Poster Presentation

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Crystal Structure of the Trypanosoma cruzi Protein Tyrosine Phosphatase TcPTP1

G. Lountos[1,2], J. Tropea[2], D. Waugh[2]

[1]Basic Science Program, Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research, Frederick, MD, USA, [2]Macromolecular Crystallography Laboratory, National Cancer Institute, Frederick, MD, USA

Chagas' disease is a neglected tropical disease transmitted by the flagellated protozoan, Trypanosoma cruzi, which affects millions of people particularly in Latin America. Only two approved drugs are available to treat the disease but they can present several side effects and are not very effective during the chronic stage of the disease. Therefore, given the large population that is at risk, there is a need to discover new molecular targets for drug design efforts. Recently, the T. cruzi protein tyrosine phosphatase, TcPTP1, was shown to play a role in the cellular differentiation and infectivity of the parasite, and therefore, raises its profile as a potential new therapeutic target. Although drug development targeting protein tyrosine phosphatases is challenging and not as advanced as in other targets such as kinases, structure-based drug design methods have shown to be vital in aiding the discovery of novel phosphatase inhibitors with high potency and improved specificity. Here, we present the 2.1 Angstroms resolution X-ray crystal structure of the T. cruzi TcPTP1 that provides structural insights into the active site environment that may be exploited in order to initiate structure-based drug design efforts to develop novel TcPTP1 inhibitors. Potential strategies to develop such inhibitors are also presented that may make it feasible to develop compounds that are specific for TcPTP1.

Keywords: phosphatase, drug target