MedicalXpress

New drug candidates show promise for cure for Chagas disease

December 26 2013

A team of researchers from Canada has developed a class of compounds which may help eradicate a neglected tropical disease that is currently hard to kill in its chronic form. The research was published ahead of print in *Antimicrobial Agents and Chemotherapy*.

Chagas disease or American trypanosomiasis, caused by *Trypanosoma cruzi*, affects about 18 million people living mostly in Latin America. The parasite is transmitted to humans by blood-sucking reduviid bugs, also known as kissing bugs due to their predilection for feeding on the faces of their victims. In the United States, Chagas disease is considered one of the neglected parasitic infections, a group of five parasitic diseases that have been targeted by CDC for public health action.

"While historically infection was largely confined to poor and rural populations in Central and South America, it has been emerging in the U.S., Canada, Europe, Japan, and Australia, due to immigration, and nonvectorial transmission is becoming a public health threat," says Deborah Nicoll-Griffith of the Merck Frosst Centre for Therapeutic Research in Kirkland, Quebec, a researcher on the study. One 2005 estimate put the number of people infected within the U.S. at 300,000 (1/1000).

There are two phases of Chagas disease: the acute phase and the chronic phase. Both phases can be symptom free or life threatening. Left untreated the disease can lead to cardiac and digestive disorders, as the parasite burrows into the heart, esophagus and colon tissue where it

causes damage over time.

The current standard of care, the drug benznidazole, has significant activity against the parasite during the acute phase, but is less effective once the disease becomes chronic.

Efforts to find new drugs focus on disrupting an enzyme, cruzipain, which the parasite uses for digestion, to produce other cellular machinery, to evade the host's immune system, and to invade heart and gastrointestinal tissues.

Nicoll-Griffith and her colleagues identified two compounds known as reversible cysteine protease inhibitors that fit cruzipain like jigsaw puzzle pieces, jamming the enzyme. In the study, they tested the efficacy of the compounds in mice against that of benznidazole. While all treatment groups showed a marked reduction in parasite burden, in all tissues, the two experimental compounds had greater cure rates of acute infections (90% and 78%) compared to benznidazole (71%.)

"The efficacy shown in these *T. cruzi* murine studies suggests that nitrile-containing cruzipain inhibitors show promise as a viable approach for a safe and effective treatment of Chagas disease," write the researchers.

More information: www.asm.org/images/Communicati … /2013/1213chagas.pdf

Provided by American Society for Microbiology