

Crucell adenovirus-based malaria vaccine candidate

THE PROJECT:
Exploring the effectiveness of a prime-boost approach

The PATH Malaria Vaccine Initiative (MVI) and the United States Agency for International Development (USAID) Malaria Vaccine Development Program (MVDP) are collaborating with the Dutch biopharmaceutical company Crucell N.V. to accelerate the development of a promising type of malaria vaccine. The partners will conduct studies to determine the effectiveness of Crucell's prime-boost vaccine approach on the malaria parasite *Plasmodium falciparum*. This approach uses adenoviruses (a type of virus associated with the common cold and other minor respiratory infections) to deliver a malaria antigen to the immune system. The vaccine is made by inserting the gene for the *P. falciparum* malaria parasite's circumsporozoite protein (CSP), the only antigen that has proven to be protective in studies, into adenoviral vectors, which act as a delivery vehicle for vaccination.

THE INNOVATION:
Using two vectors to boost immune response

The vaccine candidate uses two adenoviral serotypes—Ad35.CS and Ad26.CS—as vectors, or delivery mechanisms. Adenoviruses are recognized as being among the most potent vector systems tested to date in humans and this delivery method may elicit a more potent and comprehensive immune response to the CSP antigen.

The prime component of the vaccine, Ad35.CS, is being tested in a Phase 1 study in partnership with the National Institute of Allergy and Infectious Diseases. The partnership between MVI, Crucell, and MVDP will make it possible to clinically develop the Ad26.CS boost component of the vaccine.

Crucell's AdVac® technology supports the practice of inserting genetic material from the disease-causing virus or parasite into an adenoviral vector that has been altered so that it does not cause disease. The vector then delivers the immunogenic material directly to the immune system. However, if a person has been pre-exposed to the virus (this is common for certain adenovirus types) or previously immunized with an adenovirus-based vaccine, it may be very difficult to enhance the immune response with additional vaccine doses. This novel approach aims to circumvent that problem by immunizing first with one adenovirus (Ad35.CS) and then boosting with a different one (Ad26.CS). Since these particular adenoviruses do not regularly occur in the human population, pre-existing antibody responses should be low, which may help to ensure high immune responses against the malaria parasite.

**THE POTENTIAL:
Finding an effective
vaccine to save lives**

Malaria kills one child every 40 seconds and is a major health problem in much of the world, particularly in sub-Saharan Africa. A vaccine is viewed as a critical part of a long-term malaria-control strategy and another invaluable tool in the fight against the disease. Childhood immunization programs, which are among the most cost-effective health interventions, already save the lives of millions of children every year. A safe, effective, and affordable malaria vaccine would have the potential to save even more lives.

Supporting the development of Crucell's adenovirus-based approach is part of MVI's strategy to advance an array of vaccine approaches and candidates that have the potential to either halt the malaria parasite or greatly reduce the severity of infection.

The PATH Malaria Vaccine Initiative (MVI) is a global program established at PATH through an initial grant from the Bill & Melinda Gates Foundation. MVI's mission is to accelerate the development of malaria vaccines and ensure their availability and accessibility in the developing world. MVI's vision is a world free from malaria. For more information, please visit www.malariavaccine.org.

PATH is an international nonprofit organization that creates sustainable, culturally relevant solutions, enabling communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public- and private-sector partners, PATH helps provide appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being. For more information, please visit www.path.org.

Crucell N.V. is a global biopharmaceutical company focused on research, development, production, and marketing of vaccines, proteins, and antibodies that prevent and/or treat infectious diseases. Its vaccines are sold in public and private markets worldwide. Crucell's core portfolio includes a vaccine against hepatitis B, a vaccine against five important childhood diseases, and a virosome-based vaccine against influenza. Crucell also markets travel vaccines, such as the only oral anti-typhoid vaccine, an oral cholera vaccine, and the only aluminum-free hepatitis A vaccine on the market. The company has a broad development pipeline, with several product candidates based on its unique PER.C6 production technology. Crucell is headquartered in Leiden, the Netherlands, with subsidiaries in Switzerland, Spain, Italy, Sweden, Korea, and the United States. For more information, please visit www.crucell.com.

The USAID MVDP is a unit of the Division of Infectious Diseases of the Office of Health, Nutrition, and Infectious Diseases of the USAID Global Health Bureau. The MVDP, which was initiated in 1965 in response to the end of the first malaria eradication era, has worked with a variety of partners to contribute early research on the circumsporozoite protein and, more recently, development of blood-stage vaccine approaches leading to many of the investigational malaria vaccines fielded in recent years. Its mission is congruent with that of MVI: to develop and introduce malaria vaccines to protect vulnerable populations in the developing world. For more information, please visit www.usaid.gov.