METABOLIC REPROGRAMMING IN HUMAN MONOCYTES: UNVEILING THE ROLE OF CELLULAR METABOLISM IN *LEISHMANIA SPP.* SURVIVAL AND IMMUNE EVASION

GABRIELA DUARTE DA SILVA, AMANDA MARIA LAGO DE CASTRO, ELAINE CARVALHO DE OLIVEIRA, JULIA LOPES DE SALES, CLÁUDIA BRODSKYN

FIOCRUZ - INSTITUTO GONÇALO MONIZ, BAHIA, BRAZIL. UNICAMP, SÃO PAULO, BRAZIL.

Different *Leishmania* species have developed distinct immune evasion mechanisms, such as interference with cellular signaling and metabolic processes, to achieve effective infection in the host's mononuclear cells. This study aims to investigate the metabolic signature of *Leishmania amazonensis* and *Leishmania braziliensis* during human monocyte infection.

Monocytes were isolated from peripheral blood and infected with *Leishmania spp.* for 18 hours. Extracellular acidification rate (ECAR) and oxygen consumption rate (OCR) were measured using Seahorse. To assess the impact on metabolic pathways, the cells were pre-incubated with specific inhibitors, and parasite load was quantified. Mitochondrial mass and membrane potential were analyzed using MitoTrackers, and reactive oxygen species production was monitored using MitoSox and Cellrox. Cytokine levels were measured by Luminex.

Our data indicate that monocytes infected with *L. amazonensis* and *L. braziliensis* display a similar metabolic profile, with reduced ECAR and OCR rates. Treatment with inhibitors of glycolytic, mitochondrial metabolism, β-oxidation, and fatty acid synthesis resulted in a significant decrease in parasite load. A reduction in cytokine production was also observed in the C75 treatment, both in *L. amazonensis* and *L. braziliensis* infections. Additionally, an increase in mitochondrial mass and membrane potential was identified, and interference with monocyte metabolism was associated with increased oxidative stress, elevating cellular and mitochondrial ROS production.

This study demonstrates that infection with *L. amazonensis* and *L. braziliensis* induces similar metabolic changes in host cells, and that modulation of cellular metabolism is essential for parasite elimination.

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, MONOCYTE