Intestinal mesenchymal cells induce the differentiation of pre-cDCs into CD103+ CD11b+ DCs ex vivo

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Introduction: Classical dendritic cells (cDCs) play an essential role in intestinal immune responses by presenting antigen to naïve T cells in the draining lymph node and shaping whether tolerance or active immunity occurs. A unique population of cDC2s co-expressing CD103+ and CD11b+ is present in the intestinal mucosa, but the factors driving their development are not understood. Here we have explored the signals that pre-cDCs might receive upon entry into the intestine and show that intestinal mesenchymal cells are proficient at inducing lineage commitment towards CD103+CD11b+ cDC2.

Methods: Pre-cDCs were isolated from the bone marrow of C57BL/6 mice and cultured for 4 days in the presence of different cytokines or together with intestinal or splenic stromal cell subsets. The phenotype of resulting cDCs was analysed by flow cytometry and their ability to stimulate antigen specific OT II cells in vitro assessed.

Results: CD103+CD11b+ DCs developed when pre-cDCs were cultured with a combination of TGFβ, GM-CSF and FLT3L and these cDCs were strong inducers of antigen specific CD4+ T cell proliferation in vitro, confirming their maturity. When pre-cDCs were co-cultured with intestinal stromal cell subsets, gp38+(podoplanin+) CD31- mesenchymal cells showed a selective ability to induce the development of CD103+CD11b+ DCs. Other stromal cell subsets from the intestine and spleen stromal cells could not do this. Based on the expression of characteristic markers of CD103+CD11b+ cDC2 in vivo including CD101 and Siglec F, the CD103+CD11b+ DCs generated with intestinal stromal cells in vitro show a developmental progression from CD11b+ cDC2s. We are currently comparing the cells generated in vitro with freshly isolated intestinal cDCs at the single cell level.

Conclusion: This novel co-culture technique indicates that factors derived from intestinal mesenchymal cells may be responsible for imprinting a tissue specific signature in developing cDC2s.

Keywords : intestine, stromal cells, cDC2s
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