Transcriptomic landscape of skin lesions in cutaneous leishmaniosis reveals a strong CD8+ T cell immunosenescence signature linked to immunopathology.

Abstract

The severity of lesions that develop in patients infected by Leishmania braziliensis is mainly associated with a highly cytotoxic and inflammatory cutaneous environment. Recently, we demonstrated that senescent T and NK cells play a role in the establishment and maintenance of this tissue inflammation. Here, we extended those findings using transcriptomic analyses that demonstrate a strong co-induction of senescence and pro-inflammatory gene signatures in cutaneous leishmaniasis (CL) lesions. The senescence-associated signature was characterized by marked expression of key genes such as ATM, Sestrin 2, p16, p21 and p38. The cell type identification from deconvolution of bulk sequencing data showed that the senescence signature was linked with CD8+ effector memory and TEMRA subsets and also senescent NK cells. A key observation was that the senescence markers in the skin lesions are age-independent of patients and were correlated with lesion size. Moreover, a striking expression of the senescence-associated secretory phenotype (SASP), pro-inflammatory cytokine and chemokines genes was found within lesions that were most strongly associated with the senescent CD8 TEMRA subset. Collectively, our results confirm that there is a senescence transcriptomic signature in CL lesions and supports the hypothesis that lesional senescent cells have a major role in mediating immunopathology of the disease.

Single-cell suspensions were stained with Fixable Viability Dye eFluor 455UV and anti-CD16/CD32 (both from Thermo Fisher) in PBS prior to addition of the relevant fluorochrome-conjugated antibodies in FACS buffer supplemented with Super Bright staining buffer (Thermo Fisher).

BIOGRAPHY

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