Vaccine alternative protects mice against malaria

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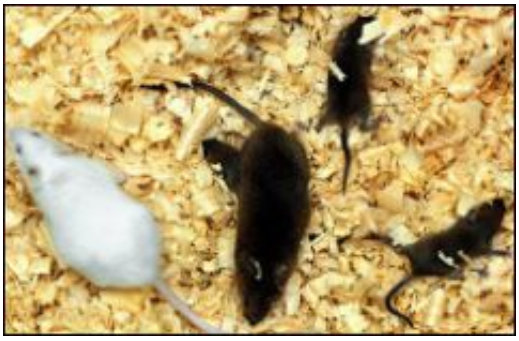

A study led by Johns Hopkins Bloomberg School of Public Health researchers found that injecting a vaccine-like compound into mice was effective in protecting them from malaria. The findings suggest a potential new path toward the elusive goal of malaria immunization.

Mice, injected with a virus genetically altered to help the rodents create an antibody designed to fight the malaria parasite, produced high levels of the anti-malaria antibody. The approach, known as Vector immunoprophylaxis, or VIP, has shown promise in HIV studies but has never been tested with malaria, for which no licensed vaccine exists.

A report on the research appears online Aug. 11 in the *Proceedings of the National Academy of Sciences* (*PNAS*).

Malaria is one of the world's deadliest infectious diseases, killing as many as 1 million people per year, the majority of them children in Africa. Malaria patients get the disease from infected mosquitoes. Of the four types of malaria that affect humans, the parasite Plasmodium falciparum is the most lethal, responsible for the majority of malaria cases. Antimalarial treatments and mosquito habitat modification have contributed to a decline in malaria mortality. But the number of cases remains high, and stemming them is a top global health priority.

In their study, researchers used a virus containing genes that were encoded to produce an antibody targeted to inhibit P. falciparum infection. Up to 70 percent of the mice injected with the VIP were protected from malaria-infected mosquito bites. In a subset of mice that produced higher levels of serum antibodies, the protection was 100 percent. The mice were tested a year after receiving a single injection of the virus and were shown to still produce high levels of the protective antibody.

"We need better ways to fight malaria and our research suggests this could be a promising approach," notes study leader Gary Ketner, PhD, a professor in the Department of Microbiology and Immunology at the Johns Hopkins Bloomberg School of Public Health.

There is a fine line between a vaccine and a VIP injection. One key difference: a VIP injection is formulated to produce a specific antibody. VIP technology bypasses the requirement of the host to make its own immune response against malaria, which is what occurs with a vaccine. Instead VIP provides the protective antibody gene, giving the host the tools to target the malaria parasite. "The body is actually producing a malaria-neutralizing antibody," says Ketner. "Instead of playing defense, the host is playing offense."

"Our idea was to find a way for each individual to create a long-lasting

response against malaria," says Cailin Deal, PhD, who helped lead the research while completing her doctorate at the School.

One advantage of this targeted approach over a traditional vaccine, the researchers note, is that the body might be able to continue to produce the antibody. With a vaccine, the natural immune response wanes over time, sometimes losing the ability to continue to resist infection, which would require follow-up booster shots. This can be challenging for people living in remote and or rural areas where malaria is prevalent but health care access limited. Any immunization protocol that involved one injection would be preferable.

"It's dose dependent," adds Deal. "Of course we don't know what the human dosage would be, but it's conceivable that the right dosage could completely protect against malaria."

"Vectored antibody gene delivery protects against Plasmodium falciparum sporozoite challenge in mice" was written by Cailin Deal, Alejandro B. Balazs, Diego A. Espinosa, Fidel Zavala, David Baltimore and Gary Ketner.

More information: Vectored antibody gene delivery protects against Plasmodium falciparum sporozoite challenge in mice, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1407362111

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