IMMUNOMETABOLISM OF LEISHMANIASIS, HOW DO THE PARASITES AFFECT THE METABOLISM OF MACROPHAGES FROM SUCCEPTIBLE BALB/C MICE?

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It is well established in the scientific community that certain intracellular parasites can modulate host cell metabolism as a strategy to promote their survival and replication among the parasites of the genus *Leishmania*. Leishmaniasis, a significant and persistent public health challenge in Brazil and other developing countries, encompasses a broad spectrum of clinical manifestations that depends on both the host's immune status and the infecting *Leishmania* species.

Given that *Leishmania amazonensis* and *Leishmania braziliensis* induce distinct clinical forms with different immunological profiles, we sought to determine whether the metabolic alterations induced by these two parasite species differ in macrophages from BALB/c mice, which is a susceptible model for Leishmaniasis

To address this, we pretreated macrophage cultures with metabolic inhibitors prior to infection, thereby preventing parasite-driven metabolic modulation. Our findings indicate that *L. amazonensis* exhibits a more quiescent profile, relying less on host cell metabolism for survival. In contrast, *L. braziliensis* displayed a distinct pattern, as metabolic inhibitors from all tested classes significantly reduced both the infection rate and parasite burden.

Furthermore, real-time metabolic assays revealed that infection did not significantly alter glycolysis or basal respiration rates. However, mitochondrial fitness parameters were substantially affected in infected groups compared to controls. Notably, previous studies in resistant macrophage lineages have shown that *L. amazonensis* and *L. braziliensis* infections enhance both glycolytic and respiratory metabolism, contrasting with our findings in the susceptible lineage.

These results reinforce the direct link between cellular metabolism and functional capacity while providing a framework for further investigation into the leishmanicidal mechanisms triggered by metabolic pre-treatment.

FUNDING: This study was supported by the Coordination for the Improvement of Higher Education Personnel (CAPES) – Finance Code 001, the National Council for Scientific and Technological Development (CNPq), and the Bahia State Research Support Foundation (FAPESB).

KEYWORDS: LEISHMANIA, IMMUNOMETABOLISM, MACROPHAGE