Potential pathway for emergence of zoonotic malaria identified

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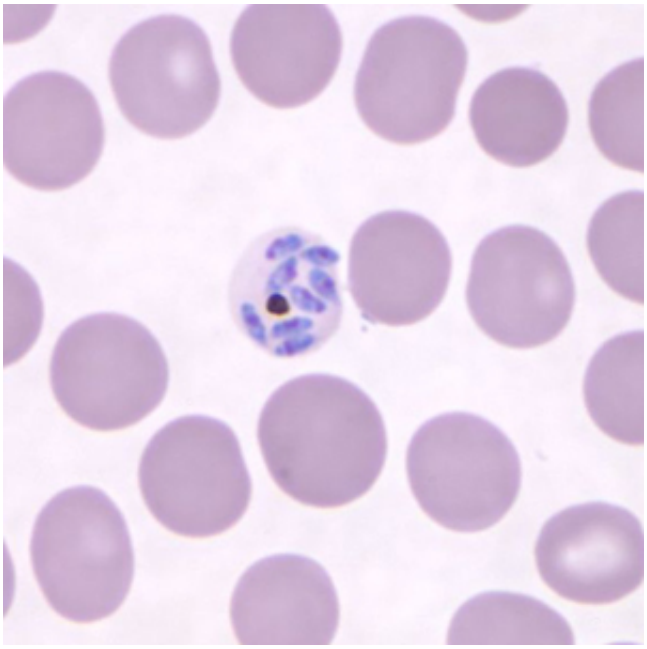

Plasmodium knowlesi sporozoites inside a Blood cells from a Blood smears. Credit: CDC

The parasite responsible for a form of malaria now spreading from macaques to humans in South Asia could evolve to infect humans more efficiently, a step towards enhanced transmission between humans, according to a new study from Harvard T.H. Chan School of Public Health. The researchers say that defining the means by which the Plasmodium knowlesi parasite invades red blood cells could lead to interventions to prevent the emergence of the zoonosis into the human

population.

The researchers identified a sugar variant on the surface of human red blood cells that currently limits the ability of P. knowlesi to invade, and demonstrated that the monkey malaria parasite has the ability to evolve to get around this barrier and pass into the human population in a more virulent form.

The study will appear online April 4, 2016 in *Nature Communications*.

"With increasing concern about the spread of P. knowlesi into human populations, it is great to be able to gain insight into what the molecular stumbling blocks are for P. knowlesi infection of humans, and how the parasite can potentially overcome them," said first author Selasi Dankwa, who carried out the work while a doctoral student in the Department of Immunology and Infectious Diseases at Harvard Chan School.

The macaque malaria parasite P. knowlesi has emerged as a major source of human infections in Southeast Asia, as the monkey's habitats are encroached upon through logging and farming. While most human infections are mild, increasing numbers of severe infections are being reported, leading to concerns that the parasite is adapting to infect humans more efficiently.

The researchers used a unique stem cell-based genetic approach for interrogating the host red blood cell to explore the parasite's ability to invade and adapt. They did an experiment that introduced the macaque sugar variant onto the human red blood cell surface and demonstrated that the parasite normally dependent on the macaque variant for invasion was unable to use the human version, limiting its virulence. However, worryingly, following prolonged adaptation to growth on human red blood cells, parasites were able to overcome their dependency on the

sugar pathway and find another way into the human cell.

The researchers call for continued monitoring of the parasite to ensure that it has not switched to using a sugar-independent pathway to invade red blood cells—a likely prerequisite for human-to-human transmission.

More information: "Ancient human sialic acid variant restricts an emerging zoonotic malaria parasite," Selasi Dankwa, Caeul Lim, Amy K. Bei, Rays H.Y. Jiang, James R. Abshire, Saurabh D. Patel, Jonathan M. Goldberg, Yovany Moreno, Maya Kono, Jacquin C. Niles, and Manoj T. Duraisingh, *Nature Communications*, online April 4, 2016, DOI: 10.1038/ncomms11187

Provided by Harvard T.H. Chan School of Public Health