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Evaluation of the lpg2 gene during *Leishmania infantum* and host cell interaction

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Abstract

INTRODUCTION: Visceral leishmaniasis is considered very severe, with high mortality rates when not treated properly. Is characterized by hepatosplenomegaly and caused by the species *Leishmania infantum* in Brazil. The promastigote form of the parasite has molecules in their surface important for the host infection, the most abundant one is the Lipophosphoglycan (LPG). The *L. infantum* promastigote also has other phosphoglycans on its surface. In response to these virulence factors, macrophages activate their microbicidal mechanisms to combat *L. infantum* infection. In this context, parasites LPG deficient, obtained by the CRISPR/Cas9 system, represent an efficient tool to evaluate the parasite-host cell interaction. **OBJECTIVES**: This study aims to investigate how the presence or absence of lpg2 can alter the microbicidal functions of murine macrophages during infection by comparing *L. infantum* wild-type (WT), *L. infantum* knockout (Δlpg2), with the deletion of the lpg2 gene and the *L. infantum* genetically restored Add-back (Δlpg2 + lpg2). **METHODS**: Macrophages derived from the bone marrow of C57BL/6 mice were cultured and subsequently infected with *L. infantum* WT, Δlpg2 and Δlpg2 + lpg2 metacyclic promastigotes. After 4, 48 and 72 hours of infection the parasite load and viability were evaluated. The culture supernatant was collected to detect nitric oxide and inflammatory mediators. **RESULTS:** We observed a reduction in the Δlpg2 parasites survival compared to WT parasites. Furthermore, macrophages infected with the *L. infantum* Δlpg2 had a significant increase in nitrite production compared to the WT and Δlpg2 + lpg2 groups, suggesting a greater microbicidal potential of macrophages infected by the Δlpg2. **CONCLUSION:** *L. infantum* Δlpg2 parasites have lower virulence and stimulate a stronger macrophage response, highlighting LPG's role as a key virulence factor. Further research is needed to understand the inflammatory mechanisms and the role of LPG2 in macrophage activation.

Keywords: Macrophage. *Leishmania infantum*. *lpg2*

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