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EBI2 marks CD8+ tissue-resident memory T cells of the skin

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Background: Inflammatory skin diseases like psoriasis, atopic dermatitis (AD) and allergic contact dermatitis (ACD) are characterized by persistent site-specific recurring lesions. Tissue-resident memory T (T_{RM}) cells remain sessile in those skin lesions and have been linked to the recurring chronic pathology. Epstein-Barr Virus-induced gene 2 (EBI2 or GPR183) mediates chemotaxis towards its ligand 7?,25-dihydroxychlesterol (7?,25-OHC). CH25H and CYP7B1 are the enzymes that synthesize 7?,25-OHC. An ever-growing number of disease pathologies are associated with the EBI2-oxysterol-axis, such as of rheumatoid arthritis, MS, COPD and IBD. EBI2 has not been described in the context of T_{RM} cells as of today.

Methods: Using an experimental murine ACD model, contact hypersensitivity (CHS), and a public raw human transcriptome bulk-RNAseq dataset, we compared mRNA-expression of EBI2-oxysterol-axis-genes in lesional vs. non-lesional skin. Utilizing high-parameter flow cytometry and clustering algorithms, we analyzed EBI2-expression of T_{RM} cells in lesional vs. non-lesional skin of biopsies from psoriasis patients and murine CHS ears.

Results: Gene-expression of EBI2-oxysterol-axis-genes is upregulated in murine (CHS) and in human (psoriasis and AD) lesional skin, compared to non-lesional skin. While only up to 40% of circulating $CD8^+$ T cells express EBI2, a striking 80 (human) to 95% (mouse) of skin $CD8^+$ T_{RM} cells are $EBI2^+$. Murine $CD8^+$ T_{RM} cells upregulate EBI2-expression during differentiation from effector cells.

Conclusion: T_{RM} cells are known to reside in ex-lesional skin and mediate chronic flare ups. We find those cells expressing EBI2 in mouse and human skin. The upregulation of EBI2-expression of skin $CD8^+$ T_{RM} cells, compared to circulating $CD8^+$ T cells, in conjunction with the upregulation of the expression of EBI2-oxysterol-axis-genes in lesional murine and human skin, is a strong indicator that the EBI2-oxysterol-axis is involved in the pathology of inflammatory skin diseases and implicates a functional role for EBI2 on T_{RM} cells that is yet to be uncovered.