Certain bacteria render mosquitoes resistant to deadly malaria parasite

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cientists have identified a class of naturally occurring bacteria that can strongly inhibit malaria-causing parasites in Anopheles mosquitoes, a finding that could have implications for efforts to control malaria. The study, led by George Dimopoulos, Ph.D., of the Bloomberg School of Public Health and the Malaria Research Institute, both of Johns Hopkins University, Baltimore, appears in the May 13 edition of *Science*. The research was partly funded by the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health.

According to the World Health Organization, an estimated 225 million malaria cases occur worldwide annually, resulting in about 781,000 deaths. Although the disease is present in 106 countries, most cases occur in sub-Saharan Africa. Insect repellent and bed nets can help prevent transmission of the malaria parasite from mosquitoes to humans, but to control malaria one step earlier, some studies are looking to eliminate infection within the mosquito itself.

Normally, when a malaria parasite infects a mosquito, it travels to the insect's gut, where its chances for survival are slim because the mosquito's immune system, digestive enzymes and resident bacteria create a hostile environment. In their new study, the scientists found that among the various types of bacteria in the mosquito gut, *Enterobacter*—a type of bacteria that occurs in some but not all mosquitoes—effectively blocked infection with the malaria-causing parasite *Plasmodium falciparum*.

"This discovery may explain why some mosquitoes are better than others at transmitting malaria to humans, even when they are of the same species," explained NIAID Director Anthony S. Fauci, M.D.

The Hopkins researchers found that in the presence of *Enterobacter*, various developmental stages of the *P. falciparum* parasite—including the stage that is transmitted to humans through a mosquito bite—were reduced by 98 to 99 percent.

"Our study used a laboratory method of *P. falciparum* infection, which causes stronger infections than those that take place in a natural environment," explained Dr. Dimopoulos. "We believe that in a natural situation, where infection levels are much lower, this bacterium would eliminate the parasite. Further, there is no evidence that *Enterobacter* is toxic to either mosquitoes or humans."

By observing the interaction between the bacteria and the parasite, the scientists determined that *Enterobacter* inhibits parasite growth by producing short-lived molecules known as reactive oxygen species (ROS). Although ROS travel through body fluids in the mosquito, they do not need to be in a mosquito to inhibit parasites.

Future research plans include sequencing the *Enterobacter* genome to better understand how it produces malaria-inhibiting ROS and studying other bacteria that reside in the mosquito gut to learn whether they have similar effects.

"If we can find a correlation between mosquitoes' malaria infection status and the presence or absence of a particular bacterium, it may suggest that the bacterium inhibits malaria parasites," said Dr. Dimopoulos. Identifying a variety of malaria-inhibiting bacteria would be especially useful since not all mosquitoes have *Enterobacter* in their guts.

The researchers hope to apply their findings to the field, where they would first modify *Enterobacter* for use in mosquitoes. The next step would be to strategically place the bacteria in the mosquitoes' natural environment, such as in their sugar food sources or breeding sites. Although these strategies have not yet been tested in malaria prevention, sugar baits have been used successfully to expose mosquitoes to toxins.

"This is a novel way of looking at how the mosquito and malaria parasite interact," said Adriana Costero-Saint Denis, Ph.D., program officer in NIAID's Vector Biology Program. "It adds another layer to the study of malaria."

Provided by National Institutes of Health

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