Research identifies first method for testing, assessing drug treatments for Chagas' disease

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Chagas' disease is a tropical parasitic sickness that currently affects more than 16 million people, with a staggering 100 million at risk, largely in the tropical areas of South and Central America. And yet the main drug used to treat the disease is highly toxic and causes serious side effects.

Now, new research just published by scientists at the University of Georgia has identified for the first time a sensitive method for testing and assessing the efficacy of treatments for Chagas' disease. The study could lead to new treatments for long-term sufferers of a disease that can be fatal.

"It is the first time we've been able to identify a set of measurements to determine whether or not a drug for Chagas actually works," said Rick Tarleton, distinguished research professor of cellular biology and a faculty member at UGA's Center for Tropical and Emerging Global Diseases.

The research was published today in the online edition of the journal *Nature Medicine*. Co-authors, also from the University of Georgia, are postdoctoral associate Juan Bustamante and master's degree student Lisa Bixby.

The research presents the first and only evidence that the current drug therapies for Chagas' disease can actually completely cure the infection. Still, current treatments have potentially severe side effects and are thought to be effective in less than 50 percent of those treated. More important, the model the team developed can be used for the development of better drugs against Trypanosoma cruzi, the parasite that causes the disease.

"We also found that the immunological markers of cure in this system, which we developed in mice, provide a means to monitor drug treatment efficacy in humans, something that has been the biggest impediment to developing new drugs," said Tarleton.

There's a fourth finding more important to the big picture of immunology, however. This study shows that chronic infections do not by default exhaust the immune system.

"Current dogma on chronic infections is that constant stimulation of the immune system eventually wears it out, which is one of the problems in treating such disorders as HIV/AIDS," said Tarleton. "This study shows that one can have an infection for more than a year, but, when cured, the immune system develops a stable, protective memory."

This idea of "memory" is at the heart of the study, and it involves T-cells, specifically one kind called cytotoxic or "killer" T-cells, which are blood-borne white blood cells that destroy T. cruzi-infected cells in the case of Chagas' disease and virally infected and tumor cells in other cases. Tarleton and his colleagues documented the development of stable killer T-cell "memory" following drug-induced cure of a chronic infection. In other words, when the body is cleared of parasites, the killer T-cells, which may have been "exhausted" by battling the persistent infection, bounce back and recall how to do their job.

The implications of the study could be considerable, Tarleton said. The T. cruzi parasite is passed to humans from the bite of blood-sucking assassin bugs, which go by many names, including "kissing bugs." The infection can also be acquired through contaminated blood transfusions and by eating food contaminated with parasites.

In its first stages, the disease often causes no more than a local swelling at the point of the bite. This

acute phase often passes, but the malady, if untreated, can then enter a chronic phase that can last for decades and cause heart disease and intestinal disorders. In many cases, Chagas', named for the Brazilian scientist who first described it nearly a century ago, is fatal.

While several hundred thousand people in the United States may have the disease, these are largely immigrants from Latin American countries. The disease, however, is a major public health issue in all of South America and kills as many as 50,000 people each year, according to some estimates, making it the most significant parasitic disease of the Americas, Tarleton said.

Source: University of Georgia