INFLUENCE OF EXTRACELLULAR ATP METABOLISM IN LEISHMANIA INFECTIVITY

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ATP released by injured cells induces the production of pro-inflammatory cytokines. On the other hand, adenosine, a product of AMP hydrolysis has immunomodulatory properties. In this study we attempted to correlate the ability of different *Leishmania* species to hydrolyze extracellular ATP, ADP and AMP with their infectivity in mice. Our results show that metacyclic forms of the most infective parasite, *L. amazonensis*, presents, after incubation for 1h at 30 °C in the presence of the respective nucleotide, higher hydrolytic activity of ATP, ADP and AMP than the same forms of the less virulent species such as *L. braziliensis* and *L. major*. This increased activity is, however, not related to the transcription levels of the parasite NTPDases, as determined by RT-PCR. In order to verify the effects of this hydrolytic pathway in the establishment of *Leishmania* infection, we treated C56BL/6 mice with adenosine at the moment of *L. braziliensis* inoculation. Adenosine induced a transient but significant increase in lesion size and parasite load, measured by the use of a dial micrometer and estimated by limiting dilution assay, respectively. This was accompanied by an increase in IL-10 production by lymph node cells, measured by ELISA's test, at 3 weeks of infection. On the other hand, administration of suramin, an antagonist of P_2 purinoreceptors and ecto-ATPase inhibitor, at the moment of *L. amazonensis* inoculation, lead to a significant decrease in lesion size and parasite load. These results strongly implicate the parasite ability to hydrolyze extracellular ATP in the establishment of *Leishmania* infection.

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