

How Adhesive Protein Causes Malaria

ScienceDaily (Sep. 27, 2007) — Researchers at the Swedish medical university Karolinska Institutet (KI) and the Swedish Institute for Infectious Disease Control (SMI) have identified the biochemical mechanism behind the adhesive protein that give rise to particularly serious malaria in children.

The knowledge of how the malaria parasite makes blood vessels become sticky paves the way for a future vaccine for the disease, which currently kills some 2 million people every year.

Severe anaemia, respiratory problems and cardiac dysfunction are common and life-threatening symptoms of serious malaria infection. The diseases are caused when the malaria bacteria *Plasmodium falciparum* infects the red blood cells, which then accumulate in large amounts, blocking the flow of blood in the capillaries of the brain and other organs.

The reason that the blood cells conglomerate and lodge in the blood vessels is that once in the blood cell the parasite produces proteins that project from the surface of the cell and bind with receptor molecules on other blood cells and on the vessel wall, and thus act like a glue. The challenge facing scientists has been to understand why certain proteins produce a stronger adhesive and thus cause more severe malaria.

The research group, which is headed by Professor Mats Wahlgren at the Department of Microbiology, Tumour and Cell Biology, KI, has studied the adhesive protein PfEMP1 in children with severe malaria. The group has identified specific parts of PfEMP1 that are likely to bond more strongly to the receptors in the blood vessels, therefore producing a stronger adhesive effect.

What the scientists show in their newly published study is that these protein parts are much more common in parasites that cause particularly severe malaria. If they can identify enough adhesive proteins causing severe malaria, it will be possible to design a vaccine that prepares the body's own immune defence.

"There are no vaccines yet that can prevent the development of malaria and cure a seriously infected person," says Professor Wahlgren. "We've now discovered a structure that can be used in a vaccine that might be able to help these people."

The study is a collaboration between Karolinska Institutet, the Swedish Institute for Infectious Disease Control, Makerere University and Medical Biotech Laboratories in Uganda, and has been financed by the Swedish International development cooperation Agency (Sida), the Swedish Research Council and the EU.

Reference: "PfEMP1-DBL1a amino acid motifs in severe disease states of *Plasmodium falciparum* malaria", Johan Normark, Daniel Nilsson, Ulf Ribacke, Gerhard Winter, Kirsten Moll, Craig E. Wheelock, Justus Bayarugaba, Fred Kironde, Thomas G. Egwang, Qijun Chen, Björn Andersson and Mats Wahlgren PNAS Online Early Edition, 24-28 September 2007

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