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Eosinophils get the party started

Eosinophils are found in the healthy intestine, yet their physiological function at this site remains poorly understood. Chu *et al.* now show that eosinophils promote the development of T helper 2 (T_H2) cell responses in the intestine by regulating the activation and migration of dendritic cells (DCs).

Most healthy tissues do not contain eosinophils. As such, these cells are typically considered to be specialized effector cells that are recruited to tissues as a result of a T_H2 cell-driven immune response. However, the fact that eosinophils are present in the healthy intestine suggests that they may have other functions at this site. Chu *et al.* examined the distribution of eosinophils in the mouse intestine and found that these cells are most frequent in the small intestine (where they account for 15–35% of all lamina propria leukocytes) and that they become less abundant along the length of the intestinal tract (representing <1% of leukocytes in the rectum).

> “eosinophils are not always the latecomers to the T_H2 cell party”

The authors therefore concentrated on exploring eosinophil functions in the small intestine. They found that ΔdblGATA1 mice (which completely lack eosinophils) were unable to develop T_H2-type immune responses in a model of peanut allergy that is induced by oral immunization with peanut butter and cholera toxin. Adoptive transfer of eosinophils to ΔdblGATA1 mice restored this ability, suggesting that eosinophils are necessary for the development of T_H2-type responses in the small intestine. By contrast, eosinophils were not required to generate other intestinal immune responses (such as IgA production and oral tolerance induction) and they were also not essential for the initiation of T_H2-type responses at other peripheral tissue sites, such as the skin, that do not normally contain eosinophils.

The ability of eosinophils to induce a T_H2-type response in the small intestine was independent of their ability to produce interleukin-4 (IL-4). Instead, the authors showed that eosinophils promote the activation and migration of $CD103^+$ DCs to the mesenteric lymph nodes during peanut sensitization. They found that challenge with a peanut extract elicited eosinophil degranulation in the small intestine, leading to the secretion of granular contents, such as the eosinophil-specific granule protein eosinophil peroxidase (EPX). Notably, EPX was shown to induce DC upregulation of the co-stimulatory molecules CD80 and CD86, as well as CC-chemokine receptor 7 (CCR7), which is required for DC migration to the draining lymph nodes. EPX also increased DC expression of OX40 ligand (OX40L; a co-stimulatory molecule associated with T_H2-type immunity) but suppressed their production of IL-12. Finally, the authors showed that EPX-deficient mice — similar to eosinophil-deficient mice — were unable to support the development of T_H2-type immune responses in the peanut allergy model.

These data suggest that eosinophils in the small intestine can drive pro-allergic responses by inducing DC activation and migration. Thus, eosinophils are not always the latecomers to the T_H2 cell party — in the intestine they can actually initiate T_H2-type immune responses.

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ORIGINAL RESEARCH PAPER Chu, D. K. *et al.* Indigenous enteric eosinophils control DCs to initiate a primary Th2 immune response *in vivo*. *J. Exp. Med.* **211**, 1657–1672 (2014)