Malaria's newest pathway into human cells identified

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Professor Alan Cowman from the Walter and Eliza Hall Institute in Melbourne, Australia, has identified a new pathway used by the malaria parasite to infect human cells. Credit: Walter and Eliza Hall Institute

Development of an effective vaccine for malaria is a step closer following identification of a key pathway used by the malaria parasite to infect human cells. The discovery, by researchers at The Walter and Eliza Hall Institute in Melbourne, Australia, provides a new vaccine target through which infection with the deadly disease could be prevented.

Each year more than 400 million people contract malaria, and more than one million, mostly children, die from the disease. The most lethal form

of malaria is caused by the parasite Plasmodium falciparum. Part of the parasite's success lies in its ability to deploy multiple ways to invade red blood cells, a process essential for the survival of the parasite within the human host.

Professor Alan Cowman, head of the institute's Infection and Immunity division, led the research with Dr Wai-Hong Tham, Dr Danny Wilson, Mr Sash Lopaticki, Mr Jason Corbin, Dr Dave Richard, Dr James Beeson from the institute and collaborators at the University of Edinburgh.

For decades, it has been known that malaria parasites use proteins called glycophorins as a means of entering red blood cells. This new research reveals an alternative pathway used by the parasite to enter red blood cells. The pathway does not involve glycophorins, instead requiring the binding of a parasite molecule named PfRh4 to Complement Receptor 1 (CR1), a common protein found on the surface of red blood cells.

"The parasite is like a master burglar - it will try a variety of different methods to get into the house, not just the front door," Professor Cowman said. "Although the human body has evolved a variety of methods to keep the parasite out, it keeps finding new ways to get in."

Professor Cowman said the PfRh family of surface proteins is involved in the recognition of red blood cell receptors, which allows the parasite to attach to the red blood cell surface and gain entry.

"We think that the parasite uses this protein to correctly identify the red blood cell and say 'Yes, this is the one we want to invade', it's like a quality assurance process," Professor Cowman said.

"The PfRh4-CR1 pathway is one of the most important of the pathways we've identified for entry of malaria parasites into cells," Professor

Cowman said. "We are now at the stage where we have identified the best combination of proteins for a vaccine, and are ready to start clinical development.

"When both glycophorin and CR1 pathways are blocked, there is a 90 per cent decrease in infection of the cells with the parasite. These results suggest that if a vaccine were to stimulate the immune system to recognise and generate antibodies to the prevalent invasion pathways, there is a good chance it would lead to a significant decrease in malaria infection."

More information: The research was published this week in the journal *Proceedings of the National Academy of Sciences USA*.

Provided by Walter and Eliza Hall Institute