

New genomic research shows why testing malaria vaccines in the clinic is as rigorous as natural exposure in the field

July 19 2022, by Heide Aungst



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Malaria is the deadliest mosquito-borne parasitic infection of humans. In 2021, after a century of research, the World Health Organization (WHO) approved the world's first malaria vaccine. That vaccine reduces

the incidence of malaria infections in young children aged 5-17 months by only 30 percent, meaning that it remains critical to continue developing and testing more effective vaccines.

WHO's goal is to find a vaccine that prevents infection as well as cases of severe [malaria](#). However, testing vaccines in the field is challenging and requires large number of volunteers and long periods of follow-up. This process increases the expense and reduces the number of trials that researchers can perform.

Now, scientists at the University of Maryland School of Medicine's (UMSOM) Institute for Genome Sciences (IGS) and the UMSOM Center for Vaccine Development and Global Health (CVD), and their collaborators report a new way to test vaccines that may be as rigorous and stringent as exposure to field strains of malaria. Their study was published in the June issue of *Nature Communications*,

Their method has two key aspects. First, they expose vaccinated volunteers to malaria in a controlled clinical environment. Secondly, for this testing, they use a strain of malaria that is genetically very different from the one used in the vaccine, as well as from strains in the geographic region to which the vaccine is intended.

This technique allows scientists to test how well the vaccine works in small numbers of volunteers under controlled settings and in a rapid fashion and predicts how well the vaccine may perform in the field. This lets researchers select the best vaccines for larger studies in the field. This method will increase the efficiency of vaccine testing and should accelerate malaria vaccine development.

"The standard for many investigators has been to test vaccines with a strain similar to the one used in the vaccine's development," explained the study's lead author, Joana Carneiro da Silva, Ph.D., Professor of

Microbiology and Immunology at UMSOM and IGS. "Using a strain that is both genetically distant from the one in the vaccine—as well as from the strains circulating in the area where malaria is rampant and the vaccine will be used— is a more stringent way to test vaccine effectiveness."

Researchers are studying the effectiveness of a vaccine (PfSPZ Vaccine) made by the company Sanaria, Inc, based in Rockville, Maryland. This vaccine uses the West African parasite strain known as PfNF54. One objective is to use this vaccine to protect individuals with little or no previous exposure to malaria, including those living or traveling in Africa. The long-term goal is to use the vaccine in mass vaccination programs to eliminate malaria from specific regions in Africa.

For the study, researchers infected mosquitoes with a Brazilian malarial strain and then exposed U.S. volunteers who had been vaccinated with the Sanaria vaccine (as well as those who received a placebo) to the bites of infected mosquitos in a controlled clinical setting. They also vaccinated research participants in Mali with the same dose of the vaccine to compare observed vaccine efficacy in the field with that in the clinic. Through [genomic sequencing](#), researchers had shown that the Brazilian strain differed greatly from 700 strains previously collected from across Africa, including the one used to make the vaccine.

The researchers looked at about 200 volunteers in four trials—two in the United States and two in Mali. In all four, they observed how many people became infected with malaria, as well as how long it took for them to become infected, comparing clinic to field. At the end of six months, they found the vaccine was just as effective in both populations.

In addition, previous comparisons had shown that those volunteers who had never been exposed to malaria developed more antibodies than those

in the field, proving that it would work well in first-time travelers to the area.

The research team included scientists from Sanaria Inc.; the Naval Medical Research Center; University of Tübingen in Germany; the Malaria Research and Training Center in Bamako, Mali; and the Laboratory of Malaria Immunology and Vaccinology at NIAID, NIH.

The World Health Organization estimates that in 2020, 241 million cases and 627,000 deaths worldwide were due to malaria, including 2,000 cases diagnosed in the United States from travelers and immigrants who were exposed elsewhere. The variety of malarial strains globally makes vaccine development particularly difficult.

"Given the diversity of malaria strains worldwide, this research demonstrates that the Brazilian strain is as diverse as any strain detected in Africa," said Kirsten E. Lyke, MD, Professor of Medicine and Director of the Malaria Vaccine and Challenge Unit at the CVD and an author of the paper.

Dr. da Silva noted this new model can be used in the future in selecting challenge strains to test the efficacy of vaccines against other parasitic diseases, using carefully controlled clinical settings to compare against field studies.

E. Albert Reece, MD, Ph.D., MBA, Executive Vice President for Medical Affairs, UM, Baltimore, the John Z. and Akiko K. Bowers Distinguished Professor, and Dean at the University of Maryland School of Medicine, says that "the world has waited decades for effective malaria vaccines. Dr. Silva and her colleagues have found a way to greatly expedite our ability to examine potential vaccine formulations in clinic to identify the most promising candidates. This study also shows how important genomics are to help establish the efficacy of new

vaccine formulations and to guide [vaccine](#) development."

More information: Joana C. Silva et al, Plasmodium falciparum 7G8 challenge provides conservative prediction of efficacy of PfNF54-based PfSPZ Vaccine in Africa, *Nature Communications* (2022). [DOI: 10.1038/s41467-022-30882-8](#)

Provided by University of Maryland School of Medicine

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