PEROXYNITRITE DERIVED FROM MACROPHAGES EFFECTIVELY PARTICIPATES IN THE CONTROL OF *T.CRUZI* INFECTION

María Noel Alvarez[1], Lucía Piacenza[1], Gonzalo Peluffo[1], Martin, C. Taylor[2], Shane R. Wilkinson[2] and Rafael Radi[1].

[1]Center for Free Radical and Biomedical Research, Departamento de Bioquímica, Facultad de Medicina. Universidad de la República. Uruguay
[2] Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine. UK.

Macrophages play a central role in the control of acute Chagas infection by the release of oxidants (nitric oxide ($^{\cdot}NO$), superoxide ($O_2^{\cdot -}$) and hydrogen peroxide (H_2O_2)) that participate in *T. cruzi* killing. We postulate that under appropriate stimuli, macrophages can produce $^{\cdot}NO$ and $O_2^{\cdot -}$ with the resulting formation of peroxynitrite ($ONOO^-$) inside the phagocytic vacuole. We explore the capacity of *T. cruzi* metacyclic trypomastigotes to activate respiratory burst, and modulate $^{\cdot}NO$ production during its interaction with macrophage. Trypomastigote-dependent $O_2^{\cdot -}$ formation by macrophages, was confirmed by luminol chemiluminescence and NBT reduction. In addition, the $^{\cdot}NO$ production and iNOS expression in infected macrophages is conserved. Infection of macrophages by trypomastigotes showed an important inhibition on intracellular parasites (~50%) in iNOS-containing activated macrophages. Killing of intracellular trypanosomes was also evaluated by [^{3}H] uridine release. To explore $ONOO^-$ participation in *T.cruzi* killing, we used *T. cruzi* overexpressers of cytosolic tryparedoxin peroxidase (CPX) that readily decomposes $ONOO^-$. Activated macrophages are incapable to control the infection by CPX-overexpressers. Our data show that $ONOO^-$ derived from macrophages effectively participates in the control of *T.cruzi* infection and the antioxidants enzymes of parasite play a central role as a virulence factors.