Small intestine epithelial cells shape the identity and fate of dendritic cells

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Within non-lymphoid and lymphoid tissues, dendritic cells (DCs) form a heterogeneous cell population, with the existence of different DC subtypes exhibiting distinct transcriptional programs and eventually, distinct functions. Particularly, the small intestine Lamina Propria (LP) is enriched in a peculiar population of cDC2s expressing the integrins CD103 and CD11b. Interestingly, a fraction of these cells can transmigrate into the epithelial layer both at steady state and in higher proportion upon infection. However, the consequences of such event of transmigration on the identity and fate of these cells is unknown. By using single cell RNA sequencing analysis, we here show that transmigration of CD103+CD11b+ DCs into the epithelium deeply modifies their transcriptomic profile: it down-regulates inflammatory gene expression and stimulates the transcription of genes associated to negative regulation of T cells as well as to cell migration. Accordingly, we found that even if intraepithelial CD103+CD11b+ DCs can capture more antigen than their LP counterpart, they barely activate T lymphocytes. Consistent with this finding, we found that intraepithelial DCs (IEDCs) express lower levels of the activation markers CD80, CD86, CD83 as well as of the chemokine receptor CCR7, than LP DCs. Strikingly, when culturing LP DCs with small intestine epithelial cells -but not with their supernatant- we observed a downregulation of the expression of these surface markers, while other IEDC markers increase. These results show that the transmigration of LP CD103+CD11b+ DCs into the epithelium leads to a significant loss of their T cell activation capacity as a result of epithelial cell imprinting.

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