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The Impact of the *lpg2* Gene on *Leishmania amazonensis* Infection in Macrophages

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Abstract

INTRODUCTION: Leishmaniasis, caused by the protozoan *Leishmania*, is a significant global health health problem. In Brazil, *Leishmania amazonensis* is responsible for two clinical forms: Localized Cutaneous Leishmaniasis (LCL) and Diffuse Cutaneous Leishmaniasis (DCL). Macrophages play a crucial role in the immune response during *Leishmania* infection. Among the glycoconjugates on promastigote parasites surface are lipophosphoglycan (LPG), phosphoglycans (PG), proteophosphoglycans (PPG), and acid phosphatases (sAP). The *lpg2* gene encodes a GDP-mannose transporter, crucial for the synthesis of phosphoglycan (PG), a common domain for the surface molecules of these parasites. The research group used CRISPR/Cas9 to develop *Leishmania amazonensis* parasites deficient in *lpg2*. **OBJECTIVES**: This study aims to explore the inflammatory mechanisms triggered by the deletion of the *L. amazonensis lpg2* gene during the infection of murine macrophages. **METHODS**: Macrophages from C57BL/6 mice were cultured and infected with wildtype (*WT*) *L. amazonensis* promastigotes and *lpg2* knockout (*Δlpg2*) promastigotes. Infection ratios of 1:5 and 1:10 were used, and parasite load and viability were assessed. The culture supernatant was then analyzed using the Griess Reaction to detect nitric oxide (NO) and inflammatory mediators using ELISA. **RESULTS:** We observed a reduction in intracellular parasite load and viability of *Δlpg2* knockout parasites compared to *WT* parasites at both ratios tested. However, nitric oxide (NO) levels did not differ significantly between the two groups of parasites. Further assessment of cytokines, lipid mediators (PGE_2 and LTB_4) is necessary in this context. **CONCLUSION:** The study highlights the significance of PG-containing glycoconjugates as virulence factors in *L. amazonensis*. These initial findings hold promise for enhancing our understanding of inflammatory mechanisms during parasite-macrophage interactions in New World *Leishmania* species.

Keywords: Macrophage. *Leishmania amazonensis*. *lpg2*

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