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BOOK REVIEW*

ANNUAL REVIEW OF IMMUNOLOGY, vol. 16, 1998; edited by William E. Paul, C. Garrison Fathman & Laurie H. Glimcher. Palo Alto, Annual Reviews Inc., 1998. 714p. ilust. ISBN : 0-8243-3016-1

The area of Infectious Diseases has been the target for several publications in previous volumes in this scientific series. In 1998, this area is covered in two chapters. In the past ten years, the field of malaria vaccines has increased enormously. Recently, a successful human trial of a vaccine aimed at sporozoites was completed. However, it is the red blood cell stage of the parasite that causes disease, and it is against this stage that it has proven very difficult to induce a protective immune response by vaccination. M. F. GOOD *et al*. review current position of this field, analyse the major obstacles to vaccine development and focus on pathways and strategies for developing a malaria blood-stage vaccine.Various studies have indicated that host genetic factors are major determinants of susceptibility to infectious diseases in humans with most of the genetic mapping outside of MHC. Candidate genes studies have implicated several immunogenetic polymorphisms in infectious diseases. HLA variation has been associated with susceptibility or resistence to malaria, tuberculosis, leprosy, HIV progression, and hepatites (B and C) virus persistence. Variation in TNF gene promoter has also been associated with cerebral malaria, mucocutaneous leishmaniasis, and lepromatous leprosy. A. V. S. HILL reviews some of the evidence on the nature and extent of the host genetic contribution to infectious diseases susceptibility. The author analyses also recent association studies of particular candidate genes. Finally, progress on immunogenetic results on malaria and HIV are summarized.

Eight chapters in this volume deal with lymphocyte development, activation, and differentiation. The interaction CD40 and CD154 (CD40 ligand) mediates contact-dependent signals between B and T cells required for the generation of thymus dependent humoral immune responses. Recent studies indicate expression of CD40 by a large variety of cells types other than B cells, and these include dendritic cells, follicular dendritic cells, monocytes, macrophages, mast cells, fibroblasts, and endothelial cells. In a excellent review, I. S. GREWAL & R. A. FLAVELL focus on the importance of CD40-CD154 interactions in non-B cell mediated cellular functions. A. HENDERSON & K. CALAME summarize recent studies on transcription factors and coativators with respect to changes in expression patterns of various genes during B cell development. NF-KB is a eucaryotic transcription factor that exists in virtually all cell types. Its responsive sites (KB sites) have been characterized in the promoters and enhancers of numerous genes, making NF-KB an important component in the inducible expression of many proteins, including cytocines, acute phase response proteins, and cell adhesion molecules. The known members of the NF-KB family of transcription factors, recent knowledge about the signaling pathways leading to their activation, and their potential role as central coordinators of the innate immune response are described by S. GHOSH *et al*. The families of proteins Jaks (Janus family tyrosine kinases) and STATS (signal transducers and activators of transcription) together constitute a signaling system triggered by cytokines and interferons that rapidly allow the transduction of an extracellular signal into the nucleous. W. J. LEONARD & J. J. O'SHEA review the basic biology of the Jak-STAT pathway and its biological implications specially in animals and humans lacking some of these molecules. D. T. CHAO & S. J. KORSMEYER analyse the BCL-2 family of proteins, a new category of oncogenes that functions in preventing programmed cell death instead of promoting proliferation. Dimerization – an important subset of physical protein–protein interactions – as a regulatory mechanism in signal transduction from the cell surface to nucleous, is reviewed by J. D. KLEMM *et al*. The authors focus on the functional consequences of dimerization and describe specific molecules that homodimerise or heterodimerise in response to a given signal. CD81 (TAPA-1) is a widely expressed cell-surface protein involved in a large variety of biologic responses. CD81 belongs to the super-family of proteins known as tetrapanins expressed in evolutionarily diverse organisms, suggesting a conserved role for these proteins. In a very intersting review, S. LEVY *et al*. summarize recent progress concerning the structural features of CD81, its known interactions with other cellular proteins, and the effects induced by cross-linking the protein on the cell surface. Finally, J. I. HEALY & C. C. GOODNOW outlined the ways that antigen receptors can trigger positive or negative responses in lymphocytes at the same or different stages of development.

The area of T Lymphocyte Receptors are examined in three chapters. As M. DAVIS *et al*. point out in a very up-to-date article, the last few years have seen the study of T cell recognition enter an exciting new phase. The authors discuss the first structures of T cell receptor molecules and, particularly, TCR-ligand complexes. They present also an analysis of the highly diverse CDR3 loops found in all antigen receptor molecules and suggest that such regions form the core of both TCR and antibody specificity. NK-cell function appears to be regulated by a balance between positive-signaling receptors that initiate, and inhibitory receptors that supress, cell activation. While positive stimulation may be initiated by an array of co-stimulatory receptors (CD16, CD2, NKR-P1, and CD40ligand), specificity is provided by inhibitory signals transduced by receptors for MHC Class I. L. LANIER analyses recent studies suggesting that inhibitory NK cell receptors (Ly 49, CD94, and KIR) are members of a larger superfamily containing ITIM sequences, the so called inhibitory receptor superfamily (IRS). The interleukin-1 receptor antagonist (IL-1Ra) is the first described naturally occurring specific

* This book is available at the Library of the Instituto de Medicina Tropical de São Paulo.

receptor antagonist of any cytokine or hormone-like molecule. Endogenous IL-1Ra is produced by hepatic cells with the characteristics of an acute phase protein in human autoimmune and chronic inflammatoty diseases. W. AREND *et al*. summarize recent information on structural variants of IL-1Ra, the role of IL-1Ra in biologic processes, and the effects of endogenous or exogenous IL-1Ra in human diseases.

E. PAMER & P. CRESSWELL review current understanding of MHC Class I – restricted antigen processing, covering antigen degradation by proteasomes, peptide transport into the endoplasmatic reticulum, the assembly and efficiency of the MHC-peptide complex, and antigen presentation by MHC Class Ia and Ib molecules. In the field of transplantation, H. AUCHINCLOSS & D. T. SACHES summarize the clinical history and rationale for xenotransplantation; types of xenotransplants and their special features; the progress that has been made in understanding the physiologic, immunologic, and potential infectious barriers to its success; and some of the strategies being pursued to overcome these obstacles such as genetic engineering and indution of tolerance – inducing approaches.

In the area of Antigen-presentation, recent results obtained in mice deficient in either Fc receptors (FcRs) or complement have revealed distinct functions for these two classes of molecules. These results led to the surprising conclusion that these two systems have evolved distinct functions in host immunity, with complement and its receptors mediating the interaction of natural antibodies (IgM) with pathogens to effect protection, while FcRs couple the interaction of IgG antibodies to effector cells to trigger inflammatory sequelae. In a exciting chapter, J. V. RAVETCH & R. A. CLYNES analyse divergent roles for Fc receptors and complement *in vivo.* Covalent attachment of activated complement C3 (C3d) to antigen links innate and adaptative immunity by targeting antigen to follicular dendritic cells and B cells via specific receptors CD21 (CR2) and CD35 (CR1). Recent studies that address the mechanism for complement regulation of B cell development within the secondary lymphoid compartment are reviewed by M. C. CARROL.

Much information has been obtained on Regulation of Immune Response. The TGF-β family of proteins are a set of pleiotropic secreted signaling molecules with unique and potent immunoregulatory properties. TGF-β is produced by every leukocyte lineage and can control the differentiation, proliferation and state of activation of these immune cells. TGF-β can also modulate expression of adhesion molecules, provide a chemiotatic gradient for inflammatory cells, and inhibit them once they have been activated. In addition to these roles, TGF-β have been linked in disease pathogenesis and oral tolerance. J. J. LETTERIO & A. B. ROBERTS focus on the ability of TGF-β to regulate the function and interaction of cells of the immune system in the development of both humoral and cell-mediated immunity. Finally, important aspects of autoimmune diseases, parasitic infections, and immunologic tolerance are also analysed in this up-to-date article. Endogenous IL-12 plays an essential role in the optimal generation of IFN-γ secreting Th1 cells. Though this action, Il-12 plays a central role in both innate and adaptative immunity important to the host defence against predominantly intracellular pathogens. M. K. GATELY *et al*. focus on more recent information on the structure and function of the IL-12 receptor and the role of IL-12 in both normal immune response and some pathologic conditions such as endotoxin-induced shock, insulin-dependent diabetes mellitus, inflammatory bowel disease, GVHD, and asthma. Immunological memory can be defined as the faster and stronger response of an animal that follows reexposure to the same antigen. The pathway to the B cell memory occurs in germinal centers and emerges after isotype switching and hypermutation of the immunoglobulin genes. By the other hand, the case for a memory T cell is less clear: it is unclear how or where memory cells arise, and the question remains whether there is also a quantitative change leading to an altered T cell that can be called a "memory" cell and, if there is a memory T cell, how can it be identified. In a informative review, R. D. DUTTON *et al*. focus on the classic T cell memory, which is long lived and is carried by small resting lymphocytes rather than ones with the characteristics of activated effectors. As H. WALDMANN & S. COBBOLD point out, one of the major goals in therapeutic immunossupression has been to achieve long-term benefit from short-term, low-impact therapy. In this field, the authors review recent information on how certain biological agents such as monoclonal antibodies, used short-term, can reprogram the immune system to become tolerant to transplanted tissues and to self-antigens in autoimmune diseases.

Two chapters in this volume are dedicated to Autoimmunity and Clinical Immunology. Recent studies have emphasized that systemic lupus erythematosus (SLE), like other autoimmune diseases, is a complex genetic trait with contributions from MHC genes and multiple non-MHC genes. Essentially all of the elements that determine genetic complexity determine susceptibility, and no particular gene is necessary or sufficient for disease expression. Although the identity of the actual genes is currently unknown, recent studies have begun to characterize how these genetic contributions may function in the autoimmune diseases, especially in terms of their role in autoantibodies production. T. J. VYSE & B. L. KOTZIN discuss genetic loci implicated in murine and human lupus. One of the characteristic features of Hodgkin's disease (HD) is the presence of a small population of large mono or multinucleated Hodgkin and Reed-Sternberg cells (HRS) within the affected tissue. In a very interesting and didatic chapter, R. KÜPPERS & K. RAJEWSKY review the origin of HRS cells and discuss studies that characterized these cells as clonal populations derived from a compartment of germinal center B cells in most if not all cases.

This volume 16 of the Annual Review of Immunology contains twenty-four chapters and introduces advanced key concepts in a manner that can be understood by postgraduates and researchers in various fields of Immunology. Therefore, it is recommended to all who wish to be brought up to date on Immunology.

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BOOK REVIEW - LIVRO*

BRIDGE, P.; COUTEAUDIER, Y. & CLARKSON, J., ed. - Molecular variability of fungal pathogens. Wallingford, CAB International, 1998. 319p. ilus.
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This volume contains a series of contributions from established European researchers, which consider aspects of molecular variability in fungal pathogens. Chapters are derived from a workshop held in Evian, France, in September 1977, supported by the EU Concerted Action Air 3-CT94-2448. The volume is divided into three sections. The first includes contributions that consider and review the major mechanism of fungal pathogenesis, the second details specific studies on variability in populations of different fungal pathogens, and the third includes contributions on methods for interpreting such variability.

The workshop brought together methods and understanding from a wide range of fungal pathogens, and this is reflected in the volume, where individual contributions include case studies and reviews of populations of fungi pathogenic on insects and nematodes as well as plant and human pathogens. The combination of mechanisms, characterization and interpretation across a wide range of applied mycology makes this a significant general text for those working on molecular characterization. The broad spectrum of topics provides a multidisciplinary reference source within mycology and the book will be suitable for postgraduate students and research scientists in applied mycology, including plant pathology, medical mycology and biological control.

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