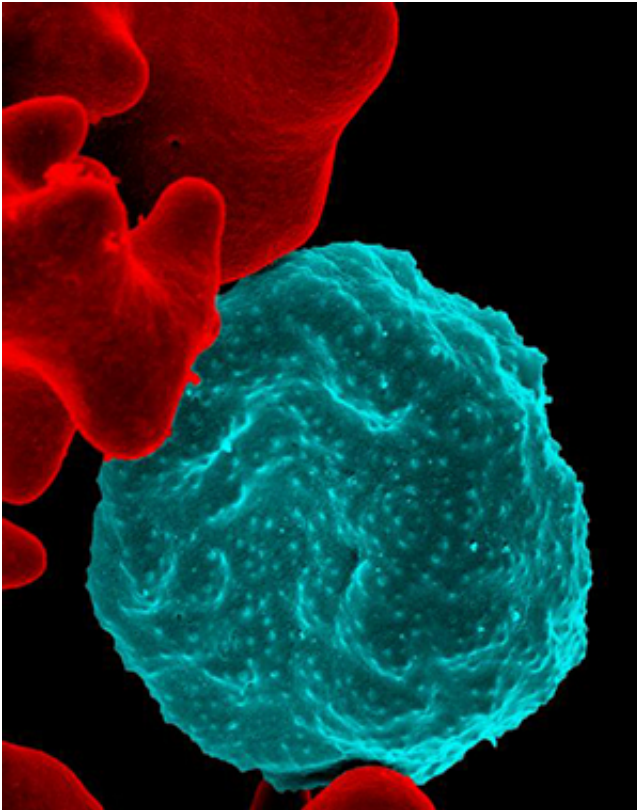


Scientists find way to trap, kill malaria parasite

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Scientists may have found a way to imprison the malaria parasite in its protective chamber inside red blood cells. In the electron micrograph, the malaria parasites appear in blue and uninfected red blood cells are shown in red. Credit: National Institute of Allergy and Infectious Diseases

Scientists may be able to entomb the malaria parasite in a prison of its own making, researchers at Washington University School of Medicine

in St. Louis report July 16 in *Nature*.

As it invades a red blood cell, the malaria parasite takes part of the host cell's membrane to build a protective compartment. To grow properly, steal nourishment and dump waste, the parasite then starts a series of major renovations that transform the red blood cell into a suitable home.

But the new research reveals the proteins that make these renovations must pass through a single pore in the parasite's compartment to get into the red blood cell. When the scientists disrupted passage through that pore in [cell cultures](#), the parasite stopped growing and died.

"The malaria parasite secretes hundreds of diverse proteins to seize control of [red blood cells](#)," said first author Josh R. Beck, PhD, a postdoctoral research scholar. "We've been searching for a single step that all those various proteins have to take to be secreted, and this looks like just such a bottleneck."

A separate study by researchers at the Burnet Institute and Deakin University in Australia, published in the same issue of *Nature*, also highlights the importance of the pore to the parasite's survival. Researchers believe blocking the pore leaves the parasite fatally imprisoned, unable to steal resources from the red blood cell or dispose of its wastes.

The [malaria parasite](#), *Plasmodium falciparum*, is among the world's deadliest pathogens. Malaria is spread mainly by the bite of infected mosquitoes and is most common in Africa. In 2012, an estimated 207 million cases of malaria occurred worldwide, leading to 627,000 deaths, according to the World Health Organization. Resistance to drug treatments is spreading among the parasite's many strains, and researchers are working hard to find new drug targets.

Senior author Daniel Goldberg, MD, PhD, professor of medicine and of molecular microbiology and a Howard Hughes Medical Institute investigator at Washington University, studies how malaria affects red blood cells.

In the new study, he and his colleagues looked at heat shock protein 101 (HSP101). Scientists named this family of proteins "heat shock" because they become active when cells are overheated or stressed. The proteins have multiple functions, including guiding the folding and unfolding of other proteins.

Previous studies have suggested that HSP101 might be involved in protein secretion. The researchers disabled HSP101 in cell cultures, expecting to block the discharge of some malarial proteins. To their surprise, they stopped all of them.

"We think this is a very promising target for drug development," Goldberg said. "We're a long way from getting a new drug, but in the short term we may look at screening a variety of compounds to see if they have the potential to block HSP101."

The scientists think HSP101 may ready malarial proteins for secretion through a pore that opens into the red blood cell. Part of this preparation may involve unfolding the proteins into a linear form that allows them to more easily pass through the narrow pore. HSP101 may also give the proteins a biochemical kick that pushes them through the pore.

Beck noted that researchers at the Burnet Institute neutralized the parasite in a similar fashion by disabling another [protein](#) thought to be involved in the passage of proteins through this pore.

"That suggests there are multiple components of the process that we may be able to target with drugs," he said. "In addition, many of the proteins

involved in secretion are unlike any human proteins, which means we may be able to disable them without adversely affecting important human proteins."

More information: Beck JR, Muralidharan V, Oksman A, Goldberg DE. PTEX component HSP101 mediates export of diverse malaria effectors into host erythrocytes, *Nature*, published online July 16, 2014. DOI: [10.1038/nature13574](https://doi.org/10.1038/nature13574)

Provided by Washington University School of Medicine

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