Innate Immunity in the Intestine

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The intestine is the largest compartment of the immune system and is bombarded continuously by an enormous variety of antigens. As a result, there is a complex array of immune effector mechanisms present in the gut, many of which are distinct from their counterparts in other parts of the body. Recently there has been an explosion of interest in innate immunity, with novel populations of myeloid cells and lymphocytes being defined, as well as distinctive mechanisms of defence. The articles in this issue will discuss some of the most interesting advances in this field, exploring the ways in which the normal intestine has adapted to live in symbiosis with its local microbiota, as well as how it responds to pathogenic organisms.

Salmonella species are important causes of food-borne disease in man and many domestic animals, producing a variety of syndromes from transient local infection to the life-threatening effects of systemic typhoid fever. These organisms employ a sophisticated range of mechanisms to subvert and evade host immune defences. In her review, Wick [1] uses the mouse model of *Salmonella enterica* serovar Typhimurium to highlight the crucial role which myeloid cells such as monocytes, macrophages and dendritic cells play in intestinal defence and in preventing systemic dissemination of this group of pathogens. The nature of mucosal macrophages is addressed in more detail by Mowat and Bain [2], who discuss the apparently paradoxical roles these cells can play

both in healthy intestine and in inflammatory bowel diseases such as Crohn's disease. In particular, they address current ideas on the possible origins and natures of the functionally distinct populations that appear under these conditions.

Until recently, eosinophils were considered to have restricted roles as effector cells in IgE-dependent inflammatory processes in the mucosa such as parasite infections and allergic hypersensitivities. However, it has become appreciated that eosinophils may be surprisingly frequent in the normal gut and Svensson-Frej [3] reviews intriguing new ideas that these cells may play also crucial roles in intestinal homeostasis. More conventional properties of eosinophils are the subject of the research paper by Johnsson et al. [4], which compares the phenotypic characteristics of blood eosinophils in patients with airway allergy, ulcerative colitis and eosinophilic oesophagitis. By combining this with measurements of chemokines and cytokines that regulate eosinophil functions, they conclude that eosinophils can acquire a variety of activities that are tailored to individual pathologies.

One of the biggest recent advances in immunology has been the identification of a number of different innate lymphoid cells (ILC) and these are especially abundant in the intestine. Aparicio-Domingo and Cupedo [5] discuss the ILC which express the nuclear hormone receptor RORC and appear to be related to lymphoid tissue inducer cells (Lti). Found in both humans and rodents, these

Lti-like ILC produce large amounts of IL22 and play important roles in healthy intestine by promoting the development of organised lymphoid tissues, regulating epithelial cell renewal and having antibacterial effects. However, during inflammation or in infection, they can switch to producing mediators such as IL17 or γ IFN, thus acting as early innate effector cells. Harrison and Maloy [6] continue this theme in more depth by discussing the role of ILC in intestinal inflammation such as that caused by *Helicobacter hepaticus* in mice and describing how plasticity amongst these cells allows them to be critical sources of different pathogenic mediators. The ways in which ILC can interact with local microbes is also the

subject of the research paper by Ohue et al. [7], who describe how this process is not restricted to effector lymphocytes but can also determine the activity of regulatory T cells. Thus they show that GroEL, a heat shock protein produced by the intestinal microbiota, drives the differentiation of naïve CD4⁺ T cells into CD25⁺ FoxP3⁺ T cells, a population known to be essential for maintaining healthy function in the gut.

Altogether this issue demonstrates the variety and sophistication of innate immune functions present in the intestine and highlights how these are beautifully adapted to maintain the delicate balance between local microbes which is essential for health.

References

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