Preface

The drug discovery process has shifted from essentially a trial and error approach toward unraveling disease and underlying molecular mechanisms with the goal to specifically target pathways and molecules. A key for understanding and exploring disease mechanisms is the availability of good models, preferably in vivo models as these more closely reflect the complexity of life.

Each organism is a highly complex integrated system and is considerably more than the sum of its parts being the net result of an evolving genome and its interactions with the environment. This volume, *Mouse Models for Drug Discovery: Methods and Protocols*, attempts to illustrate The Mouse as an exceptionally versatile and sophisticated platform which can meet this challenge.

With the development of inbred strains which are genetically invariant within a strain, it has become possible to use genetically defined animals and highly reproducible systems. This has allowed The Mouse to rise from being a pest, to a cute collectable pet, to an advanced and well-established tool for genetic and molecular research, becoming the premium instrument for drug discovery, validation, preclinical, and toxicological studies. The reasons for the mouse’s rise in prominence are many. In brief, mice are small, require relatively little space, have simple nutritional needs, a short generation time, and few special needs to reproduce. However, it is in the last 20 years with the advent of genetic engineering and the ease of manipulating the mouse’s genome that has made the mouse the most versatile mammalian experimental system. Further, the sequencing of the human and mouse genomes has clearly demonstrated that mouse and humans have direct gene and functional homologies for more than 90% of their genes. With the KOMP and other international programs, all mouse genes will be available as null alleles (i.e., knockouts) by approximately 2015. Development and distribution of these resources is aided by advances in Assisted Reproductive Technologies. With all of this in mind, it can now be truly stated that The Mouse has become a respected, indispensable tool in biomedical research and is the most commonly used animal research model.

With thousands of mouse models available covering practically all disease areas, it is beyond this volume to cover the whole field of mouse applications in the drug discovery process. In this volume, we have selected chapters which cover general background as well as a few specific disease topics with the idea of introducing those less familiar with mice as experimental model platforms. The chapters by Festing and Wiles cover general aspects of experimental design, inbred vs. outbred mice, and how to manage the risks working with live animals. The chapter by McNeish highlights a pharma approach as how to use genetically engineered mouse models for target identification and validation. Koentgen et al. has given a general overview of the many approaches used to genetically engineer mice. Rando et al. show the power of combining novel imaging tools with genetically engineered mice for drug discovery. Representatives of the young and rapidly developing field of humanized mice are provided in the chapters by Roopenian and Shultz, highlighting also the possibility of engraftment of human tissue into mouse, for example, in regenerative biology and stem cell research.
As examples for the wide field of specific disease areas and mouse models, we have included type 1 and 2 diabetes (Serreze and Baribault), cardiovascular disease (Howles), arthritis (Tak), skin disorders (Sundberg), cancer (Talmadge, Surguladze, and Li), the use of behavioral models for depression and anxiety (Kalueff), neurodegenerative diseases (Janus), neuromuscular diseases (Burgess), and infectious diseases (Medina).

We hope that this volume will stimulate those not familiar with the power of the mouse and its potential for the drug discovery process, and further, that it will encourage the development of new models as well as new ways in utilizing existing models. We also hope to promote the development of more standardized models and assays such that results can be more easily compared and reproduced.

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