

MS06-1-1 Cysteine synthase: a key enzyme in the cysteine synthesis pathway and a novel drug target for chagas disease

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Abstract

Trypanosoma cruzi, the causative agent of Chagas' disease, affects 8 million people worldwide, largely in Latin America. In the last century, this disease has begun to spread with more than 25 million people at risk of infection. Chagas' disease often has no symptoms or non-specific effects leading to the disease developing into a chronic and life-threatening infection.

Cysteine is an essential amino acid for the survival of *T. cruzi* as it allows the parasite to survive oxidative bursts imposed by the human immune system. Cysteine synthase is one of two of proteins responsible for cysteine synthesis within the *de novo* synthesis pathway of the parasite. Cysteine synthase facilitates the β -elimination of the acetate group of O-acetyl serine (produced by serine acetyltransferase) to produce cysteine. This pathway is not found in human cells and is essential to the parasite so represent a potential drug target against Chagas' disease.

Determination of the structure of cysteine synthase is critical to understanding of protein functionality and of this pathway in the parasite. Here I will present the structure of cysteine synthase from *T. cruzi*, as well as from related trypanosomatids *L. infantum* and *T. theileri*. I will also show the initial results of a fragment-based screen that will be used to produce novel inhibitors of this enzyme.