Effects of TcFLA-1BP and TcGP72 Deletion on the Infectivity and Survival of *Trypanosoma cruzi* in cell cultures

Normanda Souza-Melo[1], Giovanna Henriques de Souza[1], Wanderley de Souza[1]
1 Laboratório de Ultraestrutura Celular Hertha Meyer, Instituto de Biofísica Carlos Chagas - UFRJ – Brazil

Chagas disease, caused by the protozoan parasite Trypanosoma cruzi (Tc), is a neglected tropical disease with limited treatment options and no available vaccine. The parasite undergoes a complex life cycle with distinct morphological stages. Tc cell organization is supported by the cytoskeleton, where the flagellar attachment zone (FAZ) plays a central role in flagellum adhesion to the cell body, which is essential for parasite motility and host cell invasion. Despite the structural characterization of the FAZ in T. cruzi, its protein composition and dynamics throughout the biological cycle remain poorly understood. In this study, we characterized the role of the FAZ during T. cruzi infection in mammalian host cells using knockout parasites for FAZ-associated proteins (TcFLA-1BP$^{-/-}$ and TcGP72$^{-/-}$), generated via CRISPR/Cas9 editing. We observed that the absence of TcFLA-1BP led to heterogeneity in flagellar adhesion, with parasites displaying attached, partially detached, or completely detached flagella. In contrast, TcGP72$^{-/-}$ parasites exhibited a more homogeneous phenotype, with the flagellum consistently detached. Our findings demonstrate that TcFLA-1BP is crucial for efficient host cell infection in vitro, highlighting its essential role in parasite infectivity. Conversely, TcGP72 is nonessential for the infection process but significantly contributes to cytoskeletal remodeling during the parasite's life cycle. These results provide new insights into the distinct functional roles of FAZ proteins in T. cruzi. Furthermore, this study underscores the importance of TcGP72 in maintaining cellular architecture, reinforcing the relevance of FAZ proteins in parasite pathogenesis and structural integrity.

Supported by: FAPERJ and FINEP

Keywords: *T. cruzi,* flagellar attachment zone, infectivity