MedicalXpress

What makes the deadliest form of malaria specific to people?

December 2 2013

Researchers have discovered why the parasite that causes the deadliest form of malaria only infects humans.

The team recently showed that the interaction between a parasite protein called RH5 and a receptor called basigin was essentially required for the invasion of red blood cells by the parasite that causes the deadliest form of malaria. Now, they've discovered that this same interaction is also an important factor in explaining why the parasite seems to be remarkably specific to humans. This research will help guide eradication strategies in regions where malaria is endemic.

There are several distinct species of parasite that cause malaria. The malaria parasite species responsible for severe illness and death, *Plasmodium falciparum*, only infects humans, but is closely related to several species that infect chimpanzees and gorillas. Strangely, these species seem to be very specific – individual species appear to infect only humans, chimpanzees or gorillas, even when these primates live in close proximity. This striking observation piqued the curiosity of the team which prompted a search for the molecules that controls this specificity and revealed the important role of the RH5-basigin interaction.

"It's remarkable that the interaction of a single pair of proteins can explain why the most deadly form of malaria is specific to humans" says Dr Julian Rayner, from the Wellcome Trust Sanger Institute Malaria Programme. "This research will strengthen eradication strategies by

ruling out great apes as possible reservoirs of human infection by *P. falciparum*."

The team investigated the question of host specificity by examining two important protein interactions involved in the invasion of red blood cells - the interactions between the parasite and host EBA175-Glycophorin A and RH5-basigin.

They found that the EBA175 protein from chimpanzee specific malaria parasites could bind to human Glycophorin A, thereby ruling out this interaction as a specificity factor.

However, the RH5 protein from *P. falciparum* did not bind to the gorilla basigin protein and only bound extremely weakly to chimpanzee basigin. Therefore, the species specificity of this interaction mirrored the known infection profile of *P. falciparum* and provided a molecular explanation for why *P. falciparum* only infects humans.

"This interaction seems to explain why *P. falciparum* only infects people and not apes," says Professor Beatrice Hahn, author from the University of Pennsylvania. "This may also be an important guiding factor in the development of eradication strategies for the elimination of *P. falciparum* in endemic areas."

Until recently, studying protein interactions between the malaria parasite and great apes has been challenging. Both chimpanzees and gorillas are protected species and so obtaining blood samples that would help answer these questions is incredibly difficult.

"Today, we can produce these proteins synthetically in the laboratory to avoid the use of blood samples from endangered animals," says Dr Gavin Wright, lead author from the Wellcome Trust Sanger Institute. "In time, these scientific advances will lead to improved treatments, eradication

strategies and, vaccine development for one of the world's major health problems."

More information: Madushi Wanaguru, Weimin Liu, Beatrice H. Hahn, Julian C. Rayner, and Gavin J. Wright. (2013) 'RH5–Basigin interaction plays a major role in the host tropism of Plasmodium falciparum' Advanced online publication in *PNAS*, Dec 2, 2013. www.pnas.org/cgi/doi/10.1073/pnas.1320771110

Provided by Wellcome Trust Sanger Institute