

**MECHANISMS OF
LYMPHOCYTE
ACTIVATION AND
IMMUNE REGULATION III**

Developmental Biology of Lymphocytes

ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY

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Edited by Sudhir Gupta, William E. Paul, Max D. Cooper, and Ellen V. Rothenberg

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LYMPHOCYTE
ACTIVATION AND
IMMUNE REGULATION III**
Developmental Biology of Lymphocytes

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PREFACE

Recent advances in the understanding of the major events that shape the immune recognition system have been remarkable. The analysis of immunoglobulin (Ig) gene organization and Ig repertoire diversification in lower vertebrates has provided new insight into this process in mammals. Similarly, the understanding of the early development of lymphocytes and of the acquisition of immunological tolerance has been aided by elegant studies in quail/chicken chimeras, using the power of the distinctive markers of the constitutive cells of these birds. Great strides have been made in understanding the role played by major histocompatibility complex (MHC) molecules in antigen presentation and in repertoire selection within the thymus. The use of transgenic mice expressing specific T-cell receptor (TCR) genes has elucidated the process of both positive and negative selection. In parallel, there has been considerable progress in our understanding of tolerance, based in part on the use of markers for the $V\beta$ genes of T-cell receptors and in part on the analysis of the behavior of long term T-cell lines. This has led to the realization that both clonal deletion and clonal anergy may play critical roles in the maintenance of unresponsiveness to self antigen.

Molecular analysis of the requirements for expression of membrane immunoglobulin molecules has revealed the existence of a complex that appears to be of critical importance in mediating signalling through Ig receptors. In addition, major insights have been obtained into the regulation of expression of genes of immunologic interest. Detailed analyses of the promoter regions of such genes and of the DNA-binding proteins that control their transcription promise to yield important information for the regulation of expression of lymphokines and other lymphocyte products.

Progress in these and related areas was the theme of the Third International Conference on Lymphocyte Activation and Immunoregulation, held in Newport Beach, California on February 16-18, 1990.

The Proceedings is divided into five sections. The first section deals with the phylogeny of lymphocytes. It includes genetic mechanisms influencing the evolution of the immune recognition genes, the ontogeny of thymocytes, and the diversity of antibody repertoire during evolution from cyclostomes to mammals. The second section discusses developmental biology of T lymphocytes. It includes experimental models probing the mechanisms of selection, T cell effector gene programming via signalling, and the use of TCR transgenic mice in the study of MHC restriction and self tolerance at the level of thymus. In addition, origin, development, diversity, repertoire, ligands, and functions of $\gamma\delta$ T cells are discussed. Molecular analysis of the interaction between *p56lck* with CD4 and CD8 antigen, a likely participant in the mechanisms of intrathymic developmental choice, has also been included in this section. The third section includes discussions of multiple mechanisms of induction and maintenance of tolerance to Mls and H2, and induction and maintenance of anergy in mature T cells. Developmental biology of B lymphocytes is featured in Section IV. It includes cloning and characterization of the DNA binding protein that binds to $J\kappa$ recombination signal sequence of immunoglobulin gene, B-cell development in fetal liver, the possible role of a "gene-search" retrovirus in gene expression during lymphoid differentiation, and the components of the B-cell antigen receptor complex. Also included is the comparative study of human and murine B-cell development, and characterization of a suppressive stromal cell subclone. The final section deals with the proposed role of somatic hypermutation and gene conversion in

antibody diversity, and the molecular control of germline transcription and the role of the latter in immunoglobulin class switching. This book should be of interest to researchers not only in immunology, but also in cell, developmental, and molecular biology.

We wish to thank Miss Nancy Doman for outstanding editorial assistance and tireless preparation of the manuscript.

Sudhir Gupta
William Paul
Max Cooper
Ellen Rothenberg

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