New target identified for inhibiting malaria parasite invasion

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Credit: CDC

A new study led by researchers at Harvard T.H. Chan School of Public Health finds that a malaria parasite protein called calcineurin is essential for parasite invasion into red blood cells. Human calcineurin is already a proven target for drugs treating other illnesses including adult rheumatoid arthritis and lupus, and the new findings suggest that parasite calcineurin should be a focus for the development of new antimalarial

drugs.

"Our study has great biological and medical significance, particularly in light of the huge disease burden of malaria," said senior author Manoj Duraisingh, John LaPorte Given Professor of Immunology and Infectious Diseases. "As drug resistance is a major problem for malaria control and eradication, it is critical that that we continue to develop new antimalarials that act against previously unexploited targets in the parasite to keep priming the drug pipeline."

The study appears online June 25, 2015 in *Cell Host & Microbe*.

The research team at Harvard Chan School used cutting edge genetic and cell biological methods to provide definitive evidence of the essentiality and function of calcineurin in parasite invasion. They found that the protein allows the malaria parasite to recognize and attach to the red blood cell surface. Parasites with inhibited calcineurin failed to invade and were not infective. Studies from a group at the University of Glasgow, which are published in the same issue of the journal, show the importance of calcineurin through different stages of the malaria life-cycle, implicating the protein as a potential target for blocking malaria transmission.

In addition to opening the door to potential new malaria treatments, these studies suggest that calcineurin could be targeted to treat other parasitic diseases. Researchers at Boston College working in collaboration with the Harvard Chan group showed that calcineurin is also important for cellular attachment by a related parasite that causes toxoplasmosis.

"Our study shows that the ability of malaria parasites to engage red blood cells is driven by an ancient mechanism for cellular attachment," said lead author Aditya Paul, a postdoctoral researcher at the Harvard Chan

School. "In addition to a possible drug target, calcineurin underlies a very basic aspect of parasite biology."

More information: "Parasite calcineurin regulates host cell recognition and attachment by apicomplexans," Aditya S. Paul, Sudeshna Saha, Rays H.Y. Jiang, Bradley I. Coleman, Aziz L. Kosber, Chun-Ti Chen, Markus Ganter, Nicole Espy, Marc-Jan Gubbels, and Manoj T. Duraisingh, *Cell Host & Microbe*, online June 25, 2015, DOI: 10.1016/j.chom.2015.06.003

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