Abstract

The intestinal immune system is constantly faced with a vast variety of foreign antigens from food and commensal microbiota on top of intestinal self-antigens. To prevent pathology, the immune system developed multiple mechanisms to tolerate these harmless antigens. These mechanisms use a collaboration of thymic T-cell selection and intestinal homeostatic processes. At the same time, intestinal microbiota must be tightly controlled to prevent its overgrowth, which can lead to pathology. Thus, the intestinal immune system must use a combination of tolerogenic and immunogenic responses and keep them in equilibrium. In this thesis I first provide an overview of the current state of knowledge of these processes and then I present several original studies in which I have participated. First and foremost, in the study that is central to this thesis, we have shown that IL-17-mediated stimulation of Paneth cell antimicrobial functions is one of the important mechanisms of immune-mediated control of commensal microbiota and its perturbation results in intestinal pathology susceptibility. Additionally, I have participated in several other studies, which in combination extend the view of intestinal homeostasis, integrating intestine-specific processes with thymic T-cell selection and reactions to pathobionts. One of these studies identified a novel mechanism that ensures proper thymic T-cells selection, through the transfer of antigens from thymic epithelium to a specific population of $CD14^+$ dendritic cells. In a follow-up study, we described the complexity of the cellular network that participates in this mode of antigen transfer in the thymus. In another study, we identified a population of $Aire^+$ ILC3-like cells that were later found to play a crucial role in immune response to mucosal pathobiont *Candida albicans*. Here I discuss our original findings with previously published results, to deliver a multilayered model of establishment and maintenance of intestinal homeostasis.