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Statin, osteoporosis drug combo may help treat parasitic infections

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Researchers at the University of Georgia have discovered that a combination of two commonly prescribed drugs used to treat high cholesterol and osteoporosis may serve as the foundation of a new treatment for toxoplasmosis, a parasitic infection caused by the protozoan *Toxoplasma gondii*. They published their findings recently in *PLOS Pathogens*.

Toxoplasma gondii is a parasite capable of infecting nearly all warm-blooded animals. While healthy human adults usually suffer no lasting ill effects from infection, it can be harmful or fatal to unborn fetuses or those with weakened immune systems.

"For many years, therapies for toxoplasmosis have focused on drugs that target only the parasite," said Silvia Moreno, senior author of the article and professor of cellular biology in UGA's Franklin College of Arts and Sciences. "But in this paper, we show how we can hit the parasite with two drugs simultaneously, one that affects body chemistry in the host and one that affects the parasite."

The UGA researchers discovered that a combination of the cholesterol lowering drug atorvastatin and osteoporosis medication zoledronic acid, both more commonly known by their respective trade names, Lipitor and Zometa, produce changes in the mammalian host and in the parasite that ultimately block parasite replication and spread of the infection.

"These two drugs have a strong synergy," said Moreno, who is also a

member of UGA's Center for Tropical and Emerging Global Diseases. "The mice we treated were cured from a lethal infection using this combination approach."

Moreno and her colleagues began working on this drug combination following a series of experiments with unexpected results. They created a genetically modified version of the parasite in the laboratory that lacked a specific enzyme essential for one of the organism's most basic functions.

They thought such an experiment was an excellent opportunity to observe how the absence of this enzyme would kill the parasites. But every time they checked on the supposedly defective parasites, they were healthy and appeared completely unaffected.

"We kept asking ourselves, 'How did this happen? This enzyme should be essential to the parasite's survival,'" said Zhu-Hong Li, a UGA research scientist and lead author of the article. "It's almost like a human surviving without food or air."

What they discovered is that in order to survive, *Toxoplasma* has evolved an extraordinary ability to siphon essential compounds from its host when it is unable to make them on its own. This led them to the two-drug therapy.

Zoledronic acid prevents synthesis in the parasite and atorvastatin inhibits production in the host.

When *Toxoplasma* cannot produce these important molecules itself or steal them from its host, the parasites die.

"These drugs have been studied extensively, they are FDA-approved and safe for most people," Moreno said. "Plus, one might not have to take

the drugs for an extended period, just long enough to clear the infection ."

Moreno cautions that more research must be done before this becomes an accepted treatment for humans, but she hopes that a similar strategy might work for other serious parasitic diseases, such as malaria and cryptosporidiosis.

Early experiments with an anti-malarial drug already suggest that combining atorvastatin with fosmidomycin, an antibiotic effective against malaria parasites, creates a more potent antimalarial cocktail and it may lessen the risk of drug resistance.

Provided by University of Georgia