

Barrier in mosquito midgut protects invading pathogens

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Scientists studying the Anopheles gambiae mosquito - the main vector of malaria - have found that when the mosquito takes a blood meal, that act triggers two enzymes to form a network of crisscrossing proteins around the ingested blood. The formation of this protein barrier, the researchers found, is part of the normal digestive process that allows so-called "healthy" or commensal gut bacteria to grow without activating mosquito immune responses. But there is a downside: The barrier also prevents the mosquito's immune defense system from clearing any disease-causing agents that may have slipped into the blood meal, such as the Plasmodium malaria parasite, which in turn can be passed on to humans.

Disrupting the protein barrier, however, can trigger mosquito immune defenses to intervene and protect the insect from infection, notes the research team from the National Institute of Allergy and <u>Infectious</u> <u>Diseases</u> (NIAID), part of the National Institutes of Health. The enzymes involved in the protein barrier are called immunomodulatory peroxidase (IMPer) and dual oxidase (Duox). The researchers believe it might be possible to prevent the formation of the protein barrier by immunizing people with IMPer or the proteins that crisscross. This vaccine would generate antibodies that, after a mosquito feeds on a human, could disrupt the barrier, reduce parasite survival in the mosquito and prevent malaria transmission.

The role of IMPer-Duox in forming a protective barrier was unexpected - and previously unrecognized, according to Carolina Barillas-Mury, M.D., Ph.D., the senior study author. When her research group silenced,



or turned off, the gene for either IMPer or Duox, the mosquito's midgut immune system took over and greatly reduced Plasmodium infection, indicating that IMPer and Duox are both required for parasite survival.

The IMPer-Duox system also is found in the mucous membrane of some human tissues, such as the colon. Dr. Barillas-Mury's group is investigating whether a protective protein barrier similar to that seen in <u>mosquitoes</u> also forms in vertebrates, including humans. If so, the barrier could be part of the process that normally prevents the colon from activating immune responses against commensal bacteria, as this would be harmful and lead to chronic inflammation. The existence of such a barrier in humans could have broad implications for the prevention and treatment of diseases such as chronic inflammatory bowel disease.

More information: S Kumar et al. A peroxidase/dual oxidase system modulates midgut epithelial immunity in Anopheles gambiae. Science. DOI 10.1126/science.1184008 (2010).

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