



NEWS RELEASE

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Experimental Smallpox Vaccine Protects Against Monkeypox in Nonhuman Primates

Scientists evaluating MVA, a potential safer replacement for the licensed Dryvax smallpox vaccine, have shown that MVA elicits an immune response comparable to that of Dryvax in a monkeypox model of human disease. In addition, MVA protected nonhuman primates exposed to lethal doses of the monkeypox virus.

The study, published in the March 11th issue of the journal NATURE, is a collaborative effort involving a team of scientists from the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), the National Institute of Allergy and Infectious Diseases (NIAID), the Henry M. Jackson Foundation, and the University of Pennsylvania. Their findings represent an important step in the search for an alternative vaccine to Dryvax, which contains a live virus called *Vaccinia* that carries a high risk of adverse complications for people with suppressed immune systems.

Smallpox, a devastating disease caused by the *Variola* virus, was eradicated in 1979 through the efforts of the World Health Organization (WHO). Currently, infectious *Variola* (a species of the genus *Orthopoxvirus*) is known to exist only in two WHO-sanctioned repositories, one in Russia and the other at the Centers for Disease Control and Prevention in Atlanta. However, there is concern that undisclosed reference stocks of the virus may exist, and its potential as a biological weapon has led to the production and stockpiling of smallpox vaccine and the immunization of some healthcare workers.

Because *Variola* no longer occurs naturally, vaccines cannot be tested for their ability to prevent smallpox in humans. Thus, licensing of future vaccine candidates will include studies of immune response and protection in nonhuman primates. According to the authors, monkeypox currently provides the best nonhuman primate model of an *Orthopoxvirus* infection.

MVA is made from the same *Vaccinia* virus present in the Dryvax product. The difference is that MVA is extremely attenuated, or weakened, so it causes no adverse effects—even when given in high doses to immune-deficient nonhuman primates.

In the study, investigators divided 24 cynomolgous monkeys into four groups. Group 1 received two injections of MVA, two months apart; Group 2 received one injection of MVA followed by inoculation with Dryvax two months later; Group 3 received nothing at baseline and one Dryvax inoculation two months later; and Group 4 served as the unimmunized control group. Following the MVA and Dryvax immunizations, the team measured the immune responses of the monkeys. Results showed that after two doses of MVA or one dose of MVA followed by Dryvax, the animals' immune responses were equivalent to or higher than those induced by Dryvax alone. Two months after the last immunization, each of the 24 monkeys was challenged by intravenous injection of monkeypox virus. The unvaccinated animals became ill or died, showing signs of fever, pox lesions, weight loss, and reduced activity. The vaccinated animals were healthy overall, though minor skin lesions were seen in the group that received MVA alone and were then challenged.

According to the authors, MVA has potential use as a replacement for Dryvax, given that the immune responses elicited by one or two doses of MVA approach those of the licensed product. In addition, MVA could be useful as a pre-vaccine to Dryvax, reducing the local reaction to a subsequent smallpox vaccination without diminishing the total immune response. Further studies are planned to determine the longevity of protection, the dosage effects, and other factors. "This work is the result of a productive collaboration between federal and academic partners," said Colonel Erik A. Henchal, commander of USAMRIID. "These are the relationships that will, in the future, deliver the biodefense products the nation needs."

The research team included Bernard Moss, Patricia L. Earl, Jeffrey L. Americo, and Linda S. Wyatt of NIAID; Leigh Anne Eller of the Henry M. Jackson Foundation; J. Charles Whitbeck, Gary H. Cohen, and Roselyn J. Eisenberg of the University of Pennsylvania; and Christopher J. Hartmann, David L. Jackson, David A. Kulesh, Mark J. Martinez, David M. Miller, Eric M. Mucker, Joshua D. Shamblin, Susan H. Zwiers, John W. Huggins, and Peter B. Jahrling of USAMRIID. The work was funded by NIAID.

USAMRIID, located at Fort Detrick, Maryland, is the lead medical research laboratory for the U.S. Biological Defense Research Program, and plays a key role in national defense and in infectious disease research. The Institute's mission is to conduct basic and applied research on biological threats resulting in medical solutions (such as vaccines, drugs and diagnostics) to protect the warfighter. USAMRIID is a subordinate laboratory of the U.S. Army Medical Research and Materiel Command.

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