Malaria parasite's essential doorway into red blood cells illuminated

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Credit: CDC

Researchers at Harvard T. H. Chan School of Public Health and the Broad Institute have identified a protein on the surface of human red blood cells that serves as an essential entry point for invasion by the malaria parasite. The presence of this protein, called CD55, was found to be critical to the *Plasmodium falciparum* parasite's ability to attach itself to the red blood cell surface during invasion. This discovery opens up a

promising new avenue for the development of therapies to treat and prevent malaria.

"*Plasmodium falciparum* malaria parasites have evolved several key-like molecules to enter into human red blood cells through different door-like host receptors. Hence, if one red blood cell door is blocked, the parasite finds another way to enter," said senior author Manoj Duraisingh, John LaPorte Given Professor of Immunology and Infectious Diseases at Harvard Chan. "We have now identified an essential host factor which when removed prevents all parasite strains from entering red blood cells."

The five-year study was carried out in collaboration with labs at Harvard Medical School and the Broad Institute. It appears online May 7, 2015 in *Science*.

Severe malaria is one of the leading causes of mortality among children globally. During infection, parasites invade and replicate within red blood cells. With resistance to malaria drugs increasing, researchers are desperate to find new ways to prevent and treat the disease.

Lead author Elizabeth Egan, research fellow in the Department of Immunology and Infectious Diseases at Harvard Chan and instructor in pediatrics at Boston Children's Hospital, and colleagues developed a new technique to tap into a relatively unexplored area—identifying characteristics of a host red blood cell that make it susceptible to the parasites. Red blood cells are difficult targets for such efforts as they lack a nucleus, which makes genetic manipulation impossible.

The researchers transformed stem cells into red blood cells, which allowed them to conduct a genetic screen for host determinants of *P. falciparum* infection. They found that malaria parasites failed to attach properly to the surface of red blood cells that lacked CD55. The protein

was required for invasion in all tested strains of the parasite, including those developed in a laboratory as well as those isolated from patients, making it a primary candidate for intervention.

"The discovery of CD55 as an essential host factor for *P. falciparum* raises the intriguing possibility of host-directed therapeutics for malaria, as is used in HIV," said Egan. "CD55 also gives us a hook with which to search for new parasite proteins important for invasion, which could serve as vaccine targets."

More information: A forward genetic screen identifies erythrocyte CD55 as essential for Plasmodium falciparum invasion, www.sciencemag.org/lookup/doi/ … 1126/science.aaa3526

Provided by Harvard School of Public Health

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