

Experimental vaccine partially protects monkeys from HIV-like infection

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Results from a recent study show that novel vaccine combinations can provide partial protection against infection by Simian Immunodeficiency Virus (SIV) in rhesus monkeys. In addition, in the animals that became infected, the optimal vaccine combinations also substantially reduced the amount of virus in the blood. Results from the studies were published online today in the journal *Nature*.

This proof-of-concept study, which tested MVA, Ad26, and Ad35 vector-based vaccines, is the first to show partial vaccine protection in the stringent animal model involving heterologous, neutralization-resistant SIVmac251 viral challenges in rhesus monkeys. Preclinical studies of vaccine candidates have typically shown post-infection virologic control, however protection against acquisition of infection has previously only been reported using less rigorous viral challenges. The new Ad26/MVA and Ad35/Ad26 vector-based vaccine regimens resulted in over 80% reduction in the per-exposure probability of acquisition of infection against repetitive challenges of SIV, a virus similar to HIV that infects monkeys.

"This study allowed us to evaluate the protective efficacy of several prime-boost vaccine combinations, and these data will help guide the advancement of the most promising candidates into clinical trials," noted lead author Dr. Dan Barouch of Beth Israel Deaconess Medical Center at Harvard Medical School and the Ragon Institute of MGH, MIT, and Harvard.



Further analysis also provided insights into the immune responses that might have provided protection, called "immune correlates." The results show that antibodies to Env (the <u>envelope protein</u> that makes up the outer coat of the virus) correlated with protection against acquisition, whereas both T cell and <u>antibody responses</u> correlated with post-infection virologic control.

"These distinct immunologic correlates likely reflect fundamentally different requirements to block establishment of infection compared with controlling <u>viral replication</u> after infection," said Col. Nelson Michael, director of the U.S. Military HIV Research Program at the Walter Reed Army Institute of Research and senior author on the paper.

Barouch noted that "we have clearly shown that including Env in the vaccine is beneficial." The findings also suggest that a substantial degree of protection can be achieved against stringent virus challenges, even in the absence of high levels of tier 2 neutralizing antibodies.

These new preclinical studies provide support for advancing the Ad26/MVA prime-boost vaccine candidate into clinical development. Collaborators are planning clinical testing of this HIV <u>vaccine</u> regimen in healthy adults at research sites in the U.S., East Africa, South Africa, and Thailand.

More information: D Barouch et al., Vaccine protection against acquisition of neutralization-resistant SIV challenges in rhesus monkeys. *Nature* DOI:10.1038/nature10766 (2012).

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