
Preface

“Le savant n’est pas l’homme qui fournit les vraies réponses, c’est celui qui pose les vraies questions.”

Claude Lévi-Strauss

The immune system is able to mount an effective immune response to virtually any foreign antigen but does not react against self-components. One of the mechanisms for doing that is to create the largest repertoire of B and T cells able to recognize the most antigen candidates imaginable. This can also in some cases represent a problem as the immune system may recognize self-antigen as foreign antigens and mount an immune response leading to the destruction of self and developing autoimmune diseases. In order to avoid that, most autoreactive cells are eliminated or neutralized by a mechanism called self-tolerance. There are two components of self-tolerance: central and peripheral. Central tolerance occurs in the primary sites of lymphocytic maturation (thymus and bone marrow) where deletion of cells that react strongly with self-antigens (clonal deletion) takes place in the thymus (T cells) or bone marrow (B cells). These cells will undergo apoptosis and die (negative selection). The cells that have moderate self-recognition will survive and migrate to the periphery (positive selection). The lymphocytes that escape central tolerance come to the periphery where they can meet and also interact with self-antigen, but in the periphery there are also regulatory mechanisms which balance the activation of an immune response (immunity against pathogens) and its suppression to control the magnitude of the immune response and prevent unwanted damage or its regulation toward self-antigen (tolerance). Moreover, there are some special cases in which the immune system has to tolerate foreign antigens while requiring the capacity to respond to infections, as in the case of pregnancy. One of the goals of immunological research is to understand the mechanisms which regulate the immune system. We can define immunoregulation as a balance between activation and suppression/regulation of the immune response in order to achieve an efficient response without damaging the host. The characterization of the mechanisms of immunoregulation would not only allow us to make predictions about the outcome of a particular immune response, but also to define the ways of controlling this response either by amplification or inhibition. This would have practical consequences for certain clinical situations, e.g., the inhibition of the immune response in allergic, transplantation, or autoimmune diseases or the enhancement of the immune response in the case of infectious diseases or cancer.

Over the past several years, a high diversity of regulatory cells and suppressive molecules has taken center stage in the field of immunoregulation. Several types of regulatory cells have been described on the basis of their origin, generation, and mechanisms of action. T-regulatory cells (naturally occurring and inducible ones) were the most studied, and several subsets were identified (CD4+, CD8+, and CD4–CD8–). This book will highlight recent advances in the identification, characterization, and generation of regulatory cells not only of the T-cell lineage but also of other origins such as B, NK, myeloid, and

dendritic cells. We will also approach the role of several suppressive molecules in immunoregulation. Certain physiological situations where immunoregulation plays a central role as in pregnancy will be treated separately. Particular emphasis will be put on the characterization of the molecular mechanisms and the therapeutic applications of regulatory cells and molecules in human diseases.

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Methods and Protocols

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