DELETION OF IL-4Rα-RESPONSIVE KERATINOCYTES IN BALB/C MICE DOES NOT AFFECT THEIR SUSCEPTIBILITY TO CUTANEOUS LEISHMANIASIS

Melissa Govender[1,2], *Ramona Hurdayal*[1,3], *Berenice Martinez Salazar*[1,2], *Kaya Gqada*[1,2], *Marc Descatoire*[4], *Benjamin P. Hurrell*[4], *Noémie Oechslin*[4], *Fabienne Tacchini-Cottier*[4], *Reto Guler*[1,2], *Frank Brombacher*[1,2]

[1]*University of Cape Town, Institute of Infectious Diseases and Molecular Medicine (IDM), Division of Immunology and South African Medical Research Council (SAMRC) Immunology of Infectious Diseases, Faculty of Health Sciences, University of Cape Town, Cape Town 7925, South Africa*

[2]*International Centre for Genetic Engineering and Biotechnology, Cape Town Component, Cape Town 7925, South Africa*

[3]*Department of Molecular and Cell Biology, University of Cape Town, Cape Town 7925, South Africa*

[4]*Department of Biochemistry, WHO-Immunology Research and Training Center, University of Lausanne, Switzerland*

Background

A dominant T helper 1 (Th1) immune response is required to control cutaneous leishmaniasis (CL). Unexpectedly, early IL-4 secretion promotes protective Th1 development. Keratinocytes, which represent the major cell type in the epidermis, secrete IL-4 early during CL infection. Here we investigated whether IL-4/IL-13 signalling via the common IL-4 receptor α chain (IL-4Rα) on keratinocytes contributes to early immunity during CL.

Methods

To address this, keratinocyte-specific-IL-4Rα deficient (KRT14creIL-4Rα-/lox) BALB/c mice were generated by gene targeting and site-specific recombination (cre/*loxP*) under control of the KRT14 promotor. These mice were infected in the footpad or ear, swelling was monitored for the duration of infection, and immune response evaluated at the end of infection.

Results

KRT14creIL-4Rα-/lox BALB/c mice infected in the footpad with high-dose *L. major* IL-81 and LV39 promastigotes developed increased swelling, high parasite burdens, and cytokine and antibody secretion similar to littermate controls. In the ear infection model, KRT14creIL-4Rα-/lox BALB/c mice infected with low-dose *L. major* IL-81 and LV39 promastigotes, developed increased swelling, high parasite burdens, Th1 and Th2 cytokines, and high antibody titres, similar to littermate controls. KRT14creIL-4Rα-/lox BALB/c mice infected with *L. major* LV39 promastigotes in the ear showed significantly decreased parasite burdens in the ear, when compared to littermate controls.

Conclusions

Collectively, our results show that IL-4/IL-13 signalling through the IL-4Rα on keratinocytes does not influence the establishment of a Th1 immune response required for protection during *L. major* infection in mice.