Africa continues and cases appear in the United States and other countries, the need for long-lasting vaccines to preserve global health is imminent. Here, we evaluate the long-term efficacy of a respiratory and sublingual (SL) adenovirus-based vaccine in non-human primates in two phases. In the first, a single respiratory dose of 1.4 × 10 9 infectious virus particles (ivp)/kg of Ad-CAGoptZGP induced strong Ebola-glycoprotein (GP) specific CD8+ and CD4+ T cell responses and Ebola GP-specific antibodies in systemic and mucosal compartments and was partially (67%) protective from challenge 62 days after immunization. The same dose given by the SL route induced Ebola GP-specific CD8+ T cell responses similar to those induced by intramuscular (IM) injection, however, the Ebola GP-specific antibody response was low. All primates succumbed to infection. Three primates were then given the vaccine in an IN formulation that improved the immune response to Ebola in rodents. Three primates were immunized with 2.0 × 1010 ivp/kg of vaccine by the SL route. Diverse populations of polyfunctional Ebola GP-specific CD4+ and CD8+ T cells and significant anti-Ebola GP antibodies were present in samples collected 150 days after respiratory immunization. The formulated vaccine was fully protective against challenge 21 weeks after immunization. While diverse populations of Ebola GP-specific CD4+ T cells were produced after SL immunization, antibodies were not neutralizing and the vaccine was not protective. To our knowledge, this is the first time that durable protection from a single dose respiratory recombinant adenovirus-based Ebola vaccine has been demonstrated in primates.