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HUMAN HEMATOPOIESIS
IN SCID MICE

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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 organs² 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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