Hunter College of the City University of New York
Department of Biological Sciences
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Chasing the ICP: The endogenous inhibitor of the *Trypanosoma brucei* Cathepsin L

Trypanosomiasis is a group of diseases caused by flagellated protozoa belonging to the genus Trypanosoma, affecting humans as well as domestic and wildlife animals worldwide. However, humans and non-human primates can eliminate many of these species of trypanosomes once infection occurs due to the trypanolytic factor, TLF, a high-density lipoprotein comprising several molecules, including the lipoprotein ApoL1. ApoL1 produces pH-dependent channels in trypanosome membranes, generating an osmotic imbalance in the parasite and subsequent lysis of the parasite. Nonetheless, the intracellular mechanisms that regulate ApoL1 activity in the parasite are unclear. It has been proposed that the lysosomal enzyme Cathepsin L and its endogenous inhibitor, TbICP (*Trypanosoma brucei* Inhibitor of Cysteine Peptidase), two essential proteins for *Trypanosoma brucei* survival, could modulate the trypanolytic activity of ApoL1 within the trypanosome. We hypothesize that TbICP, rather than an inhibitor per se of the *Trypanosoma brucei* Cathepsin L, could act as a regulator or chaperone of cathepsin during its transit from the Golgi to the lysosome. To study the hypothesis, we cloned and produced both Cathepsin L and ICP from *Trypanosoma brucei* using a mammalian expression system. Our in vitro analyses showed that the enzymatic activity of cathepsin is inhibited in vitro by ICP, which could be the first evidence in vitro of the interaction between these two proteins. Cathepsin L hydrolyzed ApoL1 within the TLF as well as when it binds to lipid bilayers, supporting the hypothesis that Cathepsin L could downregulate the ApoL1 activity inside the lysosome. Finally, preliminary immunofluorescence localization analysis of TbICP using tagging inducible CRISPr-Cas9 system suggests that the possible interaction between ICP and Cathepsin L would not be in the lysosome, but more analysis must be done.

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Host: Jayne Raper