PREFACE

Ultimately, the quality of the tools available for genetic analysis and experimental disease models will be assessed on the basis of whether they provide new information that generates novel treatments for human disease. In addition, the time frame in which genetic discoveries impact clinical practice is also an important dimension of how society assesses the results of the significant public financial investment in genetic research. Because of the investment and the increased expectation that new treatments will be found for common diseases, allowing decades to pass before basic discoveries are made and translated into new therapies is no longer acceptable.

Computational Genetics and Genomics: Tools for Understanding Disease provides an overview and assessment of currently available and developing tools for genetic analysis. It is hoped that these new tools can be used to identify the genetic basis for susceptibility to disease. Although this very broad topic is addressed in many other books and journal articles, *Computational Genetics and Genomics: Tools for Understanding Disease* focuses on methods used for analyzing mouse genetic models of biomedically important traits. This volume aims to demonstrate that commonly used inbred mouse strains can be used to model virtually all human disease-related traits. Importantly, recently developed computational tools will enable the genetic basis for differences in disease-related traits to be rapidly identified using these inbred mouse strains.

On average, a decade is required to carry out the development process required to demonstrate that a new disease treatment is beneficial. However, the analysis of mouse genetic models and the application of the approaches described in this text will enable genetic discoveries to be made much more quickly. Providing insight into the genes and pathways regulating the disease-related traits among the inbred strains. The results can direct subsequent biological experimentation, clinical research, and human genetic analysis.

The book is organized into three parts: Part I: Theory and Technical Concepts, Part II: Selected Examples: Murine Models of Human Disease, and Part III: Selected Examples: The Genetic Basis for Human Disease. The chapters in the first section provide theoretical and practical overviews of the methodology used for analysis of murine genetic models of human

disease. Chapter 1 describes how new computational methods and analysis of biomedical traits among inbred mouse strains can accelerate the rate of genetic discovery. The statistical methods used for genetic analysis of murine experimental intercross progeny, which are referred to as quantitative trait locus mapping, are described in Chapter 2. Chapter 3 provides the first detailed overview of a recently developed haplotype-based computational genetic analysis method. If used by experimental mouse geneticists, this method can exponentially accelerate the rate of genetic discoveries made using murine disease models. The methods for organizing the pattern of genetic polymorphisms in the genome of inbred strains into haplotype blocks, which can be computationally analyzed, is described in Chapter 4. This chapter also compares the different methods used for generating haplotype blocks for mouse and man, and indicates how they can be used for very different applications. The section concludes with a description of the methods for discovering and characterizing genetic polymorphisms found among the commonly used inbred mouse strains in Chapter 5.

The second section provides an overview of murine models of asthma and lung disease, osteoporosis, and substance abuse. Although there are a multitude of available mouse models for many different human disease-related traits, these chapters were written by investigators who have developed the models that are used in the disease area they investigate. More importantly, they provide an overview of available mouse models and what has been learned from analysis of these models. In addition, they also indicate what models need to be developed in order to advance our understanding of these diseases. Because many disease-related processes can only be studied in vivo, it is important to examine the quality of the available disease models.

In the third section, two chapters describe how genetic analysis of human populations has provided information about the genetic basis for susceptibility to asthma and other inflammatory diseases. Hopefully, we will be able to write additional chapters about the genetic basis for many more diseases within the next few years.

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