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Alternative pathway to malaria infection identified

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Discovery of a key red cell molecule used by the malaria parasite gives renewed hope for an effective vaccine in the future, according to an international team of researchers.

Plasmodium falciparum, a blood parasite that causes malaria by invading and multiplying in the red blood cells, kills 1 to 2 million people annually.

"How the parasite invades red blood cells is not completely understood," said Jose A. Stoute, M.D., senior investigator and team leader, Department of Medicine, Division of Infectious Diseases and Epidemiology, Penn State College of Medicine. "For many years it has been known that proteins called glycophorins are used by the parasite to gain entry into the red cell."

Because infection can take place without glycophorins, researchers suspected that another protein is also involved. The identity of this protein remained a mystery for 20 years and it was named the "X" receptor. A team of researchers now reports in today's (June 17) issue of *PLoS Pathogens*, the identity of this protein as the complement receptor 1 (CR1), also known to help protect red cells from attack by the immune system. CR1 has been suspected of having other roles in the development of malaria complications. The team was able to demonstrate that this protein is important in the invasion of red cells by using several laboratory strains of malaria as well as strains obtained from Kenya.

"Our findings suggest that for many malaria strains, CR1 is an alternative receptor to glycophorins on intact red cells," Stoute said.

According to the researchers, the reasons malaria may use the CR1 protein instead of glycophorins are if the parasite encounters a variant that lacks the glycophorin receptor; if the immune system mounts a response against parasite proteins involved in the dominant pathway due to a previous infection; or if the host were to be vaccinated with a vaccine that blocks the glycophorin pathway.

"This work has important implications for the future development of a vaccine against malaria," Stoute said. "Therefore, it is imperative that all the major invasion pathways be represented in a future malaria blood stage vaccine."

Vaccines that target parasite proteins involved in the dominant glycophorin pathway, but do not block the CR1 pathway, may cause proliferation of parasites that rely on the CR1 pathway for infection.

"The demonstration that CR1 is a receptor of *P. falciparum* will facilitate the identification of additional parasite proteins that allow it to bind to the blood cell, and the future development of a vaccine that effectively blocks red cell invasion," said Carmenza Spadafora, lead author and scientist at the Institute for Advanced Science and High Technology Studies, Republic of Panama.

Provided by Pennsylvania State University