

## Generation and function of tissue resident memory T cells

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Tissue-resident memory T cells ( $T_{RM}$ ) provide superior protection against infection in extra-lymphoid tissues. We have found that  $CD8+CD103+$   $T_{RM}$  cells develop in the skin from killer lectin-like receptor G1 (KLRG-1)-negative precursors that selectively infiltrate the epithelial layer. A combination of epithelial entry in addition to interleukin 15 (IL-15) and transforming growth factor-beta (TGF-beta) signaling was required for optimal formation of these long-lived memory cells. Importantly,  $T_{RM}$  differentiation resulted in the progressive acquisition of a unique transcriptional profile that differed from those expressed by circulating memory cells and other types of T cells that permanently reside in skin epithelium. Certain differentially expressed transcription factors were found to dramatically influence  $T_{RM}$  formation and/or survival. Combined, this data provides a molecular framework for the local differentiation of a distinct peripheral memory population that forms a first-line immune defense system in barrier tissues.