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Maria-Grazia Roncarolo
DNAX Research Institute of Molecular and Cellular Biology
Palo Alto, California, U.S.A.

Bruno Péault
Institut d'Embryologie Cellulaire et Moléculaire
du CNRS et du Collège de France
Nogent-sur-Marne, France

Reiko Namikawa
DNAX Research Institute of Molecular and Cellular Biology
Palo Alto, California, U.S.A.

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CONTENTS

EDITORS

Maria-Grazia Roncarolo
DNAX Research Institute of Molecular and Cellular Biology
Palo Alto, California, U.S.A.
Chapters 3,4

Bruno Péault
Institut d'Embryologie Cellulaire et Moléculaire
du CNRS et du Collège de France
Nogent-sur-Marne, France
Chapter 1

Reiko Namikawa
DNAX Research Institute of Molecular and Cellular Biology
Palo Alto, California, U.S.A.
Chapters 3,4,8

CONTRIBUTORS

Mohammad R. Abedi
Department of Clinical Immunology
Huddinge Hospital
Karolinska Institute
Huddinge, Sweden
Chapter 5

Alessandra Cesano
The Wistar Institute
Philadelphia, Pennsylvania, U.S.A.
Chapter 9

Benjamin P. Chen
Experimental Cellular Therapy Group
SySTEMix Inc.
Palo Alto, California, U.S.A.
Chapter 2

Birger Christensson
Department of Clinical Immunology
Department of Pathology
Huddinge Hospital
Karolinska Institute
Huddinge, Sweden
Chapter 5

John E. Dick
Department of Genetics, Research Institute
Hospital for Sick Children,
and
Department of Molecular and Medical Genetics
University of Toronto
Toronto, Ontario, Canada
Chapter 10

CONTRIBUTORS

Anne H.M. Galy
Experimental Cellular
Therapy Group
SySTEMix Inc.
Palo Alto, California, U.S.A.
Chapter 2

Lennart Hammarström
Department of Clinical
Immunology
Huddinge Hospital and
Center for BioTechnology
Karolinska Institute, NOVUM
Huddinge, Sweden
Chapter 5

Hideto Kaneshima
New Enterprise Research Division
SySTEMix, Inc.
Palo Alto, California, U.S.A.
Chapter 7

Tsvee Lapidot
Department of Genetics,
Research Institute
Hospital for Sick Children,
and
Department of Molecular
and Medical Genetics
University of Toronto
Toronto, Ontario, Canada
Chapter 10

André Larochelle
Department of Genetics,
Research Institute
Hospital for Sick Children and
Department of Molecular
and Medical Genetics
University of Toronto, Canada
Toronto, Ontario, Canada
Chapter 10

Joseph M. McCune
Gladstone Institute of Virology
and Immunology
UCSF School of Medicine
San Francisco, California, U.S.A.
Chapter 7

Marcus O. Muench
DNAX Research Institute for
Molecular and Cellular Biology
Palo Alto, California, U.S.A.
Chapter 4

Yair Reisner
Department of Membrane Research
and Biophysics
The Weizmann Institute of Science
Rehovot, Israel
Chapter 6

Daniela Santoli
The Wistar Institute
Philadelphia, Pennsylvania, U.S.A.
Chapter 9

Dominique Schols
DNAX Research Institute
for Molecular
and Cellular Biology
Human Immunology Department
Palo Alto, California, U.S.A.
Chapter 3

C. I. Edvard Smith
Department of Clinical
Immunology
Huddinge Hospital and
Center for BioTechnology
Karolinska Institute, NOVUM
Huddinge, Sweden
Chapter 5

CONTRIBUTORS

Josef Vormoor
Department of Genetics,
Research Institute
Hospital for Sick Children,
and
Department of Molecular
and Medical Genetics
University of Toronto
Toronto, Ontario, Canada
Chapter 10

Jan E. de Vries
DNAX Research Institute
for Molecular and Cellular Biology
Palo Alto, California, U.S.A.
Chapter 3

PREFACE

The development, proliferation, differentiation and effector functions of cells of the hematopoietic and immune systems are regulated by a complex network of interactions. Many of these processes are controlled by signals provided by cell-cell contacts, mediated through ligand-receptor interactions in the microenvironment, and soluble factors such as cytokines. These cytokines, which are produced by activated stromal and hematopoietic cells in response to endogenous or exogenous stimuli, are pleiotropic and exhibit multiple activities on the same or different target cells. The relative importance of these activities likely depends on the local microenvironment in which the cytokines and their receptors are expressed. Therefore, it is clear that these in vivo events, which involve multiple signals in an organized manner, cannot be simply mimicked by in vitro systems. Because of this, it has been attempted for a long time to introduce human hematolymphoid systems into small animals.

With the discovery of the severe combined immunodeficient (SCID) mutant mouse, which has a genetic defect in the recombinase system, enormous progress has been made in establishing these kinds of models.[1] As a consequence of their genetic defect these mice have no T or B cells, and easily accept allogeneic and xenogeneic cells and tissues, including those of human origin. In these SCID mice transplanted with human tissues, functional hematolymphopoiesis can be induced and maintained in vivo. These SCID-hu mice function as an intermediate between the laboratory and the clinic, and they provide an excellent model for studying human hematopoiesis and immune responses in vivo. In addition, this model allows us to study the induction and manipulation of human diseases in vivo.

Two different methods were employed to introduce human cells into SCID mice, i.e., surgical implantation of fetal hematolymphoid organs[2] and injection of hematolymphoid cell suspensions into animals,[3] to develop heterochimeric animals.

This book is aimed at providing the essential information on the use of the SCID mouse for studying human hematolymphopoiesis in vivo. In the first section, studies on human hematopoietic stem cells in vivo and on the mechanisms of thymic "education" of human T cells are discussed. In addition, the effects of growth factors and toxic agents on human hematopoiesis are described. The second section contains chapters in which the human immune responses in the SCID mouse are reviewed. The third section covers SCID mouse models for studying human infectious diseases, leukemias and genetic disorders.

We hope that this book, which comprehensively covers this new epoch-making technology and its applications, will contribute to a better understanding of the use of SCID mice to study human hematopoiesis. We wish to thank the authors for their excellent chapters assembled in this book. We are grateful to Jo Ann Katheiser who assisted with the editing.

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