Birkhäuser Advances in Infectious Diseases

Infection, Immune Homeostasis and Immune Privilege

Bearbeitet von
Joan Stein-Streilein

1. Auflage 2012. Buch. XI, 153 S. Hardcover
ISBN 978 3 0348 0444 8
Format (B x L): 15,5 x 23,5 cm
Gewicht: 421 g

Preface

This book is aimed at reviewing the immune homeostatic mechanisms that regulate inflammation in the context of the innate and the adaptive immune response, the microbiome, and the environment at the level of the organ/tissue and in relation to the select infections that invade those organs.

A powerful protector of mammalian organs and tissues is an omniscient and plastic immune response. The immune response begins with innate responses that are able to respond immediately to infectious agents or foreign substances. These are induced by cells of myeloid lineage as well as select lymphocytes. The adaptive immune response results from sophisticated processes that sense antigens in the periphery and transport them to the secondary lymphoid organs where cells are poised in G_0 ready to differentiate into a variety of immune effector cells that deal with the antigenic threat both locally and peripherally. Similarly, adaptive immune responses are affected by cells of the myeloid and lymphoid lineage. Adaptive immune responses are associated with cytokines and antibodies that induce the accompanying inflammation. Both the innate and the adaptive immune responses induce inflammation that has the potential of leading to tissue damage. In order to prevent unregulated inflammation that causes tissue destruction and disease, self-imposed regulatory mechanisms are triggered almost simultaneously with the induction of the response to ensure its safe termination and restore immune homeostasis in the organ/tissue. The initiation of the immune response is dependent on secondary lymphoid tissue for the primary response to occur, but the immune regulation of the innate and the adaptive immune response occurs at the level of the tissue. Therefore, the regulatory response is fashioned to preserve the function of that tissue by limiting inflammation.

This book seeks to connect the knowledge of immune regulation in one tissue with another. In the eye the tissue is highly protected from inflammation and is left to defeat infectious invaders with mechanisms that lack inflammation. The eye, brain, reproductive tract, and (more recently) the liver are tissues that are commonly accepted to express immune privilege. The lung and gut, however, share many of the mechanisms of immune privilege as the reader will discover when reading these chapters. The lung and gut both have high levels of TGFβ and

importantly use mechanisms to suppress the antigen-presenting ability of the local dendritic cell/macrophage populations.

Much of our information on immune privilege comes from the eye. In order to protect the visual pathway, highly sophisticated mechanisms cooperated to limit damaging inflammation from occurring. Hazlett's and Stein-Streilein's chapter on the eye focuses on the innate and the adaptive immune regulatory mechanisms in detail and considers the infections that occur mostly in the anterior portion of the eye, as well as how they are treated.

The testes and the placental, both considered to be immune privileged sites, have developed similar and unique mechanisms to those we know that exist in the eye. Mark Hedger has very effectively completed his task of clarifying the meaning, mechanisms, and manifestations of immune privilege in the testes with academic grace. Like the eye, although inflammation in the testis is controlled by multiple overlapping mechanisms of immune suppression, the testes do not display an increased susceptibility to tumors or infections compared to other tissues and are actually rare compared to more distal tissues of the male reproductive tract. Nagamatsu and Schust focused their review on how the immune privilege in the placenta allows the genetically disparate fetus to thrive and grow without immune attack by the allogeneic maternal cells. They explain how gestational hormones and placenta-derived substance actively modulate maternal immunity and promote tolerance to the antigenically disparate fetus. Their well-conceived review considers the costs of immune privilege in the placenta in terms of increased infectious disease in mother and fetus.

The liver is a tissue that is unique in its ability to regenerate and is the only tissue that can be successfully transplanted across allogeneic lines without the need for immunosuppression. Not only is it accepted, but if a tissue that is normally rejected is cotransplanted with the liver, it too is protected. Wohlleber's and Knolle's review delightfully educates us on the unique qualities of the immune privilege in the liver.

Chang, DeKruyff, and Umetsu have carefully focused their review on immune homeostasis in the lungs in the regulation of asthma. Their presentation adds insight into the readers' understanding of the "Hygiene Hypothesis" and stimulates new thoughts that connect the ideas presented about the gut and microbiome to the lung.

Last, but ever so important, the bacteria in the gut are controlled by compartmentalization, monitoring, and selection of the microbial ecosystem. Some bacteria promote tolerance while others promote inflammation. Thus the prevention of harmful inflammatory responses is the result of a joint effort on the part of the host's immune system, the physiology of the host, and the members of the gut microbial community (microbiome) and can be directly influenced by the environment. Wroblewska and Nagler have elegantly simplified the complicated interactions and mechanisms of the homeostasis and privileged protection of the gut from food antigens and bacteria in their chapter.

Overall, we might conclude that if left unregulated, the inflammatory response can be the most destructive aspect of the immune response. Inflammation is the offense for both the innate and the adaptive immune response. Unlike the adaptive immune response, cells of the innate immune response are not dependent on

secondary lymphoid organs for their generation and function. Innate cells are able to respond immediately to danger, in part by their expression of receptors that recognize pathogen-associated molecular pattern (PAMP). Such receptors include Toll-like receptors, adhesion molecules, and scavenger molecules. Activation of PAMP receptors induces the production and release of inflammatory cytokines and complement factors. The adaptive immune response requires that the lymphocytes differentiate into effector cells and only after their differentiation they are capable of secreting inflammatory cytokines and contributing to tissue destruction. However, built into the immune response is the simultaneous production of suppressive molecules, the downregulation of activating receptors, the inhibitors of their signaling pathways, and the molecules that when linked to their ligands will induce apoptosis.

Within the last decade, the importance of nonlymphoid cells in immune regulation and the immune homeostasis of tissues has become known. Molecules that were thought to be markers of lymphocytes now are known to be expressed by endothelial, epithelial, and various other stromal cells. These molecules and receptors thus allow the stromal cells to interact and regulate the lymphocytes within their environment. And yes, we continue to learn.

Boston, MA Joan Stein-Streilein