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Studying the body's immune response to malaria infection could help scientists find life-saving vaccines

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Three malaria proteins that trigger an immune response in infected individuals have been identified by A*STAR researchers. These proteins could underpin a new vaccine against the world's deadliest parasitic disease.

Half a million people, mostly young children, are killed by malaria annually. Despite almost a century of research and development, no commercial vaccine exists for malaria.

Part of the problem is the complexity of the parasite, says Laurent Rénia, who led the study at the A*STAR Singapore Immunology Network. Compared with viruses, which have a maximum of 50 genes, the malaria parasite has 5,000 genes and 14 chromosomes. It also changes shape, reinventing itself as it moves from humans or monkeys to mosquitoes and back to the mammalian host. "Everything that works for viruses, doesn't work for malaria," says Rénia. "We need to think differently."

To start with, researchers need to be less haphazard in selecting potential vaccine targets. "Vaccine studies to date have been conducted like witchcraft, with no clear criteria for deciding why one protein candidate is better than another," says Rénia. "We are trying to put a bit of rationality into the process."

In 2009, Rénia and a team of researchers in the Netherlands discovered that individuals exposed to a few bites from infected mosquitos, while taking the antimalarial drug chloroquine, developed long-lasting immunity. Rénia wanted to determine the specific parasitic proteins that trigger this immune response. These antigens, he reasoned, could offer a legitimate target for potential vaccines.

He collaborated with an international team to engineer mammalian cells that express a range of malarial antigens on their surfaces. The team exposed the cells to blood samples taken from two groups of a total of 14 individuals: those who had been treated for long-lasting immunity, and those who had not. The immunized individuals produced antibodies that recognized three malaria antigens, which were generally absent in the non-immunized group.

The researchers then tested these antigens' potential as vaccine targets. They introduced one of the antigens to human liver cells growing in a dish, then exposed the cells to rabbit antibodies that recognize and block the protein's activity. The antibodies protected the liver cells against parasitic invasion.

During an infection, the malaria parasite first incubates and amplifies in the liver, before flooding the bloodstream and attacking red blood cells. Blocking the infection at this early stage could save lives.

Rénia now wants to replicate the experiment on a larger group to see if the same three proteins resurface as provokers of an immune response.

More information: Kaitian Peng et al. Breadth of humoral response and antigenic targets of sporozoite-inhibitory antibodies associated with sterile protection induced by controlled human malaria infection, *Cellular Microbiology* (2016). DOI: 10.1111/cmi.12608

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