

Development and Evaluation of an Adenovector-based Malaria Vaccine Candidate

Who: Local partners with global impact

Three Maryland-based institutions, GenVec, Inc., the U.S. Naval Medical Research Center (NMRC), and PATH's Malaria Vaccine Initiative (MVI) have partnered to develop and test an adenovirus-vectored malaria vaccine candidate. MVI will fund and provide oversight for this expansion of an existing GenVec–NMRC collaborative effort. GenVec, Inc., a biopharmaceutical company, owns rights to the adenovector technology being used. NMRC conducts applied research, development, testing, and evaluation of vaccines against infectious diseases including malaria.

What: Gene optimization and evaluation of a multi-stage malaria vaccine

The project will assess the usefulness and feasibility of including five optimized genes for *Plasmodium falciparum* malaria antigens in an adenovirus-vectored vaccine. Multi-stage vaccines are theoretically advantageous because they target the malaria parasites at different stages of their lifecycle, reducing their ability to cause clinical symptoms. The GenVec–NMRC vaccine will target the pre-erythrocytic (sporozoite and liver) and blood stages of the parasite life cycle. Vaccines directed at the pre-erythrocytic stage are designed to prevent infection, while blood stage vaccines should prevent or mitigate disease. GenVec's technology modifies the adenovirus—a common cold virus—so that it can't replicate or cause illness. It then uses the deactivated virus to deliver malaria genes that, once in the animal or human host, stimulate the production of antigens that in turn generate an immune response. GenVec adenovectors have been shown to be safe in several ongoing clinical trials.

The development program will determine the optimum gene constructs for producing three pre erythrocytic stage antigens (CSP, Ag2, and LSA1) that will induce strong T-cell responses in mice, and two blood stage antigens (MSP1 and AMA1) that will induce robust antibody responses in mice and rabbits. Antigens will be evaluated both independently and in various combinations to determine if a multi-stage approach is capable of generating effective immunity, and is as effective as a combination of single stage vaccines.

The results of this project will provide scientists with a better idea about the malaria antigen gene constructs needed to produce an effective adenovector-based malaria vaccine that can later be evaluated in clinical trials.

When: The activities described will be completed in January 2008.

Why: Adenovector technology may be part of the solution

Malaria kills more than one million people every year. Developing a malaria vaccine has proven to be a tremendous scientific and technical challenge. Scientists worldwide are working to

overcome this challenge by exploring promising technologies that could be used to develop malaria vaccines.

GenVec's adenovector technology has the potential to increase the efficacy of the vaccine. Information derived from a number of disease settings indicates that vaccines generated using adenovector technology induce strong and sustained cellular and antibody responses to the antigen. GenVec's proprietary adenovector technology is amenable to delivering multiple antigens in a single vaccine. Major obstacles

to clinical development and fielding of a multi-stage vaccine include the development and manufacturing costs, regulatory considerations, and commercialization risks associated with manufacturing each of the antigen components of such a vaccine. Vaccine constructs capable of holding multiple antigen inserts in a single vaccine backbone offer a practical solution to this problem. Many in the malaria vaccine field believe that a vaccine containing more than one malaria antigen will be necessary to adequately impact disease.

While no vaccine is currently licensed to protect against malaria, one is viewed as critical to subduing the epidemic. The CSP, Ag2, LSA1, MSP1, and AMA1 antigens, which are the target antigens of the GenVec–NMRC collaboration, are thought to have a role in protective immunity and could eventually become part of an effective and licensable malaria vaccine. CSP is also the malaria antigen included in GlaxoSmithKline's RTS,S/AS02A vaccine candidate that has demonstrated the ability to impact infection both in experimental challenge and in field trials.

How: Working Side by Side

GenVec and NMRC scientists have already engaged in a successful collaboration regarding malaria vaccines and have the expertise and the appropriate technology needed to assess whether the five well-characterized malaria proteins produce a strong immune response alone or in combination. With MVI's funding and project management support, the partnership will have the resources to evaluate an adenovectored, multi-stage malaria vaccine in animal models. This joint effort will contribute useful information to the body of knowledge about malaria vaccines, and will provide the foundation for subsequent clinical development of a multi-stage malaria vaccine.

Glossary:

Adenovirus: A DNA virus that can infect the respiratory tract. Adenovirus Type 5, the type used by GenVec, can cause a mild illness in children.

Adenovector: A modified Adenovirus, no longer able to replicate, used to deliver antigen or other gene product. The adenovector is a well-established gene delivery vector.

Antigen: For malaria, a protein from the malaria parasite that is capable of triggering an immune response.

Falciparum: The most lethal of four types of malaria in people.

Multi-stage: Containing more than one antigen.

Pre-erythrocytic: Before the parasite enters the red blood cells.

Vector: In vaccines, a bacterium or virus that does not cause disease in humans and is used to transport genes coded for antigens into the body to generate an immune response.

The PATH Malaria Vaccine Initiative (MVI) is a global program established at PATH through an initial grant of \$50 million 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 that enable 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.

The **Naval Medical Research Center (NMRC)** located in Silver Spring, Maryland, conducts research, development, tests and evaluations to enhance the health, safety and readiness of Navy and Marine Corps personnel in the effective performance of peacetime and contingency missions, as well as provide research and development support as required by the Department of Defense. NMRC's Malaria Program is developing vaccines to prevent malaria infection in military personnel and for the humanitarian mission of providing access to malaria vaccines for those who need it most. For more information, visit <http://www.nmrc.navy.mil>.

GenVec is a publicly held biopharmaceutical company developing novel therapies that improve patient care in the areas of cancer, heart disease, and vision loss. Through collaborations with the Vaccine Research Center of the National Institutes of Allergy and Infectious Diseases and the U.S. Naval Medical Research Center, GenVec is developing vaccines for HIV, SARS, malaria and dengue virus. Additional information on GenVec is available at www.genvec.com and in the company's various filings with the Securities and Exchange Commission.