DENDRITIC CELLS

Division of DC labour in the gut

As far as the immune system is concerned, the gut is full of bacterial friends and foes: commensal micro-organisms must be tolerated, whereas pathogens must be expelled. At the front line, maintaining this balance, are dendritic cells (DCs). Two groups reporting in *Immunity* have now investigated the origins and functions of lamina propria DC subsets to more fully understand how such an immune balance is achieved.

The importance of DCs in maintaining immune system homeostasis in the gut is well accepted. Although several DC subsets from the lamina propria — the gut wall mucosa — have been identified, the origin and function of these cells *in vivo* were unknown.

Through cell ablation and reconstitution experiments using specific precursor cell subtypes, Varol *et al.* and Bogunovic *et al.* showed that monocytes gave rise to one type of lamina propria DC and that pre-cDCs (DC-committed, non-monocytic precursors) gave rise to another type. The two types of lamina propria DC were characterized by the expression of different cell surface markers. Pre-cDCs gave rise to cells that were $CD103^+$, $CD11b^-$ and CX_3C-chemokine receptor 1 $(CX_3CR1)^-$. Monocytes, by contrast, produced $CD103^-CD11b^+CX_3CR1^+$ cells. CX_3CR1 is required for the formation of DC protrusions known as transepithelial dendrites, which squeeze between gut epithelial cells to sense or sample antigens from the gut lumen. So, although lamina propria DCs are known for this sampling activity, it seems that only those derived from monocytes are responsible.

Interestingly, however, it is the pre-cDC-derived cells that are the main migratory lamina propria DCs, as shown by Bogunovic *et al.* On infection of mice with *Salmonella typhimurium* it was these cells, not the monocyte-derived DCs, that carried the bacteria from the lamina propria to the draining lymph nodes, although both types of DC contained the bacteria. The monocyte-derived DCs did not traffic to the draining lymph nodes even when pre-cDC-derived cells were absent.

If only the pre-cDC-derived lamina propria DCs traffic to the lymph nodes (the main site of antigen presentation), what is the purpose of antigen sampling by the monocyte-derived lamina propria DCs? Bogunovic *et al.* propose that the monocyte-derived DCs might pass on the sampled lumen antigens to their pre-cDC-derived counterparts in a type of antigen relay — a hypothesis that the team is currently testing.

As well as being gut lumen samplers, the monocyte-derived lamina propria DCs have a pro-inflammatory role, as shown by Varol *et al.* Mice that were DC depleted and then reconstituted with monocyte precursors were susceptible to colitis. Importantly, it was the imbalanced reconstitution of DC subsets and not the initial depletion that was to blame. Mice that had their DCs depleted and were not reconstituted were only as susceptible to colitis as wild-type mice. The findings suggest that the pre-cDC-derived cells might have anti-inflammatory properties and that imbalanced representation of the lamina propria DC types, or their functions, could be a precondition to serious inflammatory bowel disorders.

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ORIGINAL RESEARCH PAPERS Varol, L. *et al.* Intestinal lamina propria dendritic cell subsets have different origin and functions. *Immunity* **31**, 502–512 (2009) | Bogunovic, M. *et al.* Origin of the lamina propria dendritic cell network. *Immunity* **31**, 513–525 (2009)