Biochemical characterisation and essentiality of proteins involved in *myo*-inositol metabolism from the parasite *Trypanosoma cruzi*

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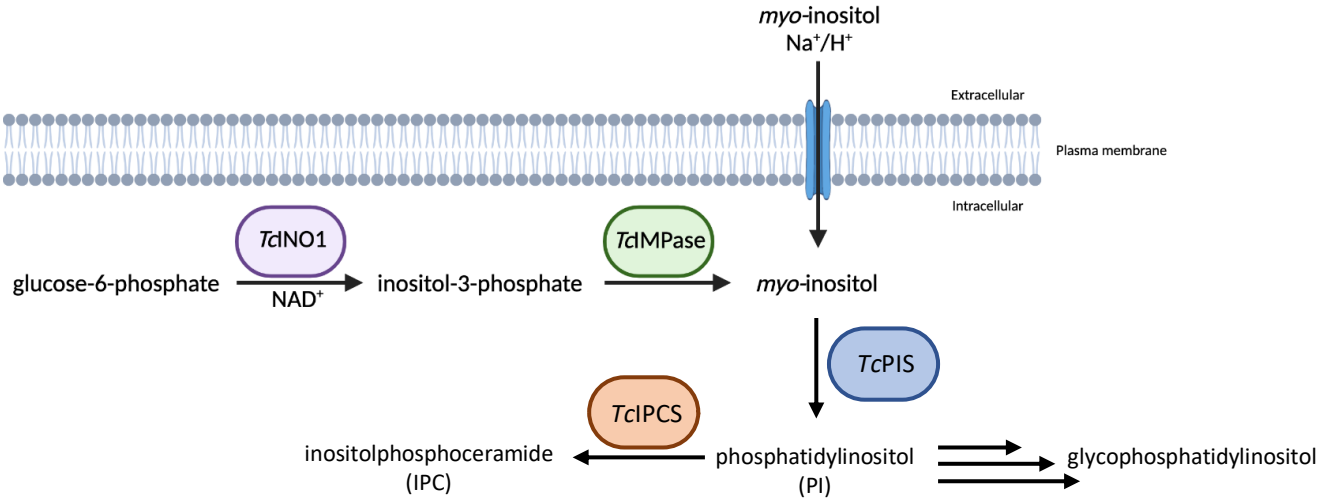

Figure 1. Putative *myo*-Inositol metabolism within *T. cruzi. myo*-Inositol may be taken up extracellularly via a Na^+ or H^+ dependent transporter or synthesised *de novo* via *Tc*INO1(purple) and *Tc*IMPase (green). *myo*-Inositol then is utilised for several phosphatidylinositol derivatives.

myo-Inositol is one of the nine naturally occurring inositol stereoisomers. It is ubiquitous amongst eukaryotes and acts as an essential metabolite with roles in signal transduction, membrane formation, and cellular physiology. In the protozoan parasite *Trypanosoma cruzi*—the causative agent of Chagas' disease—*myo*-inositol acts as a precursor to phosphatidylinositol (PI), which is an essential component to membrane lipids. In addition, PI in turn is required for formation of inositol phosphoceramide (IPC), various phosphoinositides, and glycophosphatidylinositol (GPI)-anchored mucin-type glycoproteins, which coats the parasite's cell-surface allowing the parasite to participate in multiple essential steps in parasite-host interactions. In *T. cruzi, myo*-inositol is proposed to be both *de novo* synthesised as well as scavenged from the environment, however, the proteins involved in both pathways have not been studied in *T. cruzi.* Therefore, the aim of this project is to genetically validate and biochemically characterise the putative inositol-3-phosphate synthase as well as the *myo*-inositol transporter in *T. cruzi*.