Book Reviews

Taams LS, Akbar AN, Wauben MHM, editors. Regulatory T Cells in Inflammation (Progress in Inflammation Research, Parnham MJ, series editor). Basel: Birkhäuser Verlag; 2005. 240 pages; ISBN 3764370882; price: $159.00

Fields of medicine: Immunology.

Format: Hardcover book.

Audience: Academic and industrial biomedical researchers, drug development personnel and rheumatologists, allergists, pathologists, and dermatologists.

Purpose: The book is a part of a monograph series edited by acknowledged experts, which provides up-to-date information and presents a compilation of selected articles on the latest developments in the pathology, mechanisms, and therapy of inflammatory diseases.

Content: The book is divided into two parts: the first consists of five chapters that represent an overview on the origin, function, and distribution of regulatory T cells; the second part aims to present the potential use of these cells in immunotherapy. The first chapter has been written by one of the most influential immunologists in the field, Shimon Sakaguchi, and his collaborator Noriko Sakaguchi, whose work and, I dare to say, scientific perseverance succeeded in reviving the scientific interest in a specialized cell subset important for inhibiting or suppressing aberrant or excessive immune responses to self-antigens and non-self-antigens. Although in any field it is natural and logical to first give a historical overview, in the case of regulatory T cells this is necessary. Immunologists have dwelled on different mechanisms of control of harmful and/or exaggerated immune reactions for many years. Once it was realized that the thymus is not perfect and that harmful cells could escape mechanisms of central tolerance, immunologists, including Sakaguchi, looked for other mechanisms important for immune surveillance and homeostasis (the so-called peripheral tolerance). In the past, the cells associated with immune tolerance and homeostasis were called "suppressor T cells." However, in the absence of strong and reproducible scientific data, the existence of these cells was questionable and many immunologists argued against their existence as a functionally definite cellular entity in the immune system. In the past five years, we witnessed the resurrection of the interest in this specialized cell subset. A new name, regulatory T cell, was introduced in order to reflect the current understanding that these cells do not exclusively suppress immune reaction. Other four chapters reflect

precisely the hurdle generated by the power of modern immunology or, more accurately, modern immunological techniques that revealed heterogeneity among regulatory T cells. Many inconsistencies in published data cannot be explained just by different experimental approaches or models, and scientist found that there was no specific phenotype of any among the regulatory T cell subsets. Furthermore, these cells have different cytokine dependency, antigen specificity, migratory capacity, lifespan, and actual mechanism of immunosuppression. Based on these assumptions, two main approaches have been presented in a series of chapters in Part Two, which aims to elucidate the role of regulatory T cells in human diseases: utilization of natural regulatory T cells or induction of new so-called inducible regulatory T cells. Having now the improved tools to analyze T cells, they became one of the milestones for a possible therapy of different, still incurable human diseases associated with imbalanced immune tolerance and ongoing inflammation such as multiple sclerosis, rheumatoid arthritis, type 1 diabetes mellitus, skin diseases, and transplantation tolerance. The authors of these chapters are well-known immunologists who tackled the immune mechanisms of these diseases from various angles, and not just from the angle of regulatory T cells. Some regulatory T cell popula-

tions are naturally produced in the thymus as functionally distinct populations, while others are adaptively induced from naïve T cells as a consequence of a particular mode of antigen exposure, especially in a particular cytokine milieu. This heterogeneity and apparent redundancy of regulatory T cells populations presented in these chapters may not be surprising when one considers the vital importance of maintaining immune homeostasis and self-tolerance, clearly evident by its disturbance in cases of autoimmune disease. However, one cannot but conclude that, in most of these articles, the present and past experimental findings are attributed to the action of regulatory T cells. The first two chapters in Part Two present the current knowledge on the role of different regulatory T cell subsets and immunoregulatory cytokines (interleukin-10 and transforming growth factor β), that might help restore the tolerance to self-antigens in patients with type 1 diabetes mellitus using the mouse model. In contrast to the first two, the third chapter describes the findings in patients with multiple sclerosis, in which profound changes in functional activity of regulatory T cells have now been recognized. It is evident that all these diseases develop in the presence of regulatory T cells, so it is mandatory to understand their most probable functional defect, prior to any attempts to

use these cells as targets of immunotherapy, as described in the following chapters. Adoptive transfer of antigen-stimulated regulatory T cells has indeed provided encouraging results in various animal models, but it is still a matter of debate whether these cells will be effective in blocking the chronic inflammation in diseases such as rheumatoid arthritis and allergy, as well as in maintaining the allograft tolerance. In the fifth chapter, written by Robinson and Ling, the potential role of regulatory T cells in allergy is used to explain why allergen-specific T cells do not proliferate in vitro in the presence of allergen, in contrast to allergic individuals. Based on these findings, a new concept of regulation failure (and not Th1/Th2 disbalance) has been proposed for understanding allergic diseases. This chapter also presents data on the effect of current allergic diseases therapy on regulatory T cells, such as corticosteroid therapy and immunotherapy in order to explain the lack of substantial progress both in the prevention and control of allergic diseases, which are an increasing cause of chronic illness and a great burden to national health care cost worldwide.

In several skin diseases, such as atopic dermatitis and psoriasis, the role of T cells has been demonstrated. Regulatory T cells have the ability to migrate to sites of inflammation within the skin, but as was shown in

many other diseases, these cells seem to be dysfunctional. The manipulation of regulatory T cells by either enhancing or reducing their suppressive effects may also be modulated by therapy such as phototherapy, tacrolimus, and vitamin D derivatives. In the last chapter, Wood and Akl present the current understanding of the potential role of regulatory T cells in the induction and maintenance of transplantation tolerance in humans. Since no molecule or gene has been found to fulfill the criteria of exclusivity and stability for the identification of regulatory T cells, the possible use of these cells as an add-on therapy following transplantation is still under vigorous investigation.

Highlights: The book is a good overview of the recent advances in regulatory T cell biology in inflammatory diseases, with some particularly useful chapters for those who are new in the field. These readers will also benefit from the index provided at the end. The list of literature sources at the end of each chapter is exhaustive and should help the readers to track most important papers upon which our current understanding in this field of immunology has been built on.

Limitations: As with any other fast expanding field of science, journals publishing review articles are usually more up to date with new data. For example, an entire issue of Immunological Reviews in 2001 was devoted to regulatory T cells and its 2006 June issue highlights the explosive interest in these cells.

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Iland H, Hertzberg M, Marlton P, editors. Myeloid Leukemia Methods and Protocols. Totowa, NJ: Humana Press; 2006. 306 pages; ISBN 1-58829-485-4; price: $125.00

Field of medicine: Hematology.
Format: Hardcover book.
Audience: Biomedical researchers in the field of hematology and oncology, cytogeneticists, hematologists, oncologists, immunologists, and other clinicians looking for regular scientific updates.
Purpose: To provide a diverse collection of readily reproducible methods for identifying and quantifying a large number of specific genetic abnormalities associated with the broad spectrum of myeloid malignancies. The methods range from those of immediate clinical relevance to the investigation and management of patients with myeloid malignancies, to those that relate to recently identified genetic abnormalities and are a ready source of information for the scientific community. collected in a single book.
Content: The book is divided into eighteen chapters, which include detailed protocols of advanced techniques important for diagnosis and treatment of myeloid leukemia, assessment of minimal residual disease, and discovery of gene mutations. Each chapter consists of

a short summary, introduction to the chapter, followed by materials needed for a certain protocol, methods, notes, and references. Within the materials section, each chapter provides detailed description of all required chemicals, labware, and specimens. Methods describe all applied techniques in a step-by-step manner. Protocols are followed by notes on troubleshooting that help researchers to avoid potential pitfalls. Finally, each chapter ends with the references that list the original descriptions of all methods. Also, the text is accompanied by figures and tables which make procedures more clearer. The index, at the end of the book, allows quick orientation among basic terms and selective reading of specific methods.

The first three chapters deal with techniques generally applicable to molecular biology (isolation of RNA and DNA from leukocytes and cDNA synthesis), cytogenetics, and fluorescence in situ hybridization. An overview of the expanding field of real-time quantitative polymerase chain reaction (PCR) is also included.

In the fourth chapter, the application of real time qPCR for the quantification of fusion gene BCR-ABL mRNA as the indicator of leukemic cell mass in the blood of patients with chronic myeloid leukemia (CML) is described.

The fifth chapter deals with detection of BCR-ABL mutations and resistance to imatinib mesylate, a specific tyrosine kinase inhibitor, which is the treatment option for patients with chronic myeloid leukemia.

The sixth chapter outlines the use of FISH method to identify deletions of the derivative chromosome 9 in order to detect residual disease in patients with CML after therapy.

The seventh and eight chapters deal with diagnosis and monitoring of acute promyelocytic leukemia (APL) and application of reverse transcription polymerase chain reaction for the detection of PML-RARA fusion gene as the diagnostic hallmark of APL.

The ninth and tenth chapter deal with detection of the mutation present in myeloid leukemias, qualitative and quantitative protocols for the diagnosis and minimal residual disease (MRD) monitoring in acute myeloid leukemia (AML).

In the eleventh chapter three different techniques to detect the presence of the FI1L1-PDGFRA fusion gene, characteristic for idiopathic hypereosinophilic syndrome and chronic eosinophilic leukemia are described.

The twelfth chapter describes methods for detecting internal tandem duplication and missense mutation of D38 in the FLT3 gene which is strongly associated with a poor prognosis in patients with AML.

Methods for quantification of tumor suppressor gene WT1 transcript which is overexpressed in acute and chronic leukemias are described in the chapter 13.

The fourteenth chapter outlines the use of microarrays for gene expression profiling of leukemia samples and how to approach the analysis of data.

Classification of AML using a monoclonal antibody microarray is described in the chapter 15.

In the sixteenth chapter two polymerase chain reaction-based methods for detection of the JAK2 V617F mutation in human myeloproliferative disorders are described.

The application of RT-PCR for detection of PRV-1 gene in polycythemia rubra vera and essential thrombocythemia is described in the chapter 17.

The final chapter introduces the investigation of donor and recipient derived hematopoiesis by molecular techniques, which facilitates the monitoring of engraftment kinetics in patients after allogeneic stem cell transplantation.

Highlights: Laboratory techniques featured in this book are most likely to assist "laboratory scientists and hematologists in the investigation and management of patients with myeloid malignancies." The included protocols are highly reproducible and reliable, presented in a step-by-step way, suitable even

for novice investigators who need profound and practical information to get started. The book not only provides up-dated knowledge in a specific field and detailed descriptions of related methods, but also includes into each chapter a section on troubleshooting indicated in the notes section. Therefore, it is a powerful tool for successful investigation in the hematology field.

Limitations: Although each chapter begins with an introduction, it cannot give the complete overview of rather complex pathology. One of the limitations could be that the book does not include all the molecular abnormalities associated with myeloid malignancies, but it would be hard to believe that any book can cover all possible methods in such a complex field.

Related reading: Many other books from the Methods in Molecular Biology Series would be equally powerful and high-quality source of practical information for the researchers in the field of hematology. Among many others, some recently published volumes related to hematology include Lymphoma Methods and Protocols, Multiple Myeloma Methods and Protocols, Biology and Management of Multiple Myeloma, Molecular Diagnosis of Cancer Methods and Protocols, and others. Each volume is edited by acknowledged experts and presents a reliable set of techniques in certain specific field.

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