IL-15/IL-15Rα signaling is a guardian of human hair follicle immune privilege and promotes hair growth

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The human skin harbors a haphazard pool of cytokine-resident skin immune cells (TRM) cells seeded during infections and inflammation. TRM cells are retained at the site of vital infections and provide local immunity. These cells persist for years in the skin after bone marrow transplantation but circulating ex-TRM cells indicate several potential fates. Here, we explored the clonal relationships between human T cells in different skin compartments and circulation. 10x Genomics 5 prime immune profiling coupled with feature barcoding technology was employed to investigate the clonal relationship, transcriptomic and proteomic profiles of single T cells sorted from blood, subcutis, dermis, and epidermis. A few CD8+ TRM cell clones dominate epidermis and cytotoxic CD8+ CD103+ CD49a+ showed the least diverse T cell receptor (TCR) repertoire. Clonal overlap was found between all three compartments, with some clones being specific to one of the skin sides, whereas highly abundant epidermal clones might be skin specific.

Single-cell T cell receptor (TCR) repertoire of skin and blood reveals skin-specific characteristics in health and HIV infection

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Human skin harbours a large proportion of the resident memory T (Trm) cells of the body. Trm cells promote immune homeostasis and exert anti-microbial and anti-cancer function in tissue. We recently demonstrated that skin Trm cells are permanently depleted in people living with HIV (PWH) with a low nadir and possibly replaced by blood-derived T cells. We linked the loss of Trm cells in PWH with the increased risk of developing cutaneous and mucosal cancer. The T-cell receptor (TCR) diversity analysis with next generation sequencing might give new insights into the biology of skin Trm cells at homeostasis and in HIV. We investigated the TCR profile of skin- compared to blood-derived T cells in healthy controls (HC) and PWH (n=5). We first performed bulk RNA-sequencing to get new insights into the distribution of TCR clones in the different skin and T cell clusters. We observed that only few clones are shared between skin and blood in healthy controls (8.39%), suggesting that Trm cells are quite self-sustained with scarce immune interactions with other compartments. On the contrary, the percentage of TCR clones shared between skin and blood in PWH was 24.5% and mostly represented by effector memory CD8+ T cells. Further analysis suggested an oligoclonal expansion of the TCR repertoire in CD8+ T cells, suggesting that the ongoing analysis will bring new insights into the pathogenesis of inflammatory skin diseases and cancer susceptibility of barrier organs.

Tyrosine Kinase 2 Inhibition Ameliorates the Phenotype of Lesional Alopecia Areata Scalp Skin Ex Vivo, and Reverses the Induction of Human Alopecia Areata in a Humanized Mouse Model

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Alopecia areata (AA) is an immune-mediated hair follicle (HF) disorder induced by elevated IFNα levels and a T-cell driven inflammatory response. We have previously shown that treatment with the tyrosine kinase inhibitor (TKI) BMS-986022 (BMS) has therapeutic potential for AA, by improving hair growth in lesional scalp biopsies and in a humanized mouse model. However, it is still unclear whether TKI treatment can also reverse the induction of AA in a humanized mouse model. Here, we show that treatment with BMS or tofacitinib significantly improves hair shaft number and reduces MHC class II expression, but is not able to reverse the AA phenotype. Taken together, our results suggest TKI inhibition is a novel, pharmacological approach for AA management, deserving clinical exploration.

Imiquimod perturbs amino acid metabolism in human CD8+ T cells

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Pemphigus is a rare and debilitating autoimmune blistering disease due to keratinocyte cell detachment (acantholysis). Treatments focus on immune suppression but are often associated with severe side effects. Novel therapies are therefore needed. We investigated the TCR profile of skin- compared to blood-derived T cells in healthy controls (HC) and PWH (n=5). We first performed bulk RNA-sequencing to get new insights into the distribution of TCR clones in the different skin and T cell clusters. We observed that only few clones are shared between skin and blood in healthy controls (8.39%), suggesting that Trm cells are quite self-sustained with scarce immune interactions with other compartments. On the contrary, the percentage of TCR clones shared between skin and blood in PWH was 24.5% and mostly represented by effector memory CD8+ T cells. Further analysis suggested an oligoclonal expansion of the TCR repertoire in CD8+ T cells, suggesting that the ongoing analysis will bring new insights into the pathogenesis of inflammatory skin diseases and cancer susceptibility of barrier organs.

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