

Immunization with *Leishmania major* centrin knock-out (*LmCen*^{-/-}) parasites induces skin resident memory T cells that play a role in protection against *Leishmania* infection

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Background: Leishmaniasis is a vector-borne disease transmitted through a sand fly bite with no available vaccine. Vaccination through leishmanization with *Leishmania major* has been used successfully but is not safe. Recently, we have demonstrated immunization with live attenuated *LmCen*^{-/-} parasite protects against Leishmaniasis via induction of host cellular immunity and is safe in various animal models.

Objective: Resident memory T cells (T_{RM}s) are considered the first line of defense against infections invading the host through the epithelial barrier. The goal of this study is to evaluate the generation and function of skin T_{RM}s post *LmCen*^{-/-} immunization compared to that generated through leishmanization.

Results: We examined chemokine receptors controlling the generation and survival of skin T_{RM}s, as well as effector and recruitment function of T_{RM}s in *LmCen*^{-/-} and Leishmanized immunized mice after challenge with *WT* parasites. Expression of chemokine receptors controlling the formation of T_{RM}s in the skin was significantly higher in the skin of *LmCen*^{-/-} immunized mice, compared to infected (Leishmanized) mice, at 20 weeks post immunization/infection. In addition, epithelial cytokine production, such as IL-15, IL-33 and TNF α was significantly higher in the skin of immunized mice. Upon virulent challenge, TH1 cytokines production in the skin, measured by RT PCR, was similar in immunized mice compared to healed mice. Furthermore, T_{RM} specific activation protein, ITGA-1, was higher in the treated groups compared to the nonimmunized control.

Conclusions: Results show that immunization with live attenuated parasites generates functional population of skin T_{RM}s compared to leishmanization which play an important role. Upon challenge, both immunized and leishmanized mice developed similar effector immune response.