

Preface

The term humanized mouse in this text refers to a mouse in which human tissues and cells have been transplanted and show the same biological function as they do in the human body. That is, the physiological properties and functions of transplanted human tissues and cells can be analyzed in the mouse instead of using a living human body. It should therefore be possible to study the pathophysiology and treatment of human diseases in mice with good reproducibility. Thus, the humanized mouse can be used as a potent tool in both basic and clinical research in the future.

The development of appropriate immunodeficient mice has been indispensable in the creation of the humanized mouse, which has been achieved through many years of efforts by several laboratories. The first stage on the road to the humanized mouse was the report on nude mice by Isaacson and Cattanaach in 1962. Thereafter, nude mice were studied in detail by Falanagan and, in 1968, Pantelouris found that these mice have no thymus gland, which suggested that the mice lack transplantation immunity against xenografts such as human hematopoietic stem cells. At the Nude Mouse Workshops (organized by Regard, Povlsen, Nomura and colleagues) that were held nine times between 1972 and 1997, the possibility of creating a humanized mouse using nude mice was extensively examined. The results, however, showed that certain human cancers can be engrafted in nude mice, but unfortunately engraftment of normal human tissue was almost impossible. Nevertheless, nude mice have made a great contribution to the evaluation of the effects of drugs against human cancer. In the course of this research, a system for production of a large number of germfree animals with the same high biological quality and know-how for strict microbiological and genetic quality control of the animals were established. It is now evident that highly reproducible research and experimental results could not be obtained without these achievements. This point should be taken into account in the future development of immunodeficient mice more suitable as humanized mice. Since human tissues other than certain cancer cells, especially hematopoietic cells, cannot be engrafted in nude mice, development of an even higher level of immunodeficient mice was needed. Great hopes were then placed on the SCID mice that have no T cells or B cells developed by Bosma in 1983, but the engraftment rate of normal tissue was again not as high as

expected. Thereafter, NOD-scid mice were developed as an improved version of SCID mice (Shultz et al. and Ito et al.). Using NOD-scid mice, it became possible to achieve in vivo differentiation of human blood cells from a human hematopoietic stem cell, and these mice have been used in various applications. However, human cells can be engrafted only to a certain extent and adequate differentiation is not induced even in NOD-scid mice. Further development of new immunodeficient mice was still required. Recently, during 2000–2002, NOD-scid IL2R null (Ito et al., Schultz et al.) and Rag2nullIL2R null mice (Ito et al.) were developed. These mice have been proven to show much better engraftment and differentiation states than any other previously established mice and they have attracted the attention of researchers as a basis for creation of the humanized mouse. During the last few years, remarkable results have been reported concerning the establishment and the application of humanized mice by applying newly developed immunodeficient mice such as NOD-scid IL2R null and Rag2nullIL2R null mice. Based on recent progress, the first International Workshop on Humanized Mice was held in Tokyo in October 2006. This volume of *Current Topics in Microbiology and Immunology* is based mainly on the presentations at the workshop, but all chapters were especially written for the book. A wide range of topics is discussed in this volume including the characteristics of newly developed immunodeficient mice, their rearing conditions and points to consider, as well as the creation of humanized mice using various human cells and tissues, especially human hematopoietic stem cells, their characteristics, applications, and future prospects. We hope that the present volume will contribute to the expansion of research using the humanized mouse and the development of new humanized mice in the future.

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