Researchers modify yellow fever vaccine to fight malaria

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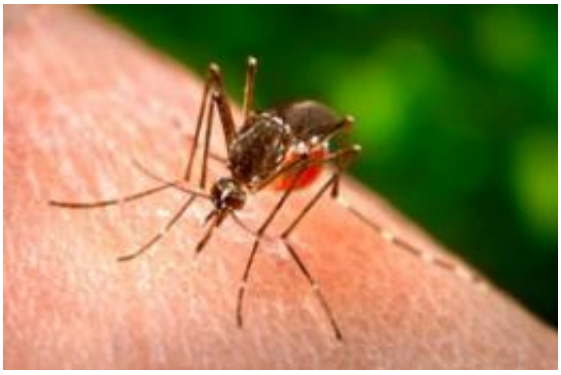

Bug off. By inserting a gene for the malaria parasite into a vaccine that originally targeted yellow fever, scientists have shown they can boost the immune system's response to infection in mice. The advance could lead to an effective way of fighting the mosquito-borne illness, among the most pressing health crises in the developing world. (Photo: James Gathany/CDC)

(PhysOrg.com) -- A genetically modified vaccine originally used to eradicate yellow fever could be the key to stopping a mosquito-borne scourge that afflicts much of the developing world.

There is no vaccine for malaria, which sickens almost a quarter of a billion people each year and kills a child every 30 seconds. That could be changing: researchers at The Rockefeller University have genetically transformed the yellow fever vaccine to prime the immune system to fend off the mosquito borne parasites that cause the disease. The

researchers found that the modified vaccine, along with a booster, provided mice with immunity to the deadly disease.

Malaria is one of the most pressing health crises of developing countries: in communities stricken by infection, attendance at work and school drops, and poverty deepens. It has been known since the 1960s that one form of the malaria parasite — called the sporozoite — can wake up the immune system and help to protect against future infection. The only way to gather sporozoites, however, is to pluck them one-by-one from the salivary glands of irradiated, malaria-ridden mosquitoes. To provide immunity, the attenuated parasites must then be injected in high doses — or delivered by the bites of hundreds of mosquitoes — a labor intensive approach not feasible for large-scale use.

“We needed to come up with another way to get the benefits of sporozoite immunization,” says Charles M. Rice, head of the Laboratory of Virology and Infectious Disease. Along with researchers from Michel C. Nussenzweig’s Laboratory of Molecular Immunology at Rockefeller and colleagues at New York University, Rice and his team considered that fighting infection with infection might be the key. They began experimenting with the attenuated yellow fever strain used in the yellow fever vaccine, known as YF17D, which has been used to successfully vaccinate more than 400 million people since 1937. Previous work in the Rice laboratory and by others had shown that this vaccine strain could be modified to include short sequences from other pathogens, including malaria.

In experiments published last month in Vaccine, the researchers inserted the nearly complete sequence of a malaria gene into the YF17D vaccine and found that the gene could produce its protein in cultured cells. The protein they chose, called CSP, covers the surface of the malaria sporozoite and is thought to be the main reason that this form of the parasite stimulates the immune system so effectively.

Immunization of mice with the YF17D-CSP vaccine led to a measurable jump in immune activity against the malaria protein, but the single shot was not enough to protect the animals from infection with the mouse form of the malaria parasite.

The group therefore added a booster shot to the vaccination regimen. Animals that had been immunized with YF17D-CSP, or with a saline solution control, were given a low dose of irradiated sporozoites. While the saline-sporozoite group was only partially protected from challenge with viable parasites, vaccination with YF17D-CSP plus the sporozoites protected 100 percent of the animals against infection.

“These results are exciting because they show the YF17D-CSP vaccine can prime the immune response against a malaria parasite,” says lead author Cristina Stoyanov. Although the utility of this approach for human immunization is not yet clear, the team hopes that further studies in other animal models might eventually lead to an effective vaccine.

More information: *Vaccine* online: May 6, 2010. Immunogenicity and protective efficacy of a recombinant yellow fever vaccine against the murine malarial parasite Plasmodium yoelii, Cristina T. Stoyanov, Silvia B. Boscardin, Stephanie Deroubaix, Giovanna Barba-Spaeth, David Franco, Ruth S. Nussenzweig, Michel Nussenzweig and Charles M. Rice. dx.doi.org/10.1016/j.vaccine.2010.04.071

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