
Preface

Since the discovery of insulin by Banting and Best in 1922, diabetes mellitus is considered the paradigmatic disease where animal models have led to a therapeutic breakthrough. In addition, this breakthrough depended on earlier studies with animal experimentation by Claude Bernard (1849), Oskar Minkowski, and Joseph von Mehring (1889), indicating that diabetes mellitus is a failure of glucose homeostasis caused by a pancreatic malfunction. Furthermore, animal models have been indispensable for the elucidation of the cellular and molecular basis of both type 1 and type 2 diabetes in the second half of the last century. In spite of the enormous research progress made so far, diabetes is still a major life-shortening health threat. However, most of the experimentation needed for the invention and test of novel therapeutic approaches cannot be performed in humans. Thus, there is no alternative to appropriate animal models which are described in this volume.

In recent years, human studies have made enormous contributions towards an understanding of the genetic basis of diabetes mellitus. Genome wide association studies have identified numerous common gene polymorphisms that are associated with an increased risk to develop diabetes mellitus. Most of these polymorphisms are located in genes whose roles in the pathogenesis are almost completely unknown. Thus, animal models such as transgenic mice will be required for further progress in this area, and these mouse lines have to be characterized with accepted methods for the study of glucose homeostasis. In addition, the so far identified human genes explain only a small fraction of the total heredity of the disease. Thus, animal models with spontaneous diabetes mellitus may be useful to discover additional genes or pathways involved in the pathogenesis of the disease.

Research in humans has identified numerous factors that modify the risk of diabetes. Some of these factors such as environmental and nutritional variables have been identified by associations, and it is still necessary to establish their causality. Again, established and accepted animal models as well as validated procedures are required in order to test the efficacy of an intervention and to prove causality of associations. This volume therefore summarizes the current status of the most important models and procedures as a timely resource in experimental diabetology.

Animal Models in Diabetes Research is an unusual volume within the *Methods in Molecular Biology* series because its first two sections do not contain lab protocols but comprise a series of reviews on model strains. With these reviews, a comprehensive overview on our current knowledge of the pathogenesis and pathophysiology of diabetes is given. Models that are being used in the study of type 1 diabetes are the NOD mouse, the *Akita* mouse, and the BB rat (Part I). Major progress has been made in elucidating the polygenic pathogenesis of type 2 diabetes in the NZO and the TALLYHO mouse, and in the GK rat. With these strains, the strategy of positional cloning by mapping quantitative trait loci and subsequently identifying the responsible genes has proven to be very effective. It can be expected that future research employing this strategy will discover many more disease genes and malfunctioning pathways with relevance to the human disease.

Other well-characterized models that are described in Part II are the *db/db* mouse, the Zucker rat, and the sand rat *Psammomys obesus*. The pathogenesis and pathophysiology of these models is in part known, and allows targeted studies of preventive or therapeutic interventions. Thus, the chapters in the first two sections of the volume should help researchers to choose the appropriate model for their specific aims. As the closest model to human type 2 diabetes, spontaneously developing diabetes in non-human primates is described in Part III.

The fourth part of the volume contains established protocols that are employed in the characterization and study of animal models of diabetes. Key methods are the study of beta cell function (Chapters 12 and 13), of glucose homeostasis in vivo (Chapters 14 and 15) and in vitro (Chapter 16) as well as of beta cell autoimmunity (Chapter 17). In addition, models or protocols for the study of renal, cardiac, or retinal secondary complications are described in the Chapters 2, 3, and 19. Finally, two chapters are devoted to pancreatic stem cells.

All authors of this volume are distinguished experts in the field of diabetes research and have previously contributed original data with the models and/or methodology they have described here. I am deeply grateful for their contributions of excellent, informative, and comprehensive chapters. The credit for the success of the volume should be given to them. Also, I am grateful to my co-editors who have carefully reviewed and edited the chapters together with me; their input has enormously improved the volume. Finally, it is my hope that *Animal Models in Diabetes Research* will be an important resource to advance diabetes research in the years to come.

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Animal Models in Diabetes Research

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2012, XI, 325 p., Hardcover

ISBN: 978-1-62703-067-0

A product of Humana Press