Sugar identified as key to malaria parasite invasion

September 10 2007

Researchers at the Johns Hopkins Malaria Research Institute (JHMRI) have identified a sugar in mosquitoes that allows the malaria-causing parasite, Plasmodium falciparum, to attach itself to the mosquito's gut. Invasion of the midgut cell layer is an essential stage in the parasite's lifecycle and in the transmission of malaria from mosquitoes to humans.

By reducing the level of the sugar, chondroitin sulfate, in the mosquito, the researchers prevented 95 percent of the parasites in the mosquito from attaching to the gut, thus blocking its development. The study is published in the online Early Edition of *Proceedings of the National Academy of Sciences*.

"This study provides significant new insights on how the parasite develops in the mosquito, complementing our earlier identification of another parasite midgut receptor that is a target for a transmission-blocking vaccine," said Marcelo Jacobs-Lorena, PhD, senior author of the study and a professor in the Bloomberg School's W. Harry Feinstone Department of Molecular Microbiology and Immunology. "This line of research could lead to new approaches for interfering with the spread of this deadly disease."

To determine whether the parasite utilizes chondroitin glycosaminoglycans to invade the mosquito midgut cells, the researchers used a process known as RNA interference to inhibit production of a mosquito enzyme that is needed to produce chondroitin sulfate. With the sugar removed, parasite adhesion and midgut invasion were substantially

decreased.

“Our study highlights the importance of sugars in parasite invasion of the mosquito gut. Previously, this phenomenon was only observed during parasite invasion of human tissues,” said Rhoel R. Dinglasan, PhD, MPH, lead author of the study and a postdoctoral fellow with the Malaria Research Institute. “It appears as if the parasite’s use of sugars as a strategy for cell invasion of tissues is similar in both man and mosquito. This may be an Achilles’ heel for the parasite, opening up the possibility of developing a vaccine that works against all stages of the parasite’s lifecycle.”

According to the researchers, many important questions must still be answered to determine if the glycosaminolgycan identified could be a potential antigen for a transmission-blocking vaccine. In a study published earlier this year in the PNAS, the JHMRI team identified a previously unknown mosquito antigen that the parasite uses for entry into the mosquito midgut, a critical step in the Plasmodium parasite’s development. The researchers produced an antibody that acts as a blanket to prevent the parasite from accessing the mosquito midgut antigen.

Their research showed that the antibodies were effective against multiple malaria parasites and could potentially provide the basis for a future ‘universal’ malaria transmission-blocking vaccine.

Source: Johns Hopkins University