Heme Oxygenase-1 Expression and its Modulation by NADPH Oxidase in *Trypanosoma cruzi* infected macrophages

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An important intracellular mechanism to control heme homeostasis is its enzymatic degradation by heme oxygenase (HO).This enzyme has an important anti-inflammatory role in the pathogenesis of many diseases and its expression can be increased by reactive species of oxygen (ROS). Another enzymatic system involved in inflammatory process is NADPH oxidase, a multimeric complex specialized in superoxide anion generation which was first characterized in phagocytes. Then, in order to investigate the correlation between these two enzymes, we analyzed the expression levels of HO-1 during *T.cruzi* infection and/or NADPH oxidase inhibitor treatments. Thus, RAW 264.7 macrophage in the exponential growth phase, were infected with *T. cruzi* trypomastigotes at a 1:10 rate and afterwards incubated with heme and/ or diphenyleneiodonium (DPI). After that, western blotting assays were performed. We observed an increase in HO-1 expression in cells infected with trypomastigotes as well as treated with heme. This augmentation was even more evident when cells were infected and incubated with heme concomitantly. On the other hand, the use of the DPI decreased HO-1 expression. NADPH oxidase inhibition by DPI was also able to diminish macrophage infection by *T. cruzi*, as analyzed by light microscopy. We have also observed that *T. cruzi* infection increases ROS production by macrophages in a NADPH oxidase-dependent manner, once it was totally abolished by pre-treatment of macrophages with DPI, as assessed by dihydrorhodamine assay. Our results show, for the first time, the modulation of HO-1 expression by *T. cruzi* infection, which seems to be a NADPH oxidase-dependent phenomenon. The impact of those enzymatic systems on macrophage infection rates are now under investigation. Supported by CNPq, CAPES and FAPERJ.