Hijacker parasite blocked from infiltrating blood

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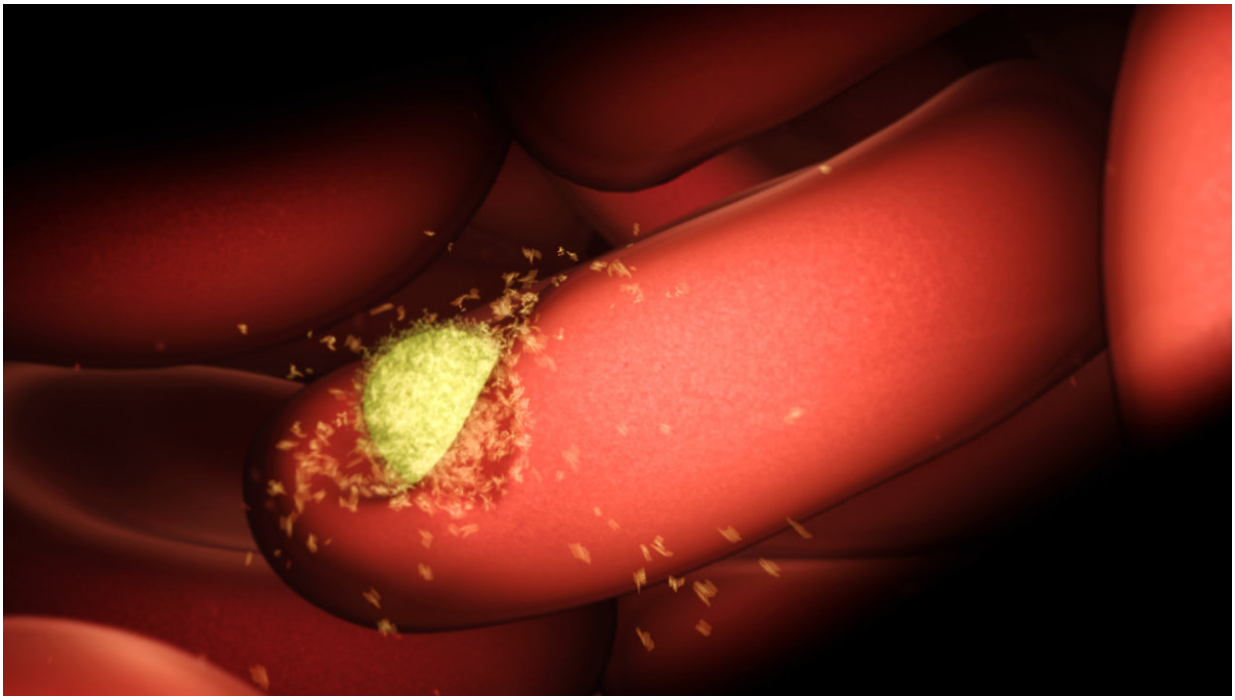


Still from WEHI.TV of malaria parasite infecting red blood cell. Credit: Dr Drew Berry, Walter and Eliza Hall Institute

A major international collaboration led by Melbourne researchers has discovered that the world's most widespread malaria parasite infects humans by hijacking a protein the body cannot live without. The researchers were then able to successfully develop antibodies that disabled the parasite from carrying out this activity.

The study, led by the Walter and Eliza Hall Institute's Associate Professor Wai-Hong Tham and Dr Jakub Gruszczyk, found that the deadly malaria parasite *Plasmodium vivax* (*P. vivax*) causes infection through latching onto the human transferrin receptor protein, which is crucial for iron delivery into the body's young red blood cells.

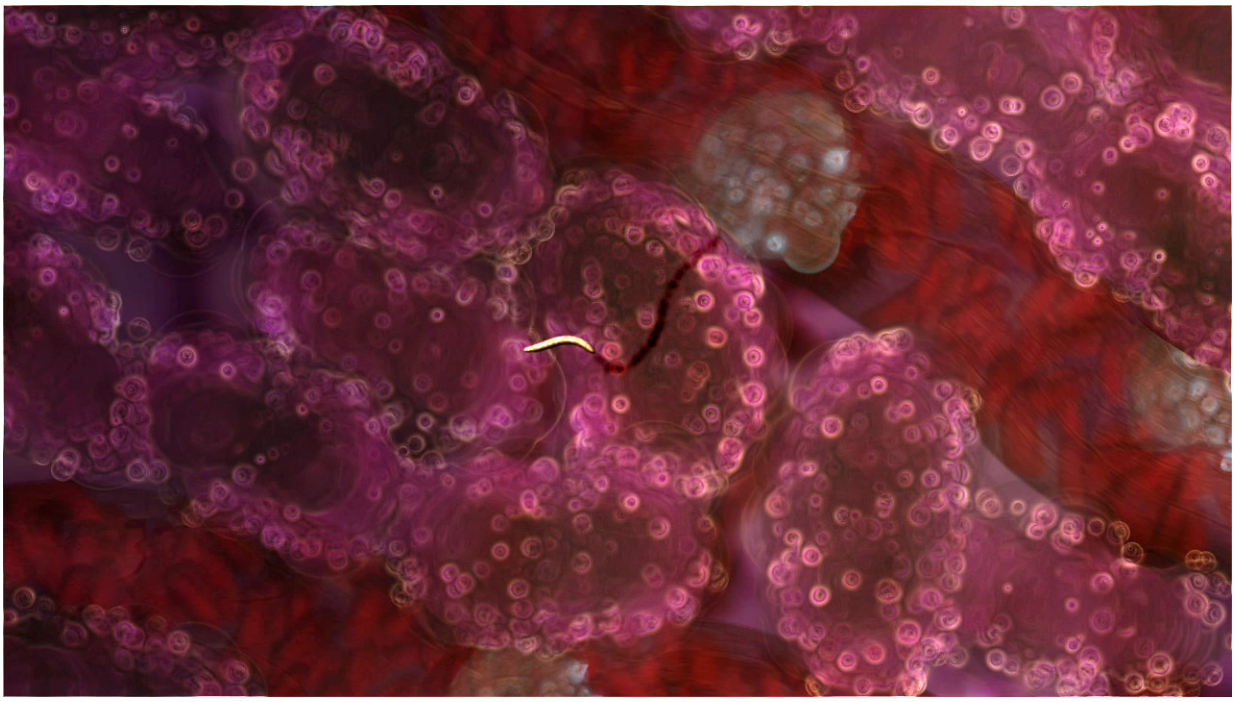
Published today in *Science*, the discovery has solved a mystery that researchers have been grappling with for decades.

Associate Professor Tham, who is also a HHMI-Wellcome International Research Scholar, said the collective efforts of teams from Australia, New Zealand, Singapore, Thailand, United Kingdom, United States, Brazil and Germany had brought the world closer to a potential effective vaccine against *P.vivax* malaria.

"*P. vivax* currently inflicts a huge burden on global health. It is the most common malaria parasite in countries outside of Africa, with more than 16 million clinical cases recorded each year.

"The parasite can lie dormant in the liver for months on end without causing any symptoms, which makes it very sneaky and difficult to treat," Associate Professor Tham said.

"We now know that *P. vivax* is hijacking the human transferrin receptor which is essential for transporting iron into the body's young red blood cells.



WEHI.TV still of malaria parasite (yellow-green) traveling in the bloodstream. Credit: Dr Drew Berry, Walter and Eliza Hall Institute

"Being able to stop *P. vivax* from latching onto this receptor and infliltrating the blood is a major breakthrough and important step towards malaria elimination," she said.

Dr Gruszczyk said once the teams understood how the parasite was gaining entry into the cells, they were able to design antibodies to block the mode of access.

"Using the Australian Synchrotron in Melbourne, we generated a 3D map of the parasite protein which is the mechanism *P. vivax* uses to latch onto the human transferrin receptor and enter the young red blood cells.

"This map provided an unprecedented view of the parasite protein's

shape, which guided the design of antibodies to block *P. vivax* from gaining entry into the human cells," Dr Gruszczyk said.

Associate Professor Tham said they were thrilled to see the antibodies successfully block *P. vivax* invasion using parasites from both Thailand and Brazil. "We are now looking to include collaborative partners in the Pacific, so we can further test the effectiveness of our antibodies," she said.

Study collaborator Dr Jonathan Abraham from Harvard University said the results of the new study aligned with a growing body of evidence that could be used to target multiple infectious diseases.

"Transferrin receptor is also co-opted by five viruses that cause Ebola-like diseases in South America. These diseases are known as New World haemorrhagic fevers.

"Our increasing understanding of how several pathogens are taking advantage of transferrin receptor, means we are getting closer to disrupting infection for a number of deadly diseases," Dr Abraham said.

More information: "Transferrin receptor 1 is a reticulocyte-specific receptor for Plasmodium vivax" *Science* (2018). science.sciencemag.org/cgi/doi … 1126/science.aan1078

Provided by Walter and Eliza Hall Institute