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# Protein helps parasite survive in host cells

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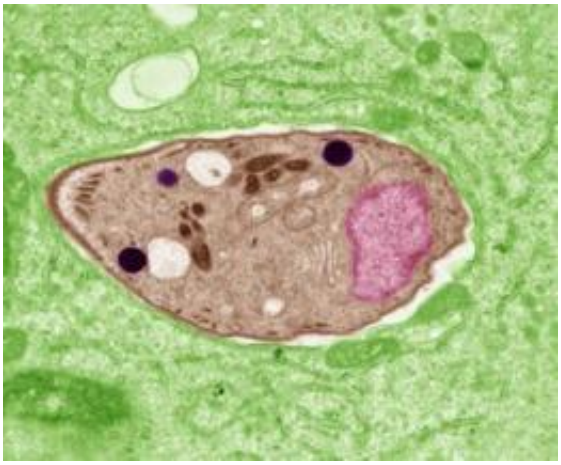

*Toxoplasma gondii* and other related parasites surround themselves with a membrane to protect against factors in host cells that would otherwise kill them. Scientists at Washington University School of Medicine in St. Louis have identified a parasite protein that protects this membrane from host proteins that can rupture it. Accoding to the researchers, disabling the parasite's defensive protein could help give hosts an advantage in the battle against infection. Credit: Wandy Beatty/Washington University School of Medicine in St. Louis

Researchers at Washington University School of Medicine in St. Louis have learned why changes in a single gene, ROP18, contribute substantially to dangerous forms of the parasite *Toxoplasma gondii*. The answer has likely moved science a step closer to new ways to beat *Toxoplasma* and many other parasites.

In a study published in *Cell Host & Microbe*, scientists show that the

ROP18 protein disables host cell proteins that would otherwise pop a protective bubble the parasite makes for itself. The parasite puts the bubble on like a spacesuit by forming a membrane around itself when it enters host cells. This protects it from the hostile environment inside the cell, which would otherwise kill it.

"If we can find therapies that block ROP18 and other parasite proteins like it, that could give the host the upper hand in the battle against infection," says first author Sarah Fentress, a graduate student in the laboratory of L. David Sibley, PhD, professor of molecular microbiology.

Infection with *Toxoplasma*, or toxoplasmosis, is most familiar to the general public from the recommendation that pregnant women avoid changing cat litter. Cats are commonly infected with the parasite, as are some livestock and wildlife.

"The exact role of ROP18 and related proteins in human disease remains to be studied," says Sibley. "But mice are natural hosts of *Toxoplasma*, so studies in laboratory mice are relevant to the spread of infection."

Epidemiologists estimate that as many as one in every four humans is infected with *Toxoplasma*. Infections typically cause serious disease only in patients with weakened immune systems. In some rare cases, though, infection in patients with healthy immune systems leads to serious eye or central nervous system disease, or congenital defects or death in the fetuses of pregnant women.

In the new study, Fentress showed that the ROP18 protein binds to a class of host proteins known as immunity-related GTPases. Tests in cell cultures and animal models showed that this binding leads to a reaction that disables the GTPases, which normally would rupture the parasite's protective membrane.

"With one exception, humans don't have the same family of immunity-related GTPases," Fentress notes. "But we do have a similar group of immune recognition proteins called guanylate-binding proteins, and we are currently testing to see if ROP18 deactivates these proteins in human cells in a similar manner."

The findings could be applicable to other parasites and pathogens. Toxoplasmosis belongs to a family of parasites that includes the parasite *Plasmodium*, which causes malaria. All surround themselves with protective membranes when they enter host cells.

"*Plasmodium* doesn't make ROP18, but it does secrete related proteins called FIKK," says Fentress. "It's possible they also act to thwart host defense mechanisms like GTPases and guanylate-binding proteins."

**More information:** Fentress SJ, Behnke MS, Dunay Ir, Mashayekhi M, Rommereim LM, Fox BA, Bzik DJ, Taylor GA, Turk BE, Lichti CF, Townsend RR, Qiu W, Hui R, Beatty WL, Sibley LD. Phosphorylation of immunity-related GTPases by a Toxoplasma gondii-secreted kinase promotes macrophage survival and virulence. *Cell Host & Microbe*, Dec. 22, 2010.

Provided by Washington University School of Medicine