Dendritic Cell Subsets And Their Role In Controlling Intestinal Inflammation

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Abstract
A proper functioning of the intestinal mucosal barrier is essential in maintaining the mutual “understanding” between myriads of commensals and the immune system. Failure in this communication can have dramatic consequences in the form of inflammatory bowel diseases (IBD) and even more insidiously, intestinal malignancies. Gut DCs, effective regulators of mucosal adaptive immune responses, potentially contribute in supporting this intestinal homeostasis. To study the crosstalk between distinct DC subsets and colonic epithelia we have exploited two new Diphtheria Toxin Receptor (DTR) transgenic mouse strains (Clec9A- and Clec4a4-DTR mice) that enable us to ablate specifically CD103+CD11b- or CD103+CD11b+ DCs in the gut during colonic epithelial damage. We show that Clec9A-DTR mice after depletion of CD103+CD11b- DCs developed severe, DSS-induced colitis, with pronounced defects in epithelial IL-18bp and Idol expression levels, both molecules important in the containment of inflammation. On the other hand, Clec4a4-DTR mice lacking the CD103+CD11b+ DCs dramatically augmented epithelium-associated anti-microbial proteins and were colitis resistant. Clearly, two distinct gut DC subsets show an antagonistic control of intestinal epithelial responses.

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