Ebola whole virus vaccine shown effective, safe in primates

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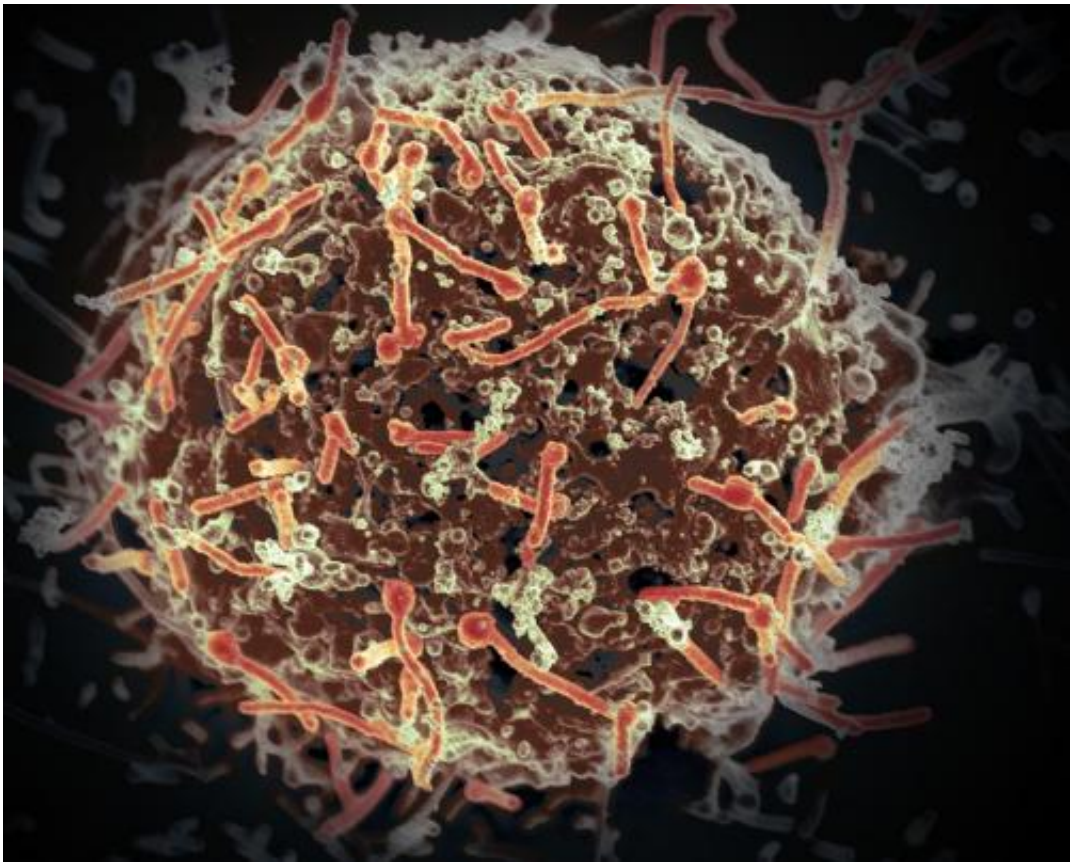

The Ebola virus, isolated in November 2014 from patient blood samples obtained in Mali. The virus was isolated on Vero cells in a BSL-4 suite at Rocky Mountain Laboratories. Credit: NIAID

An Ebola whole virus vaccine, constructed using a novel experimental platform, has been shown to effectively protect monkeys exposed to the

often fatal virus.

The vaccine, described today (March 26, 2015) in the journal *Science*, was developed by a group led by Yoshihiro Kawaoka, a University of Wisconsin-Madison expert on avian influenza, Ebola and other viruses of medical importance. It differs from other Ebola vaccines because as an inactivated whole virus vaccine, it primes the host immune system with the full complement of Ebola viral proteins and genes, potentially conferring greater protection.

"In terms of efficacy, this affords excellent protection," explains Kawaoka, a professor of pathobiological sciences in the UW-Madison School of Veterinary Medicine and who also holds a faculty appointment at the University of Tokyo. "It is also a very safe vaccine."

The vaccine was constructed on an experimental platform first devised in 2008 by Peter Halfmann, a research scientist in Kawaoka's lab. The system allows researchers to safely work with the virus thanks to the deletion of a key gene known as VP30, which the Ebola virus uses to make a protein required for it to reproduce in host cells. Ebola virus has only eight genes and, like most viruses, depends on the molecular machinery of host cells to grow and become infectious.

By engineering monkey kidney cells to express the VP30 protein, the virus can be safely studied in the lab and be used as a basis for devising countermeasures like a whole virus vaccine. The vaccine reported by Kawaoka and his colleagues was additionally chemically inactivated using hydrogen peroxide, according to the new *Science* report.

Ebola first emerged in 1976 in Sudan and Zaire. The current outbreak in West Africa has so far claimed more than 10,000 lives. There are no proven treatments or vaccines, although several vaccine platforms have been devised in recent years, four of which recently advanced to the

clinical trial stage in humans.

The new vaccine reported by Kawaoka has not been tested in people. However, the successful tests in nonhuman primates conducted at the National Institutes of Health (NIH) Rocky Mountain Laboratories, a biosafety level 4 facility in Hamilton, Montana, may prompt further tests and possibly clinical trials of the new vaccine. The work at Rocky Mountain Laboratories was conducted in collaboration with a group led by Heinz Feldmann of NIH.

Those studies were conducted with cynomolgus macaques, which are very susceptible to Ebola. "It's the best model," Kawaoka says. "If you get protection with this model, it's working."

Ebola vaccines currently in trials include:

- A vaccine based on a replication incompetent chimpanzee respiratory virus engineered to express a key Ebola protein.
- A live attenuated virus from the same family of viruses that causes rabies, also engineered to express a critical Ebola protein.
- A vaccine based on a vaccinia virus and engineered to express a critical Ebola protein.

Each of those strategies, Kawaoka notes, has drawbacks in terms of safety and delivery.

Whole virus vaccines have long been used to successfully prevent serious human diseases, including polio, influenza, hepatitis and human papillomavirus-mediated cervical cancer.

The advantage conferred by inactivated whole virus vaccines such as the one devised by Halfmann, Kawaoka and their colleagues is that they present the complete range of proteins and genetic material to the host

immune system, which is then more likely to trigger a broader and more robust immune response.

Early attempts to devise an inactivated whole virus Ebola vaccine through irradiation and the preservative formalin failed to protect monkeys exposed to the Ebola virus and were abandoned.

Although the new vaccine has surpassed that hurdle, human trials are expensive and complex, costing millions of dollars.

More information: An Ebola Whole Virus Vaccine Is Protective In Nonhuman Primates, www.sciencemag.org/lookup/doi/ … 1126/science.aaa4919

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