Efficacy of the intranasal vaccination with LACK DNA against *Leishmania (Viannia) braziliensis* infection in hamster model

Saavedra AF[1]; Couto LS[1]; Ribeiro-Romão RP[1]; Bezerra IPS[2]; Moreira OC[3]; Da-Cruz AM[1]; Rossi-Bergmann B[2]; Pinto EF[1]

[1]Laboratório Interdisciplinar de Pesquisas Médicas - Instituto Oswaldo Cruz/FIOCRUZ, Rio de Janeiro, Brazil
[2]Laboratório de Imunofarmacologia - Instituto de Biofísica Carlos Chagas Filho, UFRJ, Brazil
[3]Laboratório de Biologia Molecular e Doenças Endêmicas - Instituto Oswaldo Cruz/FIOCRUZ, Rio de Janeiro, Brazil

In the murine model, LACK DNA vaccine administrated by parenteral routes has shown protective against *Leishmania (Leishmania) major* infection, but not against *L. donovani* and *L. amazonensis* infections. On the other hand, intranasal (IN) immunisation with LACK DNA protects mice against *L. amazonensis* and *L. infantum* infections. However, vaccination studies with *L. (V.) braziliensis* are scarce. Recently, we demonstrated that the golden hamster is an appropriate model for immunoprotection studies of *L. braziliensis* infection through the protection induced by IN immunisation with whole *L. amazonensis* antigens (LaAg). Furthermore, we standardized a RT-qPCR assay for assessment of a broad panel of cytokines and molecules in hamster tissue. In this study, we investigated whether the protective effect of IN immunisation with LACK DNA can be extended to *L. braziliensis* infection using the hamster model. Hamsters received two intranasal doses of LACK DNA (50μg) or LaAg (10μg). Controls received PBS or pCI-neo plasmid. Two weeks post vaccination hamsters were challenged with $1x10^5$ promastigotes of *L. braziliensis* in the hindpaw. Five and 110 days after infection, we evaluated the immune response associated with protection through the relative gene expression quantification of IFN-ɣ, TGF-β, TNF, IL-10, IL-4, IL-6, iNOS and arginase in skin and popliteal lymph node. Hamsters vaccinated with LACK DNA did not showed significant reduction in lesion size, parasite load in skin or IgG and IgG2 anti-*Leishmania* serum levels compared to control groups. No difference was observed in IgG levels five days after immunisation or five days after infection. It was observed a slight variation in gene expression of the targets analyzed five days post infection. Cytokines gene expression 110 days post infection in skin showed no difference between groups. In contrast, in lymph node it was observed a higher expression of IFN-ɣ, TNF, IL-4 and IL-6 in LaAg group compared to control, while LACK DNA induced a slight increase in TNF gene expression. Our results demonstrated that homologous prime boost immunisation with LACK DNA did not induce protection against *L. braziliensis* infection. However, other strategies must be investigated associated with LACK DNA antigen such as adjuvants or heterologous prime boost vaccination. We showed that vaccine protection in hamster model seems to be associated with a mixed immune profile in the chronic phase of infection.

Keywords: *Leishmania (Viannia) braziliensis*; intranasal vaccine; golden hamster.

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Corresponding author: eduardo@ioc.fiocruz.br