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Weakened malaria parasites form basis of new vaccine strategy

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Using live but weakened malaria parasites as the basis of a vaccine represents a potentially encouraging anti-malaria strategy, according to results of follow-up animal studies performed after the conclusion of a recent clinical trial in humans. The research was conducted by scientists at the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, working in concert with a large team of collaborators. The findings were published online September 8 in Science Express.

The parasite that causes malaria, a disease that kills nearly one million people each year, is transmitted to humans via the bite of an infected mosquito. After the bite occurs, infectious malaria parasites in the immature, sporozoite stage of their life cycle travel to the liver, where they multiply and then spread to the rest of the body through the bloodstream.

Researchers led by Stephen L. Hoffman, M.D., of Sanaria Inc., in Rockville, Md., created a candidate malaria vaccine against Plasmodium falciparum, the most deadly of the malaria parasites, by purifying these sporozoites and then weakening them with radiation. In a clinical trial involving 80 healthy adult volunteers, the vaccine, called PfSPZ, was found to be safe and to induce a small immune response when given either intradermally (into the skin) or subcutaneously (under the skin). In a subgroup of 40 study volunteers who were given varying doses of the vaccine and then challenged with malaria, PfSPZ protected only two volunteers against infection. However, results of follow-up studies in

rhesus monkeys and in mice conducted by Robert A. Seder, M.D., of the VRC and his colleagues suggest that changing the method of vaccine delivery might improve protection by inducing specialized immune system cells, known as CD8+ T cells, in the liver, the first site of malaria infection. Specifically, the results of the animal studies indicate that delivering PfSPZ intravenously, or directly into the bloodstream, may induce a significantly stronger immune response in the liver than subcutaneous or intradermal administration and thus may have a much greater effect in actually preventing malaria.

NIAID investigators will be launching a human clinical trial with intravenous PfSPZ this fall. The trial will examine the candidate vaccine's safety and effectiveness and enable researchers to explore how it induces a CD8+ T cell response, so that future vaccine formulations can be optimized.

More information: JE Epstein et al. Live attenuated malaria vaccine designed to protect through hepatic CD8+ T cell immunity. *Science Express* DOI: 10.1126/science1211548 (2011).