Experimental vaccine protects monkeys from new Ebola virus

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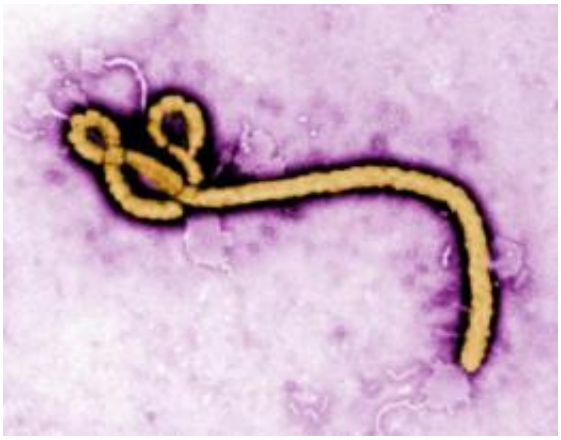

A colorized transmission electron micrograph of Ebola virus, the cause of Ebola hemorrhagic fever. The disease infects people and nonhuman primates and is frequently fatal. The first outbreak of Ebola fever occurred in 1976. Credit: CDC

New research has found that an experimental Ebola vaccine developed by researchers at the National Institutes of Health protects monkeys against not only the two most lethal Ebola virus species for which it was originally designed, both recognized in 1976, but also against a newer Ebola virus species that was identified in 2007.

Nancy J. Sullivan, Ph.D., of the Vaccine Research Center at the National Institute of Allergy and Infectious Diseases (NIAID), NIH, led the study team, which included collaborators from the U.S. Army Medical

Research Institute of Infectious Diseases in Fort Detrick, Md, and the Centers for Disease Control and Prevention in Atlanta. Their findings appear May 20 in the open-access journal *PLoS Pathogens*. Currently, there are no specific treatments or vaccines available to control Ebola outbreaks.

"The important work by Dr. Sullivan and her colleagues shows that it is possible to generate immunity to newly identified species of Ebola virus with a vaccine originally designed to protect against a different species," says NIAID Director Anthony S. Fauci, M.D. "This finding will guide future vaccine design and may open an avenue for developing a single vaccine that works against both known and emerging Ebola virus species."

The experimental Ebola vaccine being developed at NIAID has two components, a prime and a boost. The prime consists of a DNA vaccine containing a small piece of genetic material encoding surface proteins from Zaire ebolavirus and Sudan ebolavirus. The boost consists of a weakened cold virus that delivers the Zaire ebolavirus surface protein.

Previously, Dr. Sullivan and her collaborators demonstrated that the prime-boost strategy produces a strong antibody response in monkeys. More importantly, the experimental vaccine induces a robust reaction by the cellular arm of the immune system. The cellular arm includes T cells, which help orchestrate the overall immune response.

"An ideal Ebola vaccine would stimulate broad immunity so that we wouldn't have to scramble to create entirely new vaccines whenever new virus species are identified," notes Dr. Sullivan.

However, developing one vaccine to protect against multiple Ebola virus species poses a challenge, she says. To the antibody-producing arm of the immune system, each species looks different. Neutralizing antibodies

that recognize one Ebola species cannot readily recognize, or cross-neutralize, the others. T cells, in contrast, can cross-react, even when the target viruses share only small pieces in common.

After the emergence of Bundibugyo ebolavirus (BEBOV) in 2007, Dr. Sullivan's team decided to revisit the prime-boost vaccine regimen to see if the cellular immunity generated would confer protection against the new virus species.

Four cynomolgus macaques received the DNA prime vaccine. A year later, the animals were boosted with the vector vaccine. Shortly after the boost, the four vaccinated monkeys and four unvaccinated ones serving as controls were exposed to lethal levels of BEBOV. All the unvaccinated animals became ill, and three died. None of the vaccinated animals showed any sign of illness. Analysis showed that the vaccinated monkeys developed T-cell responses sufficient to prevent or control infection by the novel Ebola virus species, even though the vaccine did not contain material from BEBOV and no antibodies against BEBOV were produced. The animal study was conducted in maximum-level biosafety containment laboratories at U.S. Army Medical Research Institute of Infectious Diseases.

Now the research team is evaluating what parts of the T-cell response were critical to the vaccine's success against BEBOV. "Once we identify those critical aspects, we can design future vaccines to better elicit that desired immune cell-based activity and perhaps make a single vaccine that protects against all Ebola virus species," says Dr. Sullivan.

More information: LE Hensley et al. Demonstration of cross-protective vaccine immunity against an emerging pathogenic Ebolavirus species. PLoS Pathogens. DOI:10.1371/journal.ppat.1000904 (2010).

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