Hope for malaria may be inside African mosquitoes

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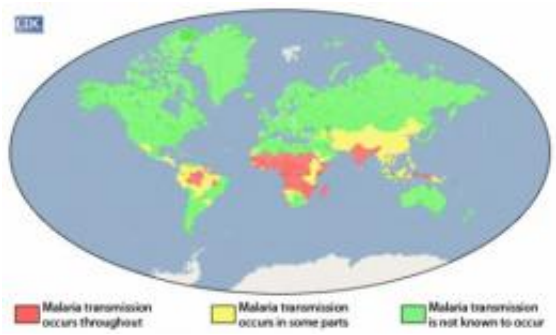

This CDC map shows an approximation of the parts of the world where malaria transmission occurs. Credit: CDC.gov

In the realm of human suffering, few diseases afflict more widespread misery than malaria, which strikes hundreds of millions of people every year and claims about a million lives -- mostly children living in sub-Saharan Africa.

No vaccines exist that can directly protect people from the disease -- which is caused by a parasite spread from person to person by mosquitoes -- but some scientists have speculated that there may be hope for protecting people indirectly by finding ways to prevent mosquitoes from becoming infected.

Now a team of scientists at the National Institutes of Health in Bethesda, Md., has demonstrated that this may be possible. In the journal *Science*

they report on experiments showing that mosquitoes infected with the malaria parasite once were able to resist it a second time.

While not exactly a silver bullet, this observation suggests the potential for controlling malaria by helping mosquitoes resist the parasite -- though the details of how to accomplish this still need to be worked out.

"It tells us that we can train mosquitoes to respond better to malaria and not allow the infection to spread," said biologist Carolina Barillas-Mury, who led the research.

A Tricky Pathogen

There is no effective human vaccine against malaria because the parasite plays a clever game of deception once inside the body. When a person is bitten, the pathogen slips into the bloodstream in the saliva of an infected mosquito. Inside, it invades the liver, setting up tiny little factories in liver cells and producing tens of thousands of new parasites over the coming days and weeks. These invade red blood cells, and the cycle begins anew when a mosquito bites and ingests some of these cells.

Malaria might not be such a problem if people were better able to resist the parasite. Like all mammals, people have a sophisticated immune defense system that monitors the blood and wipes out infections. But the malaria parasite is wildly successful at evading these defenses.

A person's spleen would typically destroy a pathogen-infected blood cell. However, the malaria parasite covers the cells it infects with molecular anchors so that the cells stick to the walls of the blood vessels, preventing entry into the spleen. The parasite also evades the body's hunter-killer immune cells by changing of appearance allows the malaria parasite to thoroughly and continually evade the immune system.

The parasite is so adept at this game of deception that people may have to be infected with malaria dozens of times before finally gaining some natural resistance to the disease. But according to Barillas-Mury, the same is not true for mosquitoes. Once infected with the parasite, they once will resist infection much better a second time.

To determine this, the researchers allowed two groups of mosquitoes to bite a mouse infected with malaria. One group became infected with the parasite and the other group did not. They found that the group infected the first time became more resistant to the parasites and could not be infected efficiently a few days later.

The resistance emerges out of the parasite's need to break through the lining of the mosquito's gut in order to survive. Only a few make it through, and those that do ruin the chances of later parasites making it out of the gut because they activate the mosquito's immune system, which prevents future infections.

That's why scientists believe that the mosquito would be a good target for intervention. If a way can be found to protect them against malaria, they may not subsequently pass it along to people.

One expert warned that much work remains to identify and test specific ways of accomplishing this. Marcelo Jacobs-Lorena, a malaria expert at the Johns Hopkins School of Public Health in Baltimore, Md., wondered if this approach will lead to new ways to prevent malaria.

"It's not quite clear at this point how this could be accomplished," said Jacobs-Lorena, who was not involved in the research. "It may [lead to new preventions], but not in the near future."

However cautious his reaction, Jacobs-Lorena was also excited about the work, calling it "a very important study." His enthusiasm was shared by

other experts this week, including Fotis Kafatos, an immunologist at Imperial College London who recognized the long-term potential for controlling malaria and other parasitic infections. Commenting via e-mail, Kafatos said he found the work extremely interesting.

"We need more such iconoclastic, path-breaking studies," Kafatos added.

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