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Researchers add crucial information on how the body's T cells react to parasitic diseases

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In the 1980s, the phrase "T cell count" burst into the world's medical vocabulary as thousands and then millions of patients died of AIDS. The public began to understand the crucial importance of T cells--cellular Pac-Men that roam the bloodstream gobbling up infection and guarding against future attacks.

While scientists understood how T cells worked in certain kinds of diseases, one area has remained murky: disorders caused by protozoan parasites. Now, because of a study just published and led by scientists at the University of Georgia, researchers are closer than ever to understanding how T cells respond to parasitic diseases that kill millions each year.

"We have needed to really know what happens in these infections," said Rick Tarleton, research professor of cellular biology and a faculty member in UGA's Center for Tropical and Emerging Global Diseases (CTEGD). "What is the body's response? This study is the first to show that one parasite, Trypanosoma cruzi, which causes Chagas Disease, elicits a T cell response focused on a few peptides, despite having some 12,000 genes capable of generating hundreds of thousands of potential targets for T cells."

The study was just published in the online journal PLOS Pathogens, a peer-reviewed, open-access journal published by the Public Library of Science. Other authors of the paper include: Diana Martin, the lead author and postdoctoral fellow at UGA; former UGA undergraduates

Melissa Cabinian and Matthew Crim; computational biologist Brent Weatherly of the CTEGD; former UGA postdoctoral fellow Susan Sullivan; doctoral students Matt Collins, Charles Rosenberg and Sarah Craven; Alessandro Sette of the La Jolla Institute for Allergy and Immunology in San Diego, Ca.; and Susana Laucella and Miriam Postan of the Nacional de Laboratorios e Institutos de Salud in Buenos Aires, Argentina.

Chagas Disease is a tropical parasitic disease that sickens as many as 18 million people a year, mostly in the Americas, and kills 50,000 of those. The parasite that carries it, T. cruzi, is transmitted to mammals and humans through the bite of several genera of flying, biting insects. What intrigued Tarleton was that T cell response to infection from T. cruzi, while important to the body's ability to fight disease, has remained somewhat cryptic because of the daunting complexity of the processes.

There are actually several kinds of T cells, and the ones Tarleton and his colleagues studied are the cytotoxic T cell, which scientists call CD8+. What they discovered is that the T cell response in T. cruzi is highly focused on a relatively small set of cellular features called "epitopes," which are part of a macromolecule that is recognized by the immune system. The specific epitopes involved are ones encoded by the trans-sialidase (or "ts") family of genes.

"The function of the ts genes is crucial for the parasite," said Tarleton, "because the parasite must have sialic acids to invade cells and infect the host. But since it doesn't have it, it must steal it from the host cells." The problem is that T. cruzi potentially expresses more than a thousand ts genes, and this pool varies from parasite to parasite--making this set of proteins a poor choice for vaccine development, Tarleton said.

The importance of the new research, however, isn't in specifically what happens in T. cruzi and Chagas Disease. Rather, it is a new

understanding of how T cells react to infection in all parasitic diseases, including malaria, which may cause as many as 500 million infections and three million deaths annually in humans. The entire area has been little understood because of the almost impenetrable complexity of the problem.

In organisms like viruses and bacteria, which have relatively small genomes, analysis can be more direct; however, understanding the targets of the T cell response in complex pathogens such as T. cruzi requires much more. Scientists must integrate information generated from the recent analysis of the T. cruzi genome and proteome, with bioinformatics and cutting-edge techniques like advanced flow cytometry to unravel what is happening.

Source: University of Georgia