Antioxidant Enzymes of *Trypanosoma cruzi* as virulence factors in Chagas Disease

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Chagas disease (CD) caused by the parasitic protozoan *Trypanosoma cruzi*, remains a major public health concern in Latin America and is now spreading worldwide. At the chronic stage, cardiac and/or intestinal symptoms develop in 20–40% of infected individuals, with no curative therapies available. The progression to the chronic phase of CD depends on host-immune response and parasite persistence in the infected tissues. In this context, a series of molecular components of *T. cruzi* have been suggested as virulence factors, which contribute to the severity of the disease. Oxidative assault to the parasite by exogenous and/or endogenous generated reactive species promoted by host cell-derived mediators has been revealed as a key mechanism accounting for parasite control. Indeed, superoxide (O$_2^-$), nitric oxide (•NO) and peroxynitrite (ONOO-) represent molecular effectors for parasite cell death, both in the acute and in the chronic stage of the disease. However, the cellular origin (*i.e.* mammalian cell vs. *T. cruzi*) and the subcellular location of the oxidizing species interacting with molecular targets in the parasite remain largely undefined. In turn, the parasite contains an array of enzyme-based antioxidant systems (*i.e.* Fe-superoxide dismutases, peroxiredoxins, glutathione peroxidases) that attenuate or neutralize the effects of oxidants allowing parasite survival for long-term periods in the infected tissues. Moreover, antioxidant enzymes may also participate in the parasite stress response to different therapeutic agents (*e.g.* Nifurtimox) and/or redox signaling processes that protect parasites from toxicity. Overall, we hypothesize that the redox balance provided by the *T. cruzi* antioxidant systems play a central role for virulence and parasite persistence in tissues leading to the progression to the chronic phase of CD.