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BOOK REVIEW - LIVRO*

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Over the last decade, HIV has been extensively characterized, and a variety of vaccine constructs and strategies have been explored. As K.B. CEASE & J.A. BERZOFSKY point out, as opposed to absolute prevention of infection, the primary goal of these strategies may be to limit infection and to assure a response to infection that prevents disease and transmission. In this chapter, the authors present the background and current state of immunobiology - driven vaccine development for AIDS.

In the field of lymphokines, S. ROMAGNANI in his excelent and didatic article, reviews current research on lymphokine production by human T cells, with particular emphasis on those responses thought to play a functional role in specific immune responses and on models that have provided general insights into the mechanisms governing immunopathology in infectious diseases, immunodeficiencies, autoimmune disorders, and other pathological conditions. Since the last review of chemoattractante receptors in the volume 2 of the Annual Review of Immunology, much information has been obtained in this area. In 1994, P.M. MURPHY reviews the issue beginning with a general introduction to leukocyte chemoattractantes. Then, he focuses on the family of leukocytes receptors and their associated G proteins. Finally, the author discusses de possible involvement of chemokines in erythrocyte function and, through molecular mimicry, in microbial pathogenesis.

Five chapters in this volume deal with lymphocyte development, activation, and differentiation . The structure and function of CD45 molecule (first referred to as leukocyte - common antigen) and its role in the immune response were reviewed in this series five years ago. CD45 is now known to be a positive growth regulator required for antigen - stimulated proliferation of T and B cells. I.S. TROWBRIDGE & THOMAS review studies of CD45 that have been performed since 1988 focusing on the importance of CD45 in lymphocyte activation and thymic development, mechanisms of CD45 activity regulation, and molecular genetics of CD45. F. MELCHERS et al. discuss the role of IgH and IgL chains and of Ig-like molecules in the development of cells of the B lymphocyte lineage. In a very interesting manner, the authors speculate that all mature, resting, primary antigen-reactive B cells in the periphery have been selected from immature sIg^+B cells by unknown antigens and have, thereby, changed their lifestyle from rapid death by apoptosis to longevity. The generation of genetically altered mice was made feasible through the combination of the gene targing with embryonic stem cell technology. K. PFEFFER & T.W. MAK discuss the present state of targeting technology and summarize the phenotypic changes observed in gene target mouse strains of immunological interest. Finally, for the first time genetic checkpoints in lymphocyte ontogeny and generation of an immune response in gene mutant mice were discussed. The presence of intestinal intraepithelial lymphocytes (IEL) has been appreciated for over 100 years. While the IEL function remains enigmatic, recent increasing evidence has secured the conclusion that the epithelium is a distint and unique primary T lymphopoietic organ. P. POUSSIER & M. JULIUS review the experiments that established that the intestinal epithelium is really a site of T cell development and selection, and correlate phenotypic and functional heterogeneity of IEL within this context. During development, T cells undergo a series of selection steps that direct differentiation processes and determine the TCR repertoire. During a second phase, T cell with self-reactive antigen receptors are eliminated by negative selection, and T cells that can recognize foreign peptides bound to self-MHC molecules are selected to mature (positive selection). E. ROBEY & B.J. FOWLKES re-

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view some of these complex developmental process including maturation signals in early T cell and the roles of thymic epithelium, hematopoietic stroma cells and peptides in the positive or negative selection of T cell repertoire.

The area of MHC and IMMUNOGENETICS includes four chapters. MHC class II molecules bind peptides predominantly derived from proteins internalized by the class II - bearing cells. A key feature of class II molecules, which has major effects on their function, is their transient association with a third glycoprotein, known as the invariant chain. In a very interesting article, P. CRESSWELL first provides a description of current understanding of the molecular and cellular mechanisms that generate complexes of MHC Class II molecules with foreing peptides. Also the mechanisms by which the invariant chain regulated MHC Class II function are discussed, after an initial description of the structural features of those molecules. Recent studies demonstrated that antigen analogs can act as powerful and specific inhibitors of T cell activation, leading to the concept that antigen analog/MHC complexes may act as antagonistis of the T cell receptor (TCR). A. SETTE et al. review basic observations that led to the concept of TCR antagonism, and describe initial usages of these antigen analogs to probe various immunological mechanism such as T cell activation, tolerance, and thymic selection. Finally, the use of the TCR antagonism phenomenon as a possible rational approach to antigen-specific immunointervention in allergies and autoimmune diseases is discussed. The polymorphic class I-a genes are encoded by H-2K, D, and L loci in the mouse and HLA-A, B, and C loci in humans. Class I-b genes in humans include HLA-E, F, G, H, I, and J, which are not orthologous to the class I-b regions in mice. This historical dichotomous categorization of MHC genes as Class-I-a and I-b is conceptually misleading according to S. SHAWAR et al. With these reservations, the authors discuss antigen presentation by MHC Class-I-b molecules with emphasis on their structure, polymophism, requirements for peptide antigen binding and tissue expression. Finally, V. ENGELHARD summarizes progress that has been made in understanding the structures of Class I and Class II MHC molecules, as well the features of the peptides that are their principal ligands.

Four chapters in this volume are dedicated to Immunoglobulins and B cell receptors. The principal mechanisms of transport of macromolecules across cells with tight junctions is via vesicular carriers, in a process known as transcytosis. In most cases studied to date, the molecule that will be transcytosed first binds to a receptor. In this article, K. MOSTOV reviews the transcytosis of polymeric immunoglobulins with emphasys on the polymeric Ig receptor (p Ig R), and transcytosis of IgG across the intestine of neonatal rats. P.A. BAEUERLE & T. HENKEL review the molecular biology of a ubiquotous primary transcription factor named NF-KB, and its possible role in cells of the immune system. Technologies have been emerging from making antibodies "in vitro" by mimiking the selection strategies of the immune system. Repertoires of antibody fragments are displayed on the surface of filamentous bacteriophage, each displaying a single antibodies species. Human antibody fragments have been isolated with specificities against both foreign and self antigens. G. WINTER et al. review recent progress on this technology, which should facilitate the construction of human antibodies of therapeutic value and of research reagents. Finally, various molecular aspects of the B cell antigen receptor complex including its structure, receptor-effector interactions and their biologic consequences are reviewed by J.C. CAMBIER et al.

Germinal centers develop in the B cell follicles of secondary lymphoid tissues during T cell-dependent antibody responses. Functions of germinal centers are now becoming apparent and some of them are reviewed by I. MAC LENNON in a very interesting article. CD40 is an integral membrane glycoprotein found on the surface of B lymphocytes, dendritic cells, follicular dendritic cells, epithelial cells, and carcinomas. CD40 binds to a ligand (CD40-L) which is expressed on activated T cells, mostly $CD4^+$ as well as basophils/mast cells. Two years ago, was demonstrated the key role of CD40/CD40-L interactions in T-cell dependent B cell activation by many groups. In an excellent chapter, J. BANCHEREAU et al. first review the CD40 and CD40-L as well as the functional consequences of CD40 engagement on human B cells. Finally, based on the kinetics and "in vivo" expression of CD40 and CD40-L, the authors propose a model for the timing and sites of CD40/CD40-L interaction during T-cell dependent immune response.

The field of Regulation of immune response has been the target for several publications in previous volumes of this series. In 1994, this important area is

examined in three chapters. Naive $CD4^+$ T cells when stimulated produce IL-2 as their major lymphokine. Upon priming, these cells develop into clones that produce IL-2, IFN-γ, and TNF-β (TH1 clones), and those that produce IL-4, IL-5, IL-6, IL-10, and IL-13 (TH2 clones). Evidence is growing that the distinctive production of IFN-γ or IL-4 in specific immune responses represents the differentiation of naive $CD4^+$ T cell populations into cells with lymphokine-producing phenotypes resembling TH1 or TH2 clones. In a very clear and didatic chapter, R.A. SEDER & W.E. PAUL review the regulation of the differentiation of naive CD4 cells into IFN-γ (TH1) or Il-4 (TH2) producers. Oral tolerance is a long recognized method to induce peripheral immune tolerance. Based on recent findings, H. WEINER et al. first delineate two pathways by which oral tolerization results in systemic hiporesponsiveness: active suppression or clonal anergy. Then, they focus on the manner by which oral tolerance may be applied to the treatment of autoimmune conditions in humans and animals. As pointed out by P. MATZINGER, one of the three fundamental questions on the regulation of immunity is how is self tolerance induced and maintened. The author describes T cell tolerance based on the view that the driving force for the immune system is the need to recognized danger and prevent destruction.

Engagement of the T cell antigen receptor (TCR) by peptide antigen bound to MHC molecules initiates a biochemical cascade involving protein tyrosine kinases (PTKs) and protein tyrosine phosphatases (PTP ases). A. CHAN et al. focus on recent advances in understanding the interactions of PTKs with the TCR complex, and mechanisms by which the PTP ases, CD45, functions in TCR signaling. No single mechanism proposed until now has satisfactorily accounted for the complete lytic process of cytotoxic T lymphocytes (CTL) and natural killer (NK) cells. Two proposed mechanisms of lymphotoxicity current valid are discussed by G. BERKE: the membranolytic one mediated by perforins and granzymes, and a non secretory mechanism initiated by receptor-mediated triggering of apoptosis-inducing target cell surface molecules. The molecular cloning of the C5a receptor places this molecule in the superfamily of G-protein coupled receptors. C. GERARD & N. GERARD focus on the state of current knowledge regarding the pro-inflammatory signalling peptide of the complement C5a, and its cellular receptor.

The area of Tumors includes only a chapter by T. BOON et al. convering tumor rejection antigens that can constitute targets for rejection responses mediated by syngeneic T cells. The authors review the identification of mouse and human tumor rejection antigens, as well as the role of T lymphocytes against them. The authors also discuss new possibilities for systemic approaches to specific immune therapy of cancer based on the identification of human tumor rejection antigens.

Transplantation tolerance can be defined as the indefinite survival of a graft in the absence of ongoing immunossuppression. Unfortunately, even today, reliable transplantation tolerance in humans is rarely achieved despite many successes in animal models. In a excellent chapter, B. CHARLTON, H. AUCHINCLOSS JR. & C.G. FATHMAN review those mechanisms of transplantion tolerance that operate throught the T cell compartment, i.e., "central" mechanisms which operate within the thymus, and "peripheral" ones which operate outside and independent of the thymus.

Much information has been obtained on Clinical Immunology. In a very clear and didatic article, B.S. BOCHENER, B.J. UNDEM & L.H. LICHTENSTEIN focus on the immunological (especially in inflammatory) alterations that accompany asthma. The potential importance of resident and recruited cells within the lung parenchyma and airways, the mediators released from these cells, and the mechanisms by which cytokines and adhesion molecules may participate in the activation and recruitment of circulating cells are also discussed. Finally, in the field of autoimmune response, M.Z. RADIC & M. WEIGERT review the genetic and structured evidence for antigen selection of anti-DNA antibodies.

This volume of the Annual Review Immunology retains the task of this series of focusing recent progress on Basis and Clinical Immunology in a attractive, didatic, and clear manner of presentation. Recent key concepts can be understood by postgraduates and researchers in various fields of Immunology.

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