METHODS IN MOLECULAR BIOLOGY

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Immunological Tolerance

Methods and Protocols

Edited by

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Preface

"Immunological Tolerance," the state in which the body is unresponsive to antigen, ensures the development of a "non-self" reactive T cell repertoire, as well as development of tolerogenic regulatory immune populations that protect us from disease. Continuing to understand how tolerance develops and, in the context of diseases such as autoimmunity and cancer, falters and breaks down will offer invaluable insight into how to manipulate these mechanisms to improve treatment of these diseases. This knowledge may also be applied to induce immunological tolerance in the setting of allogeneic transplantation as first described by Peter Medawar and Frank Macfarlane Burnet, who were awarded a Nobel Prize in 1960 for their seminal work in transplantation tolerance.

Since then the concept of immunological tolerance has blossomed into an entire, separate discipline in immunology, where advances have been regularly observed in small and large animal model systems but as of yet have largely failed to be replicated in the clinical setting. Yet, with recent advances in immunotherapy and techniques such as genome editing in concert with the isolation and characterization of novel subsets of tolerogenic cells, the prospect for harnessing the power of the immune system clinically to control unwanted responses to both self and foreign antigen now appears to be edging closer to reality than ever before.

With this in mind, I have developed this edition with a strong emphasis on techniques that can be used to understand or manipulate tolerance in human cells and to assess human disease in this setting directly. The chapters have been organized thematically into five parts. In Part 1, we focus on the isolation of tolerogenic cell types from stem cells, which are a self-renewing cell type responsible for producing and maintaining tissues in the body. While their biology in this respect is well established, different classes of stem cells and their progeny are now emerging as potential agents of immunomodulation, and we explore this capacity from both ex vivo isolated stem cells and laboratory-engineered stem cells (so-called induced pluripotent stem cells). Part 2 extends the premise of isolating tolerogenic cell populations for study and therapeutic utility by covering the ex vivo isolation of tolerogenic lymphocytic cells, including recently characterized B regulatory populations. In Part 3, we explore multiple methods to study the mechanisms underpinning tolerance, as well methods to induce tolerance through thymus progenitors which may be utilized in the future to reconstruct the thymus, the key site for central tolerance induction. How such methods of tolerance induction are invoked practically, as first envisioned by Medawar and Burnet, in context of transplantation, is considered in Part 4. Finally, Part 5 includes methods to assess the breakdown of immune tolerance in specific pathological conditions.

When I was asked to compile this special edition of *Methods in Molecular Biology* on "Immunological Tolerance" I was both honored and somewhat daunted by the task of covering the massive scope of the field. I have attempted to focus on what I consider to be important contemporaneous issues and methods, which I sincerely hope you will enjoy and find useful in your quest to further advance the field.

Finally, it would be remiss of me not to acknowledge my husband, Neil, for his steadfast support of my academic career (and in life in general), and to our daughter, Olivia, the light of our lives, who makes us realize what really matters in the end.

London, UK ***Ashleigh S. Boyd***

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