A Leak in the Dike

In the 19th century poem *A Leak in the Dyke* by the American writer Phoebe Cary, a young Dutch boy saves his community by jamming a finger into a leaking levee, illustrating the importance of barrier integrity but also the need of supportive measures. A similar view on epithelial linings as simple physical barriers of the body is often taken, but in recent decades, a broad spectrum of dynamic functions has been described for the epithelial cells. These include chemokine production to recruit immune cells, synthesis of antibacterial molecules, and interaction with the adaptive immune system during immunization [1–4]. In this issue, Carl Persson [5] takes a thought-provoking and maybe unorthodox viewpoint on host defense at the mucosal surfaces in his review. He discusses the importance of non-sieved plasma proteins/peptides at the surface of intact mucosal barriers in vivo. These proteins, including antimicrobial proteins, are likely to play important roles in host defense.

Often adjacent to the mucosal lining, macrophages display a large plasticity and can be divided into numerous subsets that often are tissue specific where they exert broad sets of functions [6–10]. In an experimental study, van Riet et al. [11] show that subsets, i.e., M(GM-CSF) and M(M-CSF) macrophages, respectively, play different roles during inflammation, enhancing epithelial innate immunity and wound repair to different extents. Macrophages are important gatekeepers and recognize intruding pathogens at an early stage. TLR9 is localized in their endosomes, acting as a sensor for unmethylated CpG motifs that are present in bacteria, DNA viruses (e.g., HSV-1), and fungi. In an important study presented in this issue, Zyzak et al. [12] show that the MyD88 adapter-like

(Mal) adapter molecule, considered important for recognition of bacteria through TLR2- and TLR4-dependent pathways, is engaged in TLR9-dependent expression of genes encoding IFN β and TNF α in macrophages infected by *Herpes simplex*.

Another important cell in proximity of epithelial linings is the mast cell, commonly associated with its content and release of histamine and heparin but also a broad set of immunoregulatory functions through production of cytokines and eicosanoids. It has become evident that mast cell proteases play important roles in the immunobiology of mast cells and their roles in disease. In an intriguing review, Gunnar Pejler [13] provides an overview of the current understanding of mast cell chymase. Mucosal-associated invariant T (MAIT) cells are getting increasing attention as they produce proinflammatory cytokines in an innate-like manner and play an important role in controlling the host immune response [14]. Inflammatory bowel disease, particularly in the case of ulcerative colitis, is characterized by mucosal inflammation. Ju et al. [15] found that circulating MAIT cell levels were reduced in these patients. Furthermore, MAIT cell deficiency was correlated with disease activity, and their state of activation was increased. Taken together, this suggests important roles for MAIT cells in inflammatory bowel disease.

In conclusion, this issue mainly focuses on the mucosa and cells in its neighborhood. We hope that the articles will provide interesting reading to the readership of the journal!

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Conflict of Interest Statement

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