ENHANCED EXPRESSION OF ANTIOXIDANT ENZYMES AS A VIRULENCE FACTOR IN *TRYPANOSOMA CRUZI* INFECTION

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Overexpression of antioxidant enzymes in *Trypanosoma cruzi*, including mitochondrial (MPX) and cytosolic (CPX) tryparedoxin peroxidases, ascorbate peroxidase (APX) and iron-containing superoxide dismutases (Fe-SODs) is being revealed as a key mechanism for immune evasion. Different isoforms of Fe-SOD have been detected in *T. cruzi* which readily eliminate superoxide radicals ($O_2^{\cdot -}$) at the site of generation. We have recently shown that overexpression of mitochondrial Fe-SOD (*Tc*SODA) is capable to inhibit programmed cell death under conditions associated to enhanced mitocohondrial $O_2^{\cdot -}$ formation. Moreover, the release of an extracellular form of Fe-SOD during the acute phase of infection has been reported and can be postulated as a defense mechanism against macrophage-derived $O_2^{\cdot -}$. Using *T. cruzi* CPX and MPX overexpressers we found that both cell lines readily decompose cytotoxic and diffusible peroxides generated *in vitro* or released by activated macrophages, including hydrogen peroxide (H_2O_2) and peroxynitrite ($ONOO^-$). Most notably, *T. cruzi* strains overexpressing CPX became more resistant to $ONOO^-$-dependent cytotoxicity, being more capable to effectively infect and survive in mammalian macrophages. Our data together with other recent contributions indicating the overexpression of antioxidant enzymes during metacyclogenesis and an increased expression of Fe-SOD in drug-resistant *T. cruzi* strains place the antioxidant enzyme network of *T. cruzi*, and most likely of other trypanosomatids such as *Leishmania*, as an emerging virulence factor.