Cells, inside and outside

Annual Review of Cell Biology 1989. Vol. 5, Palade, G. E., Alberts, B. M. and Spudich, J. A., eds. Annual Reviews, Palo Alto, USA, 1989, 542 pp. Price: USA $35; elsewhere $39.

This compilation has reviews on various subjects, including molecular traffic in cells, control of DNA replication and the cell cycle, transgenic systems, and growth factors in embryogenesis. Interestingly, the volume includes a discussion of every representative system: yeasts, *Drosophila*, plants and mammals.

The review of the latest literature on transgenic systems discussed by Westphal and Gruss is very informative and thought-provoking. The shortest article in the volume, it represents the state of the field and reflects the potential that transgenic systems hold for the understanding of molecular biology of development and to achieve gene targeting as demonstrated by the authors' own contributions to the field.

The review on growth factors during development by Melton and Whitman effectively combines the early observations of Spemann and Mangold (1924), which implied that regions of embryos were inducers of development, with the recent search for the chemical basis of embryonal inductions. The discussion principally focuses on evidence implicating peptide growth factors as morphogens or intercellular signals during development, thus providing a basis for study of signal transduction during specific developmental events.

Kendall A. Smith discusses the interleukin-2 (IL-2) receptor system from the interesting viewpoint of a typical hormone–receptor system. The article provides a brief but systematic status review, including the interesting kinetic cooperation in the IL-2 receptor–ligand interaction invoking high-affinity and low-affinity binding sites. Apart from the discussion on signal transduction and its biological consequences in the IL-2 system, the review includes a brief discussion on the development of IL-2 analogues as agonists and antagonists in immune-response pathways.

There are two articles whose subject matter is DNA replication and control of the cell cycle. The review by Bruce Stillman deals with initiation of eukaryotic DNA replication. Most of the information is obtained from studies on cell-free systems. The role of proteins other than DNA polymerase is discussed; in these studies animal viruses like adenovirus, SV-40 and Epstein–Barr virus have yielded valuable information. The requirement of linear DNA by adenovirus and circular DNA by SV-40 for initiation of replication suggests variations in mechanism of replication initiation in eukaryotes. The author rightly points out the risks in simple extrapolation of our knowledge of prokaryotic systems to eukaryotes.

A related article by F. Cross, J. Roberts and H. Weintraub extensively discusses control of the cell cycle at various phases. This is an almost exhaustive review of the literature, including data from various systems such as *Aspergillus*, *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, frog eggs and mammals. Major data in the field come from studies on *S. pombe*, *S. cerevisiae* and frog egg. The authors have very effectively compared the data from different systems at every step and have also given comprehensive models wherever available/feasible.

The extracellular matrix (ECM) has been reviewed in two articles. Tenascin, a protein present in ECM, is discussed by H. P. Erickson. The review includes a historical background, biochemical characterization, primary structure, intermolecular interactions, and the interaction of tenascin with the cell surface. The distribution of tenascin is restricted to embryonic tissues and certain adult tissues; however, the protein offers enough diversity to implicate it as a multifunctional protein. ECM of *Drosophila* is discussed by Fessler and Fessler. This review includes a discussion on *Drosophila* ECM in general and the mojor components of the matrix. There is a discussion of the expression of matrix proteins, specifically collagen IV, laminin and integrins, the transmembrane proteins. Thus the unifying concepts of cell function and structure have traversed across the boundary of the cell and ECM seems to constitute yet another feature that tumour cells share with early embryonic cells.

The other topics dealt with in this volume relate to protein and lipid traffic in cells, evolution of mitochondrial DNA, chloroplasts of land plants, intracellular matrix, and biogenesis of lysosomes.

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Antigen recognition the preeminent problem

Annual Review of Immunology 1989. Vol 7. William E. Paul, Garrison Fathman, C. and Henry Metzger, eds. Annual Reviews, Palo Alto, USA, 1989. 730 pp. Price: USA $34; elsewhere $38

The articles of this volume focus on the developmental biology of the cellular immune elements, *in vivo* regulation of inflammation and immune response, antigen recognition by T cells through their surface receptors, induction of effector immune responses, and the influence of antibodies on immune response.

In an introductory chapter, George and Eva Klein nostalgically recall their tryst with various aspects of tumour immunology. This should certainly inspire young scientists pursuing immunologic studies.

The part on developmental immunobiology includes two detailed reviews, 'Heterogeneity of mast cells in relation to IgE antibody response' by Yukihiko Kitamura and 'Cellular elements which regulate B lymphocyte development in bone marrow' by Paul W. Kinkade and his colleagues. *Xenopus* frogs have been extensively used in research in immunogenetics and it is timely that an update appears, viz. 'Immune system of the *Xenopus*' by Louis Du Pasquier and his colleagues. Mathew L. Thomas describes the biology and genetics of the 'Leukocyte common antigens', which perform a vital role in lymphocyte activation.

The 'Microanatomic changes in the lymphoid system during immune response' by A. K. Szakal and his colleagues outlines antigen recognition, antigen processing and antigen presentation functions of the lymphoid tissue with lucid pictures. The fundamental event in immune recognition is the discrimination of self from nonself, and 'Immunogenetics of cell surface antigen differentiation and expression' is a valuable article, contributed by Wolfgang J. Rettig and Lloyd J. Old.

These trend-setting reviews have been followed by others on *in vivo* regulation of inflammation and immune response. Bruce Beutler and Anthony Cerami elaborate on the biology of the cachectin/tumour necrosis factor and their central role in host immune response. The regulatory role of the 'Decay accelarating factor' in complement-mediated tissue injury has been analysed by Douglas M. Lublin and John P. Atkinson. Stuart H. Orkin presents an interesting chapter on 'Chronic granulomatous disease', in which phagocytic cells fail to produce anti-microbial oxidants resulting in increased susceptibility to microbial infections.

The initiation of amplified immune responses through T-cell activation has been elucidated by a series of reviews which focus primarily on T cell receptors (TCR), TCR–antigen–MHC interaction and effector-cell responses.

Although the $\alpha\beta$ TCR has been sufficiently well characterized, the $\gamma\delta$ TCR has been an enigmatic molecule. David H. Raulet defines the structure, function and genetics of the latter type of TCR. They are expressed in unusual anatomic sites and are proposed to perform unusual immune surveillance involving the recognition of a restricted set of self antigens.

Barbara E. Bierer and her colleagues have covered the biology of the cluster differentiation (CD) surface antigens of lymphocytes, which are critical for their function. They are involved in adhesion of cells, transmission of co-stimulatory signals and antigen-dependent and -independent lymphocyte activation The significance of the variable-region connectivity of the TCR has also been elaborated by P. Pereira and his colleagues

Alain Townsend and Helen Bodmer present an exciting review on 'Antigen recognition by class I restricted T lymphocytes', where the mechanisms of peptide binding to the Bjorkman's groove are discussed, culminating in the unifying hypothesis that all T cells recognize peptides bound to class I and class II MHC proteins on the cell surface. The TCR–antigen–MHC complex subsequently initiates a wide array of effector responses through the helper $CD4^+$ and cytotoxin $CD8^+$ T cells.

Daniel L. Mueller and his colleagues show that T-cell proliferation and development of an effector function is essentially a consequence of the peptide occupancy of TCR and a co-stimulatory signal received through an accessory cell. The development and functional studies have been analysed in depth for helper T cells by T. R. Mosman and R. L. Coffman. Abraham Kupfer and S. J. Singer follow with a detailed study on the 'Cell biology of the cytotoxic and helper T cell functions'. Jean Charles Cerrottini and H. R. MacDonald complete this part of the story by presenting the 'Cellular basis of T cell memory'. Unlike B-cell memory, it appears that T memory cells can be phenotypically typed. The availability of monoclonal antibodies to these markers is expected to increase the pace of research into the mechanism of immunologic memory

Ryo Abe and Richard J. Hodes describe the importance of the Mls gene products, which probably play a role in non-MHC-product-mediated selection of the T-cell repertoire. The limitation appears to be that the system has been recognized only in murine animals.

Ingrid Muller and her colleagues show that the antigen specificities of two populations of T helper cells are different when they are correlated with resistance and susceptibility to infection with *Leishmania major*. This finding has novel implications for the development of vaccines for parasites in that defined antigens may be needed to focus on protective immunity alone.

When TCR binds peptides of self proteins in conjunction with the MHC complex, an autoimmune self-destructing process can be initiated. To prevent such a TCR–peptide interaction, as a therapeutic or prophylactic measure, various strategies could be developed The use of antibodies to TCR, TCR-blocking peptides and deletion of T-cell subsets have been exemplified by Hans Acha Orbea and his colleagues and Vipin Kumar and his colleagues. 'Manipulation of the TCR by monoclonal antibodies' by Herman Waldman illustrates how antibodies could be used to suppress, enhance or modify immune responses. These reviews draw our attention to the innovative field of immunotherapy of human diseases.

Finally, the elegant use of the Epstein–Barr virus to study the B-cell repertoire has been outlined by Paulo Casali and Abner Louis Notkins. The impact of B-cell differentiation pathways on the regulation of immune response has been elucidated by C. Kocks and Klaus Rajewsky.

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Annual Review of Immunology 1990. Vol 8. William E. Paul, Garrison Fathman, C. and Henry Metzger, eds. Annual Reviews, Palo Alto, USA, 1990. 819 pp. Price: USA $38; elsewhere $42.

The topics covered in this volume largely relate to three critical events in the biology of immune recognition: binding and internalization of antigen by cell-bound or free immune molecules; intracellular processing and presentation of antigenic moieties on cell surface through the major histocompatibility complex (MHC); and recognition of such moieties by T-cell receptors, which eventually leads to the elaboration of amplified immune responses. The culmination of such responses in the generation of either protective immunity or self-damaging autoimmunity has also been appropriately exemplified.

The review begins with an introductory chapter by Brigitte Askonas whose work on antibody synthesis and the role of cytotoxic T lymphocytes (CTL) and antibodies in viral immunity is well known.

The genetics and biology of the human immunodeficiency virus (HIV) and other retroviruses have been covered by two articles by Warner C. Greene and Ronald C. Desrosiers. Retroviruses are now playing havoc with human health and it is apt that they have been

analysed in this volume with particular reference to the development of appropriate vaccines. Monte S. Meltzer and his colleagues in fact present the unusual role of macrophages in the regulation of the pathogenesis of the HIV infection. Hitherto, the $CD4^+$-receptor-bearing T cells were thought to be the only major target of the HIV.

Antonio Lanzavechhia elaborates on 'Receptor-mediated uptake of antigens and its relevance to immune recognition through class II MHC complex'. Exciting findings are the role of membrane-bound immunoglobulin and Fc receptors in antigen capture and their influence on subsequent intracellular antigen processing. The perplexing presence of high levels of antibodies which do not have any protective immunity in some diseases like tuberculosis could perhaps be explained by ascribing them a role in capture and intracellular processing of antigens.

In a related review, Ian A. Wilson and Nancy J. Cox present detailed analysis of the structural basis of immune recognition of the influenza virus haemagglutinin (HA), which is one of the extensively studied viral adhesion molecules. Analysis of the conserved and variable amino-acid sequences in its structure has shown that the virus evades immune recognition through mutational changes in the HA molecule. Similar antigenic variation of coat proteins of many microbes has prevented development of rational vaccines, as exemplified by this review and another on 'Cellular and genetic aspects of antigenic variation in trypanosomes' by George A. M. Cross. Wilson and Cox discuss the importance of studying adhesion molecules for the development of drugs that prevent microbial entry and pathogenesis.

Antigenic peptides are intracellularly synthesized or processed prior to expression in conjunction with MHC class I and class II proteins on the cell surface. Although specific classes of T cells recognize these peptides and then initiate effector immune responses, peptide–MHC expression remains a seminal event in immune recognition.

The evolution, genetics and biology of the MHC proteins have been updated in four reviews by David A. Lawlor and colleagues, Warner C. Greene, Iwona Stroynowsky, and Cristophe Benoist and Diane Mathis.

The recognition of MHC-bound peptides by T-cell receptors is a multitudinous process which in turn results in the initiation of an effector immune response. The developmental biology of T cells has been updated by Harald Von Boehmer in his review on the expression of TCR in transgenic mice. The genetics and mutational analysis of TCR has been further elucidated by J. D. Ashwell and Richard Klausner. The molecular basis of T-cell specificity has been highlighted by Louis Matis. Finally, the intracellular events following the binding between TCR and the MHC-bound peptides have been covered by Katherine Ullman and her colleagues.

These reviews have elegantly tried to answer how the structures of the TCR and of the TCR–antigen–MHC trimolecular complex determine the initiation of the biochemical events that lead to effector immune responses. It is, however, implied that there are some critical lacunae, like the crystallographic structure of TCR, the link between the membrane activation and the nucleus in the T cell, and the mechanism of interaction between TCR and superantigens. The latter are expected to be of major clinical importance.

In recent years, there has been considerable interest in the immune response to stress proteins, which show a remarkable degree of conservation of structure across prokaryotic and eukaryotic organisms. Although they perform essential cellular functions in protein assembly, transport and disposal, particular attention has been focused on their being responsible for autoimmune diseases. Richard Young details the mechanisms by which they may be involved in autoimmune pathogenesis. Related reviews by Scott S. Zamvil, Lawrence Steinman, Luis Castano and George Eisenbarth focus on the role of T cells in generating allergic encephalomyelitis and induction of autoimmune diabetes.

The pre-eminent immunoglobulin molecule has certainly not been left behind in this volume. Charlotte Esser and Andreas Radbruch present the latest data on the enigmatic immunoglobulin class switching, although the nature of the recombinase and the molecular connection between transcription and recombination remain elusive.

Lymphocyte control of immunoglobulin isotype selection has also been described by Fred D. Finkelman. The exciting field of catalytic antibodies has been covered by K. M. Shokat and P. G. Schultz, and there appears to be a promising use for new 'tailorable catalysts' in biology, chemistry and medicine.

Finally, the mechanism of action of CTL has been elaborated by a detailed study of perforins by Jurg Tschopp and Markus Nabholz. There is also an interesting chapter on the leukocyte integrin receptor family by Martin E. Hemler.

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Brief notes

Studies of High-temperature Superconductors. A series in 10 volumes. A. V. Narlikar, ed. Nova Science Publishers, Inc., 283 Commack Road, Suite 3000, Commack, NY 11725-3401, USA. 1989–.

With Bednorz and Muller's pioneering discovery of high-temperature superconductors in 1986, superconductivity has ceased to remain an area of mere academic curiosity and a preserve of a small community of low-temperature physicists and cryogenicists. Renouncing their cold confines and freed from the grip of liquid helium, superconductors have stepped into the realm of high temperatures. The area has been transformed into a rich field of intensive and highly competitive research, encompassing diverse disciplines such as structural chemistry, ceramic engineering, metallurgy, solid state electronics, and experimental and theoretical condensed matter physics.

Each chapter in these volumes comprises a detailed review or an extended paper focusing on one or more of the frontal aspects of research and applications, including state-of-the-art technology pertaining to HTSCs. The contributors are recognized authorities in the field. The editor, A. V. Narlikar, is deputy director of the National Physical