IFN-g-dependent and NOS2-independent mechanisms of resistance to *Leishmania amazonensis*

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The main mechanism involved in control of *Leishmania* in mice is the production of NO by activated machrophages. However, mice that do not express the nitric oxide synthase (iNOS-/-) present some resistance to infection when compared to mice that do not express interferon-gamma (IFN-γ-/-), the main macrophage-activating cytokine. Hence, we raised the hypothesis that reactive oxygen species (ROS) might be responsible for the partial resistance to infection in iNOS-/- mice. To test this hypothesis, iNOS-/-, phox-/- and wild type (wt) mice were used for *in vivo* and *in vitro* assays to establish what phenotypes were connected with susceptibility to *Leishmania amazonensis*. Elicited peritoneal machophages from iNOS-/- were more permissive to infection *in vitro*, and macrophages from phox-/- mice did not differ from macrophages from wt animals. On the other hand, *in vivo* infection revealed an important role of ROS in the inhibition of parasite growth, since phox-/- mice had larger footpad lesions than wt. When treated with an inhitor of iNOS, aminoguanidine, these mice showed augmented parasite load and lesion size in the footpad. Our data suggest the presence of an important mechanism independent of nitric oxide, and introduce another model of study involving reactive oxygen species and the immunology of parasitic disease.
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