

Researchers characterize potential protein targets for malaria vaccine

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Researchers from Nijmegen and Leiden have now characterized a large number of parasite proteins that may prove useful in the development of a human malaria vaccine. Details are published October 31st in the open-access journal *PLoS Pathogens*.

Every day 2000 children die from malaria in Africa alone. The infection is transmitted from human to human by biting mosquitoes. Despite many years of effort, a vaccine is still not available to fight the deadly disease.

Once injected by a mosquito, parasites migrate to the liver where they mature and then their sporozoites (infective cells) are released into the blood, causing disease and fatal complications. A promising method for vaccination is to sufficiently weaken these parasites such that they invade liver cells and stimulate an immune response, but don't develop further. This can be achieved by genetically inactivating individual parasite genes that are active during the parasite's growth in the liver. The researchers achieved this by modifying the proteins essential for sporozoite development, which their study identified.

Collaborators had previously shown how to successfully vaccinate mice using a rodent malaria which had one of these liver stage genes removed, specifically p36p. In a related article, published October 28th in *PLoS ONE*, this collaborating group shows the first transition of such a vaccination from the rodent system to humans, by inactivating the equivalent gene (p52) in the major human malaria parasite, *P. falciparum*. Similar to the results with the rodent parasite, these human

parasites are unable to develop in liver cells.

This is the first time that genetic modification of a human parasite results in its growth arrest in a liver cell, opening up promising possibilities for its use as a human vaccine. These studies show how results obtained in rodent models of malaria can be pipelined to form the basis for clinical development of anti-malaria vaccines in humans.

Citation: Lasonder E, Janse CJ, van Gemert G-J, Mair GR, Vermunt AMW, et al. (2008) Proteomic Profiling of Plasmodium Sporozoite Maturation Identifies New Proteins Essential for Parasite Development and Infectivity. PLoS Pathog 4(10): e1000195.

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