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Discovery may aid vaccine design for common form of malaria

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A form of malaria common in India, Southeast Asia and South America attacks human red blood cells by clamping down on the cells with a pair of proteins, new research at Washington University School of Medicine in St. Louis has revealed.

The study provides details that will help scientists design better vaccines and drug treatments for the strain, *Plasmodium vivax*.

"More people live at risk of infection by this strain of malaria than any other," said senior author Niraj Tolia, PhD, assistant professor of molecular microbiology and of biochemistry and molecular biophysics. "We now are using what we have learned to create vaccines tailored to stop the infectious process by preventing the parasite from attaching to red blood cells."

The finding appears Jan. 9 in *PLOS Pathogens*.

The World Health Organization estimates there were more than 200 million malaria cases in 2012. The deadliest form of malaria, Plasmodium falciparum, is most prevalent in Africa. But *P. vivax* can hide in the liver, re-emerging years later to trigger new infections, and is harder to prevent, diagnose and treat.

Earlier studies had suggested that one *P. vivax* protein binds to one protein on the surface of red blood cells. Tolia's new study reveals that the binding is a two-step process that involves two copies of a parasite

protein coming together like tongs around two copies of a host protein.

"It's a very intricate and chemically strong interaction that was not easily understood before," Tolia said. "We have had hints that other forms of malaria, including the African strain, may be binding in a similar fashion to host cells, but this is one of the first definitive proofs of this kind of attack."

Tolia suspects blocking any of the proteins with drugs or vaccines will stop the infectious process.

"For example, some people have a mutation that eliminates the protein on red blood cell surfaces that *P. vivax* binds to, and they tend to be resistant to the parasite," he said. "This is why this strain isn't prevalent in Africa—evolutionary pressure has caused most of the populations there to stop making this protein."

Tolia also found evidence that other people with immunity to *P. vivax* have developed naturally occurring antibodies that attach to a key part of the parasite's binding protein, preventing infection.

"The parasite protein is very large, and human antibodies bind to it at many different points along its length," Tolia explained. "We have observed that the ones that are most effective so far are the antibodies that bind to the protein at the region highlighted by our new research."

More information: Batchelor JD, Malpede BM, Omattage NS, DeKoster GT, Heinzler-Wildman KA, Tolia NH. Red blood cell invasion by Plasmodium vivax: structural basis for DBP engagement of DARC. *PLOS Pathogens*, online Jan. 9, 2014.