A matter of life and death: ROS and intracellular parasites

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The study of intracellular parasites and their relationship with hosts has implicated reactive oxygen species (ROS) as players in the resistance to these parasites. This role in resistance may be direct by ROS or, when macrophages are activated, in conjunction with nitric oxide. Results from our laboratory show that ROS may have a detrimental effect on parasite growth, an effect promoting this growth or may not affect parasite growth at all. *Trypanosoma cruzi* infect macrophages from wild-type C57BL/6 (wt) mice and mice lacking phagocyte NADPH oxidase (phox ko) equally. However, parasite growth is largely impaired in phox ko macrophages. Growth of *L. amazonensis* is similar in wt and phox ko mice, while *L. infantum* grow better in phox ko macrophages. In vivo, phox ko mice were more susceptible to *T. cruzi*, as shown by higher mortality. However, parasite burdens were indistinguishable between phox ko and wt mice, and the mortality seems to be due to cardio-vascular effects: infected phox ko presented lower blood pressure and cardiac arrythmia. Phox ko mice presented larger lesions when infected with *L. amazonensis*. These lesions were not due to higher number of parasites, but to a larger inflammatory infiltrate in these mice, when compared to wt. A larger inflammatory infiltrate was also found in *L. infantum*-infected phox ko mice. In both cases of infection with *Leishmania*, we found that neutrophils migrated to the site of infection in phox ko mice and died at this site by necrosis rather than apoptosis, promoting, therefore, more inflammation. We conclude that ROS, besides its known effect in the resistance to intracellular parasites, promotes signaling for parasite growth and participates in the host homeostasis regulating the inflammatory response and systemic cardio-vascular responses.

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