EVALUATION OF THE PROTECTIVE CAPACITY OF KHARON-DEFICIENT *Leishmania mexicana* AGAINST CHALLENGE WITH *Leishmania braziliensis*

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Abstract

Leishmaniasis is still a serious public health problem worldwide. There are currently no safe and effective vaccines available for humans, and disease control depends exclusively on chemotherapy, which, in addition to being toxic, has high rates of therapeutic failure. Thus, the search for vaccine development remains urgent. It is known that developing protective immunity in patients cured of leishmaniasis is possible, which shows the importance of an active infection in inducing protective immunity against *Leishmania*. The use of live attenuated parasites of the genus *Leishmania* as vaccine candidates has been resumed and widely studied, as they mimic natural infections without causing the disease, allowing interaction with essential antigens in the development of immunity. Previous studies have shown that deletion of the kharon1 gene results in defects in the development of the amastigote form, leading to intracellular death and rendering the parasites incapable of sustaining the infection. We previously showed that *L. infantum* deficient in Kharon (Δ*Likh1*) induces protection against a challenge with virulent *L. infantum*. In this work, we evaluated the ability of a Kharon-deficient *L. mexicana* strain (Δ*Lmexkh1*) to induce cross-protection against *L. braziliensis*, Brazil's leading etiological agent of Cutaneous Leishmaniasis. Our results show that Δ*Lmexkh1* cannot survive in infected macrophages, although promastigote forms showed normal growth. We will evaluate the effect of immunization with Δ*Lmexkh1* against a challenge with *L. braziliensis* in a preclinical infection model.

Keywords: live attenuated *Leishmania* vaccine, leishmanization, kharon