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Klaus Aktories

Medizinische Fakultät, Institut für Experimentelle und Klinische Pharmakologie und Toxikologie, Abt. I Albert-Ludwigs-Universität Freiburg, Albertstr. 25, 79104 Freiburg, Germany

Richard W. Compans

Department of Microbiology and Immunology, Emory University, 1518 Clifton Road, CNR 5005, Atlanta, GA 30322, USA

Max D. Cooper

Department of Pathology and Laboratory Medicine, Georgia Research Alliance, Emory University, 1462 Clifton Road, Atlanta, GA 30322, USA

Jorge E. Galan

Boyer Ctr. for Molecular Medicine, School of Medicine, Yale University, 295 Congress Avenue, room 343, New Haven, CT 06536-0812, USA

Yuri Y. Gleba

ICON Genetics AG, Biozentrum Halle, Weinbergweg 22, 06120 Halle, Germany

Tasuku Honjo

Faculty of Medicine, Department of Medical Chemistry, Kyoto University, Sakyo-ku, Yoshida, Kyoto 606-8501, Japan

Yoshihiro Kawaoka

School of Veterinary Medicine, University of Wisconsin-Madison, 2015 Linden Drive, Madison, WI 53706, USA

Bernard Malissen

Centre d'Immunologie de Marseille-Luminy, Parc Scientifique de Luminy, Case 906, 13288 Marseille Cedex 9, France

Fritz Melchers

Max Planck Institute for Infection Biology, Charitéplatz 1, 10117 Berlin, Germany

Michael B. A. Oldstone

Department of Immunology and Microbial Science, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA

Rino Rappuoli

Novartis Vaccines, Via Fiorentina 1, Siena 53100, Italy

Peter K. Vogt

Department of Molecular and Experimental Medicine, The Scripps Research Institute, 10550 North Torrey Pines Road, BCC-239, La Jolla, CA 92037, USA

Honorary Editor: Hilary Koprowski (deceased)

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Thomas Boehm · Yousuke Takahama
Editors

Thymic Development and Selection of T Lymphocytes

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 Springer

Editors

Thomas Boehm
Department of Developmental Immunology
Max-Planck-Institute of Immunobiology
and Epigenetics
Freiburg
Germany

Yousuke Takahama
Division of Experimental Immunology
Institute for Genome Research
University of Tokushima
Tokushima
Japan

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Preface

The thymus is an evolutionarily ancient primary lymphoid organ common to all vertebrates in which T-cell development takes place. Remarkably, in jawed vertebrates the overall histological structure of the thymus has not changed over several 100 million years, as illustrated by the fact that the thymus of cartilaginous fishes already possesses an outer cortical and inner medullary region. This surprising stability of tissue organization underlies a conserved mechanism of T-cell differentiation that is a characteristic of the adaptive immune functions in all vertebrates.

The two major aspects of thymopoiesis, namely the development of the stromal microenvironment of the thymus and the development of T-cells, are addressed by the papers in this volume. Yousuke Takahama and Graham Anderson and their colleagues discuss cell biological and molecular aspects of epithelial differentiation in the cortical and medullary regions of the thymus. Although these two compartments are functionally interconnected, their properties are quite distinct as they support different stages of thymocyte development. Lo and Allen discuss the molecular basis of positive selection, the process by which the thymic microenvironment influences the formation of the repertoire of the T-cell receptors (TCRs) expressed on developing T-cells. Because TCRs can also exhibit self-reactivity, this property needs to be carefully controlled to avoid undesired autoimmunity; in their chapter, Maria Mouchess and Mark Anderson address the mechanisms by which the thymus imposes the essential central tolerance on T-cells. The last two chapters elaborate additional important aspects of haematopoietic cell differentiation: Zhang and Bhandoola discuss recent progress in understanding the many factors that regulate the homing of T-cell precursors to the thymic rudiment and also touch upon the question of which cell type(s) colonize the thymus; finally, Tanaka and Taniuchi discuss how genetic and epigenetic mechanisms regulate the decision between CD4 and CD8 lineage differentiation.

The contributions in this volume not only provide state-of-the-art overviews of the various aspects of thymopoiesis written by leading experts in the field, they also illustrate how far we have come in our understanding of thymus development and T-cell differentiation and how these observations might be translated into improved diagnosis and treatment of various immunodeficiency and autoimmune disorders disrupting thymus function.

Thomas Boehm
Yousuke Takahama

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