

An old plant virus inspires the design of a modern vaccine to fight against malaria

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This photomicrograph of a blood smear contains a macro- and microgametocyte of the Plasmodium falciparum parasite. Credit: Wikipedia.

Scientists from the Walter Reed Army Institute of Research have demonstrated that a novel, secondgeneration malaria vaccine candidate based on the tobacco mosaic virus may offer protection against Plasmodium falciparum malaria in the upcoming issue of the journal *Proceedings of the National Academy of Sciences*.

Malaria, infecting approximately 228 million individuals in 2018, remains a meaningful threat to public health and regional stability. Large human populations live in malaria-infested regions of Africa, Southeast Asia and South America, where mosquitoes continuously transmit the malaria parasites from sick to healthy individuals. Though infection rates have been decreasing, this decline has stagnated in recent years, necessitating novel interventions. While malaria has been eradicated from the United States, it remains one of the top five infectious disease threats to deployed Service Members.

The first generation malaria vaccine, RTS,SProvided(Mosquirix), developed through a collaborationProvidedbetween GlaxoSmithKline Vaccines and the WalterResearchReed Army Institute of Research, is based on theResearch

circumsporozoite protein of Plasmodium falciparum. While RTS,S has conferred high level protection in controlled human malaria infection trials, its potency and duration of protection against natural malaria infection needs to be improved.

In an attempt to develop a second-generation CSPbased malaria vaccine, Dr. Sheetij Dutta's laboratory at the WRAIR Malaria Biologics Branch, has used the nano-sized disk and rod shaped particles of the <u>tobacco mosaic virus</u>. TMV was one of the earliest known viruses that causes mottling of tobacco leaves; this research shows that the TMV coat protein can also be highly effective as a vaccine scaffold to refocus the host immune system to the most vulnerable epitopes on CSP. Since the TMV-based malaria vaccine was produced using recombinant DNA technology in <u>bacterial cells</u>, it is non-infectious to humans and will pose no risk to plants.

Dutta added, "The TMV-malaria vaccine showed a 10X improvement over a comparator vaccine in mice, and the superiority of this vaccine was confirmed in Rhesus monkeys. Serum antibodies from the vaccinated monkeys potently blocked parasite entry into human liver cells up to 11 months following vaccine administration. We are now exploring the utility of TMV particles for rational design of second generation vaccines against other infectious diseases."

More information: Mark D. Langowski et al, Optimization of a Plasmodium falciparum circumsporozoite protein repeat vaccine using the tobacco mosaic virus platform, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.1911792117

Provided by Walter Reed Army Institute of Research



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