Journal club

DCs TAILOR T CELLS TO THE TISSUE

This seminal study published in 2005 by William Agace and colleagues marked an important step forward in our understanding of mucosal immunology and dendritic cell (DC) biology. It not only phenotyped the antigen-presenting cell (APC) type that is responsible for imprinting T cells with the ability to return specifically to the intestinal mucosa but also led to an explosion of information on intestinal DCs, which are now one of the most intensively studied immune cell populations in the body.

Previous work by this group and others had shown that tissue-specific homing of lymphocytes to the intestine required the presentation of antigen in intestinal draining lymphoid tissues. However, the type of APC responsible for such antigen presentation was not defined. Agace and colleagues showed that this is specifically a property of CD103$^+$ DCs that migrate from the lamina propria of the intestine to the draining lymph nodes and induce the expression of 'homing' receptors on T cells. This was the first description of a defined role for DCs expressing CD103 in the intestine, and it was one of the first definitive studies of CD103$^+$ DCs anywhere in the body.

> "the tissue of origin has a crucial role in determining DC behaviour"

Studies by many groups have since underlined how the tissue of origin has a crucial role in determining DC behaviour. We now know that intestinal CD103$^+$ DCs are particularly important for inducing the differentiation of forkhead box protein P3 (FOXP3)$^+$ regulatory T cells, which regulate immune responses in the intestine. Furthermore, unlike CD103$^+$ DCs elsewhere in the body, it has been shown that those in the intestine are heterogeneous; there is a distinct lineage of interferon-regulatory factor 4 (IRF4)-dependent CD103$^+$ DCs, in addition to the cross-presenting, BATF3-dependent CD103$^+$ DCs that are found in other tissues.

Both of these effects of CD103$^+$ DCs on T cells (gut-homing specificity and effector function) have been shown to depend on DC production of retinoic acid from the metabolism of dietary vitamin A. The immunoregulatory role of retinoic acid has now become a major topic of research, underpinning the idea that vitamins and other dietary constituents might modulate immune function. The early insights provided by this 2005 paper have been of crucial importance in helping us to understand this and many other aspects of immune regulation in the intestine.

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The author declares no competing interests.

ORIGINAL RESEARCH PAPER
Johansson-Lindbom, B. *et al.* Functional specialization of gut CD103$^+$ dendritic cells in the regulation of tissue-selective T cell homing. *J. Exp. Med.* **202**, 1063-1073 (2005).