Single dose protection against lethal Ebola virus challenge

Ebola virus disease (EVD) is a fast-progressing, highly lethal illness that poses significant threat to global public health when not contained. The current outbreak in the Democratic Republic of the Congo, as of February 26, 2019, has totaled 879 cases with a 63% fatality rate according to the World Health Organization. The main strategy to stop transmission of EVD is isolation of contacts and wearing proper protective equipment. However, most new EVD cases occur in individuals not on known contact lists, undermining traditional interventions. An ideal countermeasure would be the development of a safe and effective vaccine. An experimental vaccine, rVSV-ZEBOV, has proven protective against Ebola virus (EBOV) and has been administered in the region of the current outbreak. In an initial trial, severe adverse events to vaccination were reported which included fatigue, chills, headache, and muscle pain (Regules et al., 2017). An additional drawback to this vaccine is the requirement for storage at -60°C or colder. This creates a logistical nightmare to vaccinate in rural areas with year-round high temperatures.

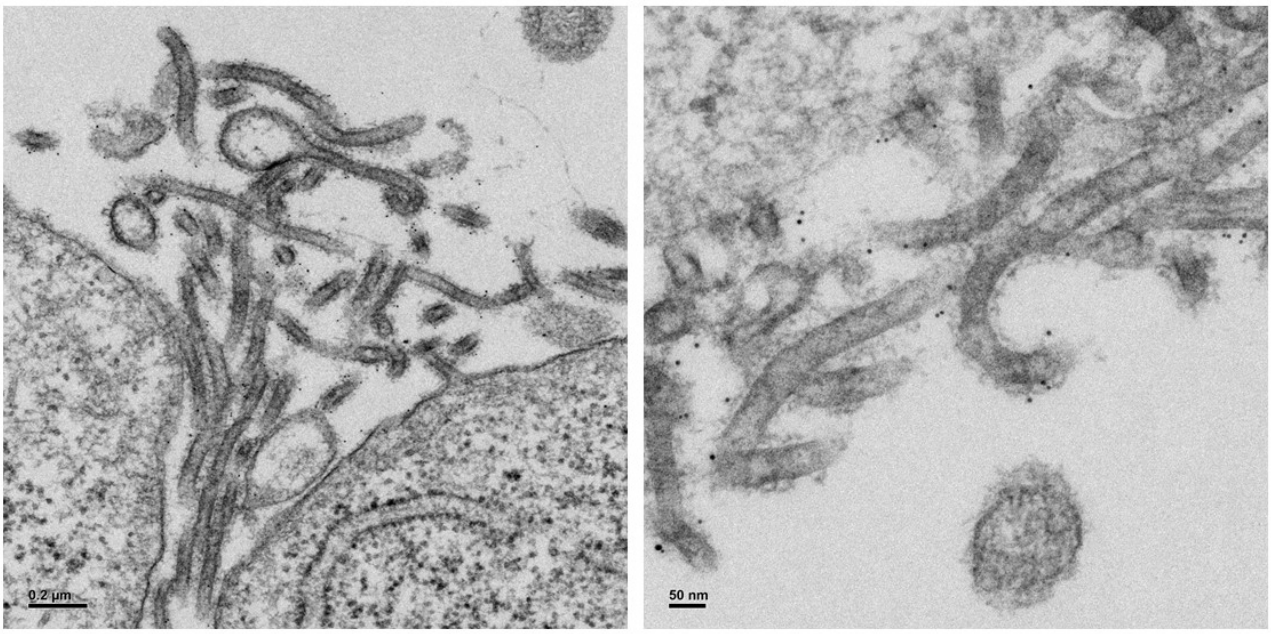

Fig. 1. Electron micrograph showing formation of MVA-EBOV VLPs. Immunogold staining (black dots) depicts Ebola virus GP on surface of VLPs.

We constructed and carried out pre-clinical testing of a vaccine using Modified Vaccinia Ankara (MVA) as a delivery vector for induction of immunity to EBOV. Although not directly tested here, MVA can be freeze-dried without compromising the ability to stimulate an immune response. Dried vaccine has a longer shelf life and would be highly beneficial in terms of handling and transport for distribution in the event of an outbreak. Our vaccine has the added benefit of producing non-

infectious virus-like particles (VLPs) as shown below in Figure 1. This allows the immune system to see the EBOV antigens in an arrangement closely resembling the natural virus which leads to robust antibody production and cellular responses. The VLPs form following expression of EBOV matrix (VP40) and glycoproteins (GP), which have been engineered to be expressed by the replication defective MVA vector. The MVA-VLP platform is not only safe in comparison to replication competent vaccines, but also highly immunogenic and is considered as best-in-class potential vaccine candidate against EBOV (Lazaro-Frias et al., 2018).

In animal experiments, we demonstrate that just a single administration of our vaccine, MVA-EBOV, provides complete protection from a deadly dose of EBOV. First, we achieved successful protection of guinea pigs and hamsters from a fatal dose of EBOV by immunizing animals twice (prime/boost regimen) with MVA-EBOV. Next, we evaluated the ability of MVA-EBOV vaccine to protect non-human primates (NHPs) from lethal EBOV challenge. Figure 2a shows that animals receiving one dose of MVA-EBOV vaccine were fully protected from death. Furthermore, there was no detectable live EBOV in the blood of challenged animals that had been immunized with MVA-EBOV (Fig 2b). Analysis of immune responses revealed that similar levels of antibody against EBOV proteins were produced in NHPs that received the vaccine once or twice. These antibodies protected animals through virus neutralization and cellular cytotoxicity, an activity that kills infected cells.

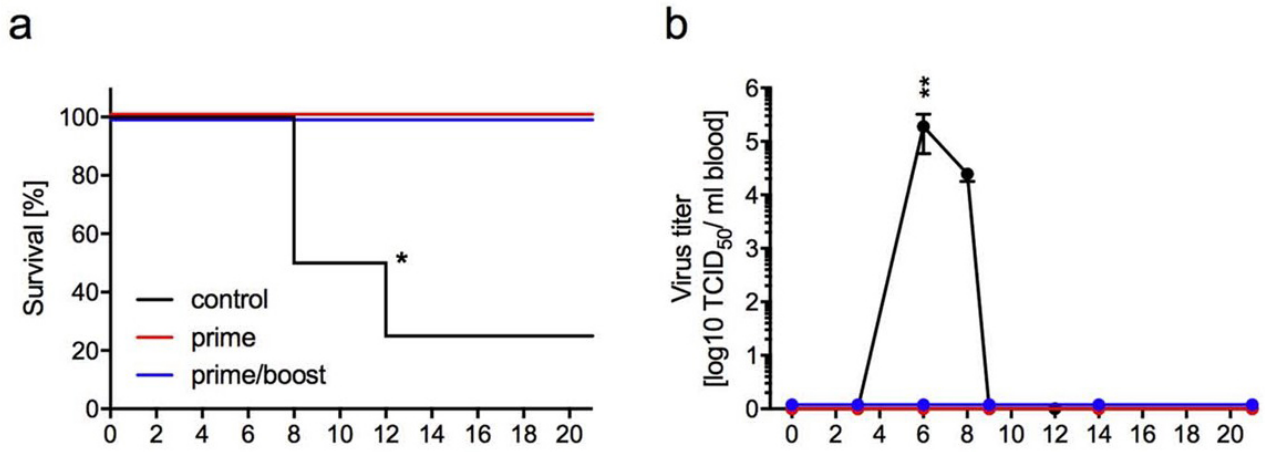

Fig. 2. Single-dose immunization provides complete protection in NHPs against lethal EBOV challenge. (a) Survival curves of animals receiving one (red) or two (blue) doses of MVA-EBOV vaccine or the sham control (black). (b) Viremia in whole blood following challenge.

In sum, GeoVax's MVA-EBOV vaccine would provide a safer, single-dose alternative to the current experimental vaccines as it is not associated with adverse side effects. Importantly, this vaccine can be formulated into a more stable dried vaccine overcoming operational hurdles of delivering vaccines that require a -60°C cold-chain. Priorities for the continued development of

MVA-EBOV vaccine include determining how quickly it can provide protection and how long protective responses last.

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Publication

A Single Dose of Modified Vaccinia Ankara expressing Ebola Virus Like Particles Protects Nonhuman Primates from Lethal Ebola Virus Challenge.
Domi A, Feldmann F, Basu R, McCurley N, Shifflett K, Emanuel J, Hellerstein MS, Guirakhoo F, Orlandi C, Flinko R, Lewis GK, Hanley PW, Feldmann H, Robinson HL, Marzi A.
Sci Rep. 2018 Jan 16