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BOOK REVIEW*

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Recently, several new approaches have been shed light on " in vivo" antigen presentation, cell proliferation, death, migration, tolerance induction, and memory cell generation. In a very interesting chapter, **M.K. JENKINS** *et al*. focus on these new findings with emphasis on unique features of the " in vivo" response that normally were not analyzed in cell culture studies.

The area of **T Lymphocytes and NK Cells** is covered in 3 chapters. NK cells express inhibitory receptors specific for MHC class I proteins, and stimulatory receptors with diverse specificities. NK cells can discriminate between normal cells and cells that do not express adequate amounts of MHC class I molecules. However, the triggering receptors responsible for positive NK cells stimulation remained elusive until recently. In an excellent review, **A. MORETTA** *et al*. report on recently identified human activating NK receptors and co-receptors and the molecular mechanisms responsible for the induction of NK-mediated natural cytotoxicity in humans. In the same field, **D.H. RAULET** *et al*. review the regulation of the NK cell receptor repertoire in a model in which NK cells are regulated by the balance of signaling via stimulatory receptors, specific for ligands, and inhibitory receptors, specific for MHC class I molecules. Elevation of intracellular free calcium is one of the key triggering signals for T cell activation by antigen and other stimuli that cross-link the T cell antigen receptor. The molecular and cellular mechanisms that generate Ca^{2+} signals in T cells, the ways in which they may interact to generate complexity, and the consequences of calcium signaling on gene expression are focused by **R. LEWIS** .

Early experiments examining the nature of MHC-restriction during T cell priming showed that minor MHC antigens were capable of being transferred from cells expressing these antigens to the host APCs, and such antigen presentation was termed cross-presentation. In a very didactic chapter, **W.R. HEATH & F.R. CARBONE** summarize current knowledge of the cross-presenting APC and examine the role of cross-presentation in tolerance and immunity.

Much information can be obtained on the field of **Lymphocyte Development, Activation and Differentiation**. A complicated set of T cell regulatory mechanisms have been implicated on immune regulation. One such mechanism is the requirement of two distinct signals for effective activation of antigen-specific T cells: an antigen-specific signal via the T cell receptor and a noncognate costimulatory signal that is provided by soluble factors or cell-surface molecules on APC. In a very didactic review, **B. SALOMON & J.A. BLUESTONE** summarize current understanding of these complex costimulatory pathways including the individual roles of the CD28, CTLA-4, B7-1 (CD80), and B7-2 (CD86) molecules, and the CD40/CD154 pathway. Finally, the authors summarize recent data on the utility of the selective blockade of these T cell costimulation pathways for use in the treatment of autoimmune diseases and transplantation in nonhuman primates and humans. In the same area, **C.A. CHAMBERS** *et al*. analyze the effectiveness of CTLA-4 blockade in enhancing anti-tumor responses in experimental systems which offer the possibility of translating basic knowledge of costimulatory regulation into new strategies for tumor therapy. T cell activation requires sustained T cell receptor interaction with MHC-peptide complexes in the immunological synapse (IS) between T cell and antigen-presenting cell (APC). The required duration of signaling is on the order of hours, while the activating and inhibitory molecular interactions in the IS have half-lives on the order of seconds. **S.K. BROMLEY** *et al*. review the concept of immunological synapse as a dynamic structure and its formation as it relates to membrane structure, T cell polarity, signaling pathways, and the antigen-presenting cell. Two general classes of IgGFc receptors are now recognized – the activation receptors and the inhibitory receptor – which function in concert and are usually found coexpressed on the cell surface. "In vivo" studies and the implication of those studies for the role of these receptors in maintaining tolerance, shaping the antibody repertoire, and determining the cellular outcome of engagement of FcRs by IgGs are reviewed by **J.V. RAVETCH & S. BOLLAND**. Progress in characterizing stages of developing B cells focusing on genes critical in the early stages of this process, the central role of the pre-B cell receptor and elimination of self-reactive B cells are reviewed by **R.R. HARDY & K. HAYAKAWA.**

Four chapters deal with **Cytokines and Chemokines** in a very didactic manner. The chemokines are a family of low-molecular-weight proteins involved in leukocyte activation and migration. Chemokines which are implicated in the regulation of leukocyte traffic as well as in establishing lymphoid organ architecture constitute the homeostatic chemokines. Another large subset of chemokines appears to provoke inflammatory cell migration into tissues and are named inflammatory chemokines. Both chemokine subsets mediate their function by interacting with specific receptors belonging to the family of seven-transmembrane, G protein-coupled receptors, expressed on the leukocyte surface. **M. MELLADO** *et al.* discuss the JAK/STAT activation pathway, the chimokine receptor dimerization and activation of the Tyrosine Kinase Pathway. Finally, the mechanisms through which the chemokines promote their effect in the context of the prevention of HIV-1 infection are analyzed. IL-18 is a new member of the IL-1 family and its receptor (IL-18R) and its signal transduction pathway are analogous to those of the IL-1R. IL-18 has the capacity to stimulate innate immunity and both Th1 and Th2-mediated responses, and plays important physiological roles in host defense. In a very interesting chapter, **K. NAKANISH** *et al*. review recent advances in the patophysiological roles of IL-18.

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

T. TANIGUSHI *et al*. focus on the historical background of the interferon regulatory factors (IRF) family of transcription factors and discuss its role in the biological systems that operate during host defense. IL-10 is a multifunctional cytokine with diverse effects on most hemopoietic cell types and its principal function appears to be to limite and terminate inflammatory responses. As pointed by **K.W. MOORE** *et al*., their review was written at the tenth anniversary of IL-10's discovery, and the authors emphasizes more recent developments illuminating the role of IL-10 in normal and pathological immune responses "in vivo", as well IL-10 and IL-10 receptor structure and signalling.

Tolerance and Autoimmunity are discussed in two chapters. Insulin-dependent diabetes mellitus (IDDM) ensues from the selective aggression against insulin-secreting β cells of the islets of Langerhans by autoreactive T cells. Both autoreactive CD4+ and CD8+ T cells specific to autoantigens are present in most normal individuals but are kept under control by a number of peripheral tolerance mechanisms, among which CD4+CD25+CD62L+T cell-mediated regulation probably plays a central role. In a very interesting chapter, **J.F. BACH & L. CHATENOUD** discuss main questions as the peaceful coexistence of such "physiologic" autoreactive T cells with the organ expressing the target autoantigen in health individuals; how this equilibrium may be disrupted by inappropriate activation of autoantigen-specific T cells following to local inflammation; genetic and environmental influences; and, restoration of self-tolerance by administration of β-cell antigens or CD3 antibodies or NK T cell stimulation. **M. FELDMANN & R.N. MAINI** review many features of anti-TNF-α therapy of rheumatoid arthritis such as the inhibitors of TNF-α in current clinical use, and the clinical efficacy and the mechanism of action of anti-TNF-α therapy.

The area of **Immunodeficiency** is covered in 2 chapters. The bare lymphocyte syndrome (BLS) is a rare form of hereditary immunodeficiency characterized by the lack of expression of MHC class II molecules, which leads to severe immunodeficiency and recurrent infections. W. **REITH & B. MACH** review clinical features of BLS, its molecular basis, and the current understanding of the mechanisms regulating the expression of MHC class II genes. X-linked lymphoproliferative disease (XLP), a familial disorder affecting males with a rapidly fatal course in response to EBV infection was first reported more than 25 years ago. This disorder is clinically characterized by three major phenotypes: fulminant infectious mononucleosis, B cell lymphomas, and dys-gammaglobulinemia. The gene that is altered in XLP (SAP/SH2D1A) was cloned 2 years ago, and its recent analyses by **M. MORRA** *et al*. suggest that the development of dys-gammaglobulinemia and B cell lymphoma can occur without evidence of prior EBV infection.

The field of Immunology of Infectious Diseases is examined in 5 chapters. As pointed by **L.G. GUIDOTTI & F.V. CHISARI** in their excellent chapter, "the accepted dogma is that complete clearance of intracellular virus by the immune response depends on the destruction of infected cells by NK and cytotoxic T cells". The authors challenge this notion showing evidence that tissue-sparing, noncytolytic antiviral mechanisms mediated by the innate and adaptative immune response can be envolved as a host survival strategy to control infections of vital organs that would otherwise be destroyed if the only way to eliminate the infections was to kill all infected cells. The host defense and pathogenic mechanisms operative in *Mycobacterium tuberculosis* infection are discussed by **J.L. FLYNN & J. CHAN**. The authors summarize current understanding of the host immune response, with emphasis on the roles of macrophages and the ability of the organism to survive within macrophages. They also focus on the effector function of CD4+ and CD8+ T cells and on the roles of cytokines and chemokines. *Helicobacter pylori* is a bacteria that is mostly acquired during childhood and, if not treated, persists chronically, causing chronic gastritis, peptic ulcer disease, and in some individuals, gastric adenocarcinoma and gastric B cell lymphoma. The current treatment of *H. pylori*-symptomatic patients with a proton pump inhibitor and antibiotics is efficatious but face problems such as antibiotic resistance and patient compliance. **G. Del GIUDICE** *et al*. discuss the promising antigens for vaccine development against *H. pylory*, such as urease and the vacuolating cytotoxin. Some aspects of the immune response induced by the natural infection are also analyzed. The HIV-1 envelope glycoproteins, gp 120 and gp 41, mediate HIV-1 entry into target cells, initiating the HIV-1 replication cycle. They are a target for entry-blocking drugs and for neutralizing antibodies that could contribute to vaccine protection. **P. POIGNARD** *et al*. summarize the recent progress in the understanding of the gp 120 structure and function. The human T cell leukemia virus-1 (HTLV-1) is a retrovirus that causes adult T cell leukemia, which is a malignancy of CD4+T cells, and a neurological disorder, the tropical spastic paraparesis. **M. YOSHIDA** reviews the molecular biology of Tax-protein, which is a key regulator of viral replication, focusing on the possible mechanisms of host-cell regulation.

This volume of the **Annual Review of Immunology** offers a broad updated information on selected topics for students and researchers focusing recent progress on Basic and Clinical Immunology in a didactic manner of presentation.

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