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COMPARATIVE ANALYSIS OF INITIAL EVENTS OCCURRING DURING MACROPHAGE INTERACTION WITH *LEISHMANIA BRAZILIENSIS* ISOLATES CAUSING DISTINCT CLINICAL FORMS

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Abstract

INTRODUCTION Cutaneous Leishmaniasis (CL) is caused by *Leishmania braziliensis* (*Lb*) and can manifest as localized cutaneous (LCL), mucosal (ML), or disseminated leishmaniasis (DL). The interaction between *Leishmania* parasites and macrophages, the primary host cells, plays a crucial role in determining the establishment and outcome of the disease. Although the involvement of phospholipase C (PLC) and Akt in phagocytosis has been extensively studied, their specific role in *Lb* phagocytosis remains unexplored. **OBJECTIVE** This study aims to characterize the initial events of *Lb* entry into macrophages using isolates obtained from patients with LCL or DL. **METHODOLOGY** Genetically characterized *Lb* isolates from LCL or DL patients were utilized. Parasite intracellular viability was assessed at 12 h post-infection in THP-1 cells to examine potential differences in infectivity between *Lb*-LCL and *Lb*-DL. The impact of PLCγ and Akt on infection outcomes was evaluated by treating THP-1 cells infected with *Lb*-LCL or *Lb*-DL with specific inhibitors (U73122 and GSK 690693, respectively), and the parasite viability was measured at 4 and 12 hours post-infection. To assess free radical production, THP-1 cells were labeled with the superoxide probe H2DCFDA, incubated with Lb-LCL-19432 or Lb-DL-18211, and analyzed under fluorescence microscopy. **RESULTS** *Lb*-DL isolate showed lower viability compared to *Lb*-LCL after 4 and 12 hours of infection. Inhibition of PLCγ significantly reduced parasite viability in cells infected with both *Lb*-LCL and *Lb*-DL, while Akt inhibition did not affect the viability of any isolate tested. In addition, *Lb*-LCL promastigotes induced greater production of reactive oxygen species (ROS) compared to *Lb*-DL. **CONCLUSION** PLCγ appears to play a role in *Lb* phagocytosis for both LCL and DL tested isolates. Further experiments are ongoing to compare the influence of initial events in the outcome of infection caused by LCL and DL isolates in THP-1 cells.

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