Researchers discover 'map' in malaria vaccine hunt

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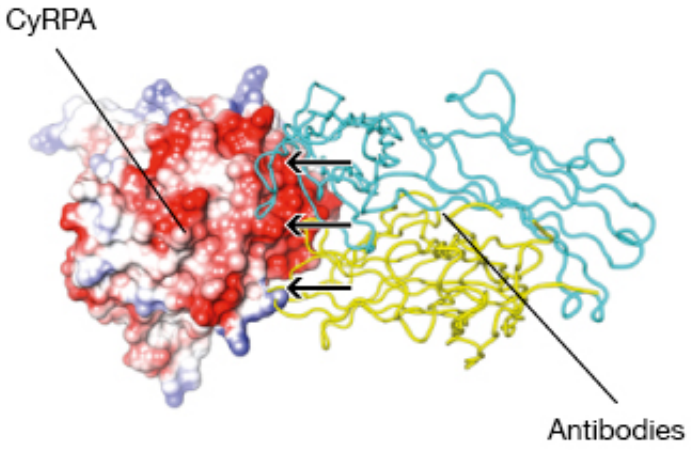

The parasite protein CyRPA blocked by antibodies. Credit: Walter and Eliza Hall Institute of Medical Research

A promising vaccine target for the most deadly type of malaria has had its molecular structure solved by Institute researchers, helping in the quest to develop new antimalarial therapies.

Using the Australian Synchrotron, the researchers mapped the parasite protein CyRPA in atomic detail for the first time, and established how antibodies that block the function of CyRPA disrupt the parasite's ability to bind to and infect human red blood cells.

The study, led by Professor Alan Cowman, Associate Professor Mike

Lawrence, Dr Yibin Xu and Dr Lin Chen, was published in the journal *eLife*.

Plasmodium falciparum is the most deadly strain of malaria parasite, and is predominantly found in Africa, where it causes up to half a million deaths each year. It is widely accepted that malaria vaccines will play a crucial role in eliminating malaria infections, and the eventual eradication of the parasites.

Professor Cowman said this was the first time the potential vaccine candidate CyRPA had been visualised at the atomic scale.

"CyRPA forms a complex with two other parasite proteins – PfRh5 and PfRipr – and together the complex is essential for the parasite to be able to burrow into red blood cells," Professor Cowman said.

Professor Cowman and his team have spent more than 30 years unravelling the complicated processes used by the malaria parasite to invade the human host.

"Plasmodium falciparum has co-existed with humans for millions of years, and developed an arsenal of weapons to aid it in infecting humans, as well as substantial evasion tactics," Professor Cowman said. "We are gathering intelligence to develop new and much-needed tools that will exploit these strategies to stop infection."

This study has shown at the atomic scale how key antibodies block the parasite from infecting the human red blood cell which was previously unknown.

"With these maps, we can see in clear detail that antibodies to CyRPA act as a shield, blocking critical interactions with the PfRh5 protein, and stopping the parasite in its tracks," Professor Cowman said.

"This binding is absolutely essential for parasite survival, marking CyRPA as a potential malaria vaccine candidate."

More information: Lin Chen et al. Structural basis for inhibition of erythrocyte invasion by antibodies toprotein CyRPA, *eLife* (2017). DOI: 10.7554/eLife.21347

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