In vitro and *in vivo* leishmanicidal activity of a fungal peptide produced in culture by *Aspergillus terreus* P63

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Leishmaniasis is a disease caused by more than 20 species of *Leishmania* parasites. *Leishmania amazonensis* and *L. braziliensis* are among the main causative agents of Cutaneous Leishmaniasis (CL) in the New World, presenting a wide spectrum of clinical forms. As these pathologies have no satisfactory treatment outcomes, the discovery of alternative chemotherapeutic options is in pressing need. In this scenario, we aimed at studying novel bioactive molecules produced by an *Aspergillus* sp. strain. Bioassay-guided fractionation and purification of the growth media organic extract produced by *A. terreus* P63 led to the isolation of a peptide (which structure is under investigation). We assessed the viability of *L. amazonensis* and *L. braziliensis* and L929 fibroblasts using the MTT assay in A. *terreus* P63 peptide (AtP63p)-incubated cultures for 24h. *L. braziliensis* promastigotes were more sensitive to AtP63p (EC_{50} = 1.9 ± 0.3 μM) than *L. amazonensis* (EC_{50} = 4.5 ± 0.2 μM). 50% cytotoxic concentration of AtP63p was >10 times higher for L929 fibroblasts when compared to parasites' EC_{50}. *L. amazonensis* amastigotes were more sensitive to AtP63p than promastigotes (EC_{50} of 2.4 ± 0.1 μM), leading us to establish a good selectivity index = 18.8. Next, *in vivo* assays were conducted using BALB/c mice infected in the tail base with stationary-phase promastigotes of *L. amazonensis* (n=5/group). After the establishment of the skin lesions, animals were randomly distributed in groups I and II, that received intraperitoneal injections of 0.9% NaCl + 10% DMSO + AtP63p at 5 and 10 mg/kg/day, respectively, for 15 days. Group III received 0.9% NaCl + 10% DMSO only for the same period. There was a significant reduction in lesion parasite load (p = 0.0157) for both AtP63p -treated groups. A second round of experiment was performed to assess the efficacy of topical

use of AtP63p at 5 mg/kg/day for 32 days (n=5/group). In this case, a significant reduction of the total ulcerated area was observed in AtP63p -treated vs. untreated animals (AUC; p= <0.0001). Our results showed promising *in vitro* and *in vivo* leishmanicidal effects of AtP63p, emphasizing that systemic inoculation of AtP63p led to a decrease in the parasite load in the lesion site, whereas it is the topical administration delayed the progression of ulcers, a cure criterion established for CL management. Financial support: CAPES, CNPq, FAPESP.