The Mouse in Biomedical Research, 2nd Edition

Volume I
History, Wild Mice, and Genetics
THE MOUSE IN BIOMEDICAL RESEARCH, 2ND EDITION

Volume I
History, Wild Mice, and Genetics

EDITED BY

James G. Fox
Division of Comparative Medicine, MIT
Cambridge, MA

Muriel T. Davisson
The Jackson Laboratory
Bar Harbor, ME

Fred W. Quimby
Laboratory Animal Research Center
The Rockefeller University
New York, NY

Stephen W. Barthold
Center for Comparative Medicine
Schools of Medicine and Veterinary Medicine
University of California
Davis, CA

Christian E. Newcomer
Research Animal Resources and Department of
Molecular and Comparative Pathobiology
Johns Hopkins University
Baltimore, MD

Abigail L. Smith
School of Veterinary Medicine
University of Pennsylvania
Philadelphia, PA

AMSTERDAM • BOSTON • HEIDELBERG • LONDON • NEW YORK • OXFORD
PARIS • SAN DIEGO • SAN FRANCISCO • SINGAPORE • SYDNEY • TOKYO

Academic Press is an imprint of Elsevier
# Table of Contents

**Volume I History, Wild Mice, and Genetics**

<table>
<thead>
<tr>
<th>Section</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>List of Reviewers</td>
<td>x</td>
</tr>
<tr>
<td>List of Contributors</td>
<td>xi</td>
</tr>
<tr>
<td>Foreword</td>
<td>xiii</td>
</tr>
<tr>
<td>Preface</td>
<td>xv</td>
</tr>
<tr>
<td>1. Building a Better Mouse: One Hundred Years of Genetics and Biology</td>
<td>1</td>
</tr>
<tr>
<td>Herbert C. Morse III</td>
<td></td>
</tr>
<tr>
<td>2. Systematics of the genus <em>Mus</em></td>
<td>13</td>
</tr>
<tr>
<td>Priscilla K. Tucker</td>
<td></td>
</tr>
<tr>
<td>3. The Secret World of Wild Mice</td>
<td>25</td>
</tr>
<tr>
<td>Grant R. Singleton and Charles J. Krebs</td>
<td></td>
</tr>
<tr>
<td>4. Breeding Systems: Considerations, Genetic Fundamentals, Genetic Background, and Strain Types</td>
<td>53</td>
</tr>
<tr>
<td>Melissa L. Berry and Carol Cutler Linder</td>
<td></td>
</tr>
<tr>
<td>5. Mouse Strain and Genetic Nomenclature: an Abbreviated Guide</td>
<td>79</td>
</tr>
<tr>
<td>Janan T. Eppig</td>
<td></td>
</tr>
<tr>
<td>6. The Mouse Genome</td>
<td>99</td>
</tr>
<tr>
<td>Mark D. Adams</td>
<td></td>
</tr>
<tr>
<td>7. Gene Mapping</td>
<td>115</td>
</tr>
<tr>
<td>Muriel T. Davisson</td>
<td></td>
</tr>
<tr>
<td>8. Genetic Monitoring</td>
<td>135</td>
</tr>
<tr>
<td>Richard R. Fox, Michael V. Wiles, and Petko M. Petkov</td>
<td></td>
</tr>
<tr>
<td>9. Cytogenetics</td>
<td>145</td>
</tr>
<tr>
<td>Muriel T. Davisson and Mary Ann Handel</td>
<td></td>
</tr>
<tr>
<td>10. Mouse Embryology: Research Techniques and a Comparison of Embryonic Development between Mouse and Man</td>
<td>165</td>
</tr>
<tr>
<td>Matthew H. Kaufman</td>
<td></td>
</tr>
<tr>
<td>11. Gamete and Embryo Manipulation</td>
<td>211</td>
</tr>
<tr>
<td>K.C. Kent Lloyd</td>
<td></td>
</tr>
<tr>
<td>12. Chemical Mutagenesis in Mice</td>
<td>225</td>
</tr>
<tr>
<td>Martin Hrabé de Angelis, Dian Michel, Sibylle Wagner, Sonja Becker, and Johannes Beckers</td>
<td></td>
</tr>
<tr>
<td>13. Gene-Specific Mutagenesis</td>
<td>261</td>
</tr>
<tr>
<td>K.C. Kent Lloyd</td>
<td></td>
</tr>
<tr>
<td>Robert G. Pergolizzi and Ronald G. Crystal</td>
<td></td>
</tr>
<tr>
<td>15. Mouse and Human Pluripotent Stem Cells</td>
<td>281</td>
</tr>
<tr>
<td>Leslie F. Lock</td>
<td></td>
</tr>
<tr>
<td>16. Drugs and the Mouse: Pharmacology, Pharmacogenetics, and Pharmacogenomics</td>
<td>289</td>
</tr>
<tr>
<td>Lucia F. Jorge-Nebert, Sandrine Derkenne, and Daniel W. Nebert</td>
<td></td>
</tr>
<tr>
<td>Index</td>
<td>321</td>
</tr>
</tbody>
</table>
Volume II Diseases

List of Reviewers
List of Contributors
Foreword
Preface

Viral Diseases

DNA Viruses

1. Murine Cytomegalovirus and Other Herpesviruses
   Geoffrey R. Shellam, Alec J. Redwood, Lee M. Smith, and Shelley Gorman
   1

2. Mouse Adenoviruses
   Katherine R. Spindler, Martin L. Moore, and Angela N. Cauthen
   49

3. Mousepox
   R. Mark L. Buller and Frank Fenner
   67

4. Parvoviruses
   Robert O. Jacoby and Lisa Ball-Goodrich
   93

5. Polyoma Viruses
   Thomas L. Benjamin
   105

RNA Viruses

6. Mouse Hepatitis Virus
   Stephen W. Barthold and Abigail L. Smith
   141

7. Lymphocytic Choriomeningitis Virus
   Stephen W. Barthold and Abigail L. Smith
   179

8. Lactate Dehydrogenase-Elevating Virus
   Jean-Paul Coutelier and Margo A. Brinton
   215

9. Reoviridae
   Richard L. Ward, Monica M. McNeal, Mary B. Farone, and Anthony L. Farone
   235

10. Retroelements in the Mouse
    Herbert C. Morse III
    269

11. Sendai Virus and Pneumonia Virus of Mice (PVM)
    David G. Brownstein
    281

12. Cardioviruses: Encephalomyocarditis Virus and Theiler’s Murine Encephalomyelitis Virus
    Howard L. Lipton, A.S. Manoj Kumar, and Shannon Hertzler
    311

13. Chlamydial Diseases
    Roger G. Rank
    325

14. Clostridial Species
    Kimberly S. Waggie
    349

15. Enterobacteriaceae, Pseudomonas aeruginosa, and Streptobacillus moniliformis
    Hilda Holcombe and David R. Schauer
    365

16. Aerobic Gram-Positive Organisms
    Cynthia Besch-Williford and Craig L. Franklin
    389

17. Helicobacter Infections in Mice
    James G. Fox and Mark T. Whary
    407

18. Mycoplasma pulmonis, Other Murine Mycoplasmas, and Cilia-Associated Respiratory Bacillus
    Trenton R. Schoeb
    437

19. Pasteurellaceae
    Werner Nicklas
    469

20. Fungal Diseases in Laboratory Mice
    Virginia L. Godfrey
    507

Mycotic and Parasitic Diseases

TABLE OF CONTENTS
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>Protozoa</td>
<td>517</td>
</tr>
<tr>
<td></td>
<td>Katherine Wasson</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Helminth Parasites of Laboratory Mice</td>
<td>551</td>
</tr>
<tr>
<td></td>
<td>Kathleen R. Pritchett</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Arthropods</td>
<td>565</td>
</tr>
<tr>
<td></td>
<td>David G. Baker</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Miscellaneous Diseases</strong></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>The Tumor Pathology of Genetically Engineered Mice: A New Approach to Molecular Pathology</td>
<td>581</td>
</tr>
<tr>
<td></td>
<td>Robert D. Cardiff, Robert J. Munn, and Jose J. Galvez</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Spontaneous Diseases in Commonly Used Mouse Strains</td>
<td>623</td>
</tr>
<tr>
<td></td>
<td>Cory Brayton</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>Zoonoses and Other Human Health Hazards</td>
<td>719</td>
</tr>
<tr>
<td></td>
<td>Christian E. Newcomer and James G. Fox</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Index</strong></td>
<td>747</td>
</tr>
</tbody>
</table>

# Volume III Normative Biology, Husbandry, and Models

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gross Anatomy</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Vladimír Komárek</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Mouse Physiology</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Robert F. Hoyt, Jr., James V. Hawkins, Mark B. St. Claire, and Mary B. Kennett</td>
<td></td>
</tr>
</tbody>
</table>

**List of Reviewers**
x

**List of Contributors**
xii

**Foreword**
xiii

**Preface**
xv

**Normative Biology**

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gross Anatomy</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Vladimír Komárek</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Mouse Physiology</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Robert F. Hoyt, Jr., James V. Hawkins, Mark B. St. Claire, and Mary B. Kennett</td>
<td></td>
</tr>
</tbody>
</table>

**Health Delivery and Quality Assurance Programs for Mice**

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Nutrition</td>
<td>321</td>
</tr>
<tr>
<td></td>
<td>Graham Tobin, Karla A. Stevens, and Robert J. Russell</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Health Delivery and Quality Assurance</td>
<td>385</td>
</tr>
<tr>
<td></td>
<td>Diane J. Gaertner, Glen Otto and Margaret Batchelder</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Environmental and Equipment Monitoring</td>
<td>409</td>
</tr>
<tr>
<td></td>
<td>J. David Small and Rick Deitrich</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Biomethodology and Surgical Techniques</td>
<td>437</td>
</tr>
<tr>
<td></td>
<td>Alison M. Hayward, Laura B. Lenke, Erin C. Bridgeford, Elizabeth J. Theve, Courtnye N. Jackson, Terrie L. Cunliffe-Beamer, and Robert P. Marini</td>
<td></td>
</tr>
</tbody>
</table>
TABLE OF CONTENTS

Overview

1. The Molecular Basis of Lymphoid Architecture in the Mouse 57
   Carola G. Vinuesa and Matthew C. Cook

2. The Biology of Toll-Like Receptors in Mice 109
   Osamu Takeuchi and Shizuo Akira

3. Genomic Organization of the Mouse Major Histocompatibility Complex 119
   Attila Kumánovics

4. Some Biological Features of Dendritic Cells in the Mouse 135
   Kang Liu, Anna Charalambous, and Ralph M. Steinman

5. Mouse Models Revealed the Mechanisms for Somatic Hypermutation and Class Switch Recombination of Immunoglobulin Genes 155
   Maria D. Iglesias-Ussel, Ziqiang Li, and Matthew D. Scharff

6. Mouse Natural Killer Cells: Function and Activation 169
   Francesco Colucci

7. Cytokine-Activated JAK-STAT Signaling in the Mouse Immune System 179
   Bin Liu and Ke Shuai

8. Signal Transduction Events Regulating Integrin Function and T Cell Migration in the Mouse 195
   Lakshmi R. Nagarajan and Yoji Shimizu

9. Mouse Models of Negative Selection 207
   Troy A. Baldwin, Timothy K. Starr, and Kristin A. Hogquist

Index 759
<table>
<thead>
<tr>
<th>No.</th>
<th>Chapter Title</th>
<th>Authors</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Peripheral Tolerance of T Cells in the Mouse</td>
<td>Vigo Heissmeyer, Bogdan Tanasa, and Anjana Rao</td>
<td>223</td>
</tr>
<tr>
<td>11</td>
<td>The Genetics of Mouse Models of Systemic Lupus</td>
<td>Srividya Subramanian and Edward K. Wakeland</td>
<td>243</td>
</tr>
<tr>
<td>12</td>
<td>Inhibitory Receptors and Autoimmunity in the Mouse</td>
<td>Menna R. Clatworthy and Kenneth G.C. Smith</td>
<td>261</td>
</tr>
<tr>
<td>13</td>
<td>Mouse Models of Immunodeficiency</td>
<td>B. Anne Croy, James P. Di Santo, Marcus Manz, and Richard B. Bankert</td>
<td>275</td>
</tr>
<tr>
<td>14</td>
<td>Mouse Models to Study the Pathogenesis of Allergic Asthma</td>
<td>Chad E. Green, Nicholas J. Kenyon, Scott I. Simon, and Fu-Tong Liu</td>
<td>291</td>
</tr>
<tr>
<td>15</td>
<td>The Mouse Trap: How Well Do Mice Model Human Immunology?</td>
<td>Christopher C.W. Hughes and Javier Mestas</td>
<td>303</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Index</td>
<td>313</td>
</tr>
</tbody>
</table>
List of Reviewers for Chapters in this Volume

Avner, Phil
Pasteur Institute, Paris, France

Bucan, Maja
University of Pennsylvania, Philadelphia, PA

Bult, Carol
The Jackson Laboratory, Bar Harbor, ME

Carlton, Michael D.
National Museum of Natural History, Washington, D. C.

Cook, Susan A.
The Jackson Laboratory, Bar Harbor, ME

Donovan, Peter J.
Johns Hopkins Medicine, Baltimore, MD

Eicher, Eva M.
The Jackson Laboratory, Bar Harbor, ME

Gardner, Murray
University of California, Davis, CA

Johnson, Kenneth R.
The Jackson Laboratory, Bar Harbor, ME

Mobraaten, Larry E.
The Jackson Laboratory, Bar Harbor, ME

Nachman, Michael
University of Arizona, Tucson, AZ

Paigen, Beverly J.
The Jackson Laboratory, Bar Harbor, ME

Papaioannou, Virginia
Columbia University, New York, NY

Pinkert, Carl A.
University of Rochester School of Medicine and Dentistry

Rowe, Lucy B.
The Jackson Laboratory, Bar Harbor, ME

Vesell, Elliot
Hershey Medical Center, University of Pennsylvania, PA

Watters, James W.
Merck & Co., West Point, PA

Wilshire, Tim
Genomics Institute of the Novartis Research Foundation, San Diego, CA

Womack, James E.
Texas A & M University, College Station, TX
Contributors

Mark D. Adams
Department of Genetics
Case Western Reserve University
Cleveland, OH 44106

Sonja Becker
GSF National Research Center for Environment & Health
Institute of Experimental Genetics D-85764
Neuherberg
Germany

Johannes Beckers
GSF National Research Center for Environment & Health
Institute of Experimental Genetics D-85764
Neuherberg
Germany

Melissa L. Berry
The Jackson Laboratory
Bar Harbor, ME 04609-1500

Ronald G. Crystal
Department of Genetic Medicine
Weill Medical College of Cornell University
New York, NY 10021

Muriel T. Davisson
The Jackson Laboratory
Bar Harbor, ME 04609-1500

Sandrine Derkenne
Department of Environmental Health and Center for Environmental Genetics (CEG)
University of Cincinnati Medical Center
Cincinnati, OH 45267-0056

Janan T. Eppig
Informatics Program
The Jackson Laboratory
Bar Harbor, ME 04609

Richard R. Fox
The Jackson Laboratory
Bar Harbor, ME 04609-1500

Mary Ann Handel
The Jackson Laboratory
Bar Harbor, ME 04609-1500

Martin Hrabé de Angelis
GSF National Research Center for Environment & Health
Institute of Experimental Genetics D-85764
Neuherberg
Germany

Lucia F. Jorge-Nebert
Department of Environmental Health and Center for Environmental Genetics (CEG)
University of Cincinnati Medical Center
Cincinnati, OH 45267-0056

M.H. Kaufman
School of Biomedical and Clinical Laboratory Sciences
University of Edinburgh
Edinburgh
UK

Charles J. Krebs
Institute for Applied Ecology
University of Canberra
Canberra ACT 2601
Australia

Carol Cutler Linder
Natural Sciences
New Mexico Highlands University
Las Vegas, NH 87701

K. C. Kent Lloyd
Center for Comparative Medicine
School of Veterinary Medicine
University of California at Davis
Davis, CA 95616
Leslie F. Lock  
Departments of Developmental and Cell Biology and Biological Chemistry  
University of California Irvine, CA 92697-3940

Herbert C. Morse, III  
Laboratory of Immunopathology  
National Institute of Allergy and Infectious Diseases  
NIH Bethesda, MD 20892

Dian Michel  
GSF National Research Center for Environment & Health  
Institute of Experimental Genetics D-85764 Neuherberg  
Germany

Daniel W. Nebert  
Department of Environmental Health and Center for Environmental Genetics (CEG)  
Department of Pediatrics & Molecular Developmental Biology, Division of Human Genetics  
University of Cincinnati Medical Center Cincinnati, OH 45267-0056

Robert G. Pergolizzi  
Department of Genetic Medicine  
Weill Medical College of Cornell University New York, NY 10021

Petko M. Petkov  
The Jackson Laboratory Bar Harbor, ME 04609-1500

Grant R. Singleton  
International Rice Research Institute  
Las Baños, Laguna  
Philippines

Priscilla K. Tucker  
Dept. of Ecology and Evolutionary Biology  
University of Michigan  
Ann Arbor, MI 48109

Sibylle Wagner  
GSF National Research Center for Environment & Health  
Institute of Experimental Genetics D-85764 Neuherberg  
Germany

Michael V. Wiles  
The Jackson Laboratory  
Bar Harbor, ME 04609-1500
Mice are centuries old as an interest of humans. Probably initially pets, eventually they became a research interest, even by Gregor Mendel in the 1800s. But it was the achievement of an inbred strain by Clarence Cook Little in 1909 that launched the mouse as a focus for understanding the biology and genetics of ourselves. The establishment of inbred strains nearly 100 years ago led the way to defined strains with animals of repeatable and also repeatedly different genotypes for biomedical study. They soon offered the exciting initial understanding that genetics played a role in cancer.

With large mouse populations under observation, natural mutations of many varieties appeared, some morphological, some debilitating, others subtle with defined biochemical problems. And so it was recognized early that the mouse had similar (sometimes nearly identical) diseases to humans and that it could provide a powerful basis for a practical understanding of the human medical condition. For researchers it was obvious the mouse provided us as well with a tool for understanding the whole mammalian biology, including physiology, immunology, and development. Thus the mouse became essential for basic research. And the mouse was small, easily and economically maintained. It bred quickly and aged 30 times as fast as humans. It had everything.

A hope early on was that the powerful combination of genetics and chromosomal anatomy so well exploited in Drosophila would be found in the mouse. This hope was temporarily dashed when it was discovered that except for the X chromosome, all the chromosomes of the mouse were acrocentric. Except for their length, the mouse chromosomes were essentially indistinguishable. But soon after in the 1960s with the development of techniques for banding chromosomes, this drawback was fully overcome. The positioning of mouse genes on specific chromosomes and the studies of chromosomal aberrations and disease quickly advanced. We were all amazed at how many huge chunks of chromosomal segments were conserved between mouse and human since their separation some 65 million years ago. That finding alone has helped scientists to find genes controlling human disease, already found in the mouse. It cannot be understated that advancements in understanding of animal health and control of mouse diseases was essential for these wide ranging and exponential opportunities in research. Similarly, the parallel exponential advances in computer technology, capacity, and availability was essential.

The mouse has never since disappointed researchers as was evidenced by the first four volumes of The Mouse in Biomedical Research published in 1981-1983. In those volumes the word “exponential” was used many times. The success of the studies described there was a milestone for researchers to learn and reflect on the variety of scientific advancements and understanding the biology of the mouse. It provided as well a description of the fundamental guidelines and techniques for raising mice, essential for effective and humane experimentation. “Exponential” continues to be the word for our times; it characterizes so many human endeavors and certainly research avenues, methodologies, and successes. Various new breeding schemes have revealed much about linkage and biological effects of specific genes, segments, and single chromosomes. A better understanding of mutagenesis has made the production and study of mutants an experimental science. Genes and other segments of chromosomes can now be moved around and exchanged among species. Gene therapy and stem cell research in the mouse have the promise of great immediate medical benefit. Every new research approach of course does not work, but the plasticity of biological systems and their seeming “willingness” to be maneuvered is surprising.

In the last two decades the rapid advances in DNA technology have made it now possible to study essentially complete known sequences of the genomes of mouse and human. It now does not surprise us that the human and mouse genomes each contain about 30,000 genes and that the DNA sequences are for the most part the same. Perhaps only a few hundred genes uniquely differentiate the species. Much non-protein coding DNA is also conserved, but for what reasons? Comparative genomics is providing awesome insights and raising revolutionary new questions.

It is timely now for this second edition of The Mouse in Biomedical Research where the state of the art in mouse research is captured again. Much has happened since the first edition. Much basic information has remained the same with modifications. The first volume entitled History, Wild Mice, and Genetics begins with three chapters by Morse, Tucker, Singleton, and Krebs on the background of the mouse in history, systematics, and natural environment. A researcher will find this fascinating background useful, because appropriate interpretation of laboratory findings may depend on it. Berry and Linder’s chapter on Breeding Systems reveals the years of
development of such a variety of systematic mating schemes
that manipulate the genome to better understand linkage and
genetic effects. The following chapter by J. T. Eppig describes
many years of thought given to systematic and agreed-upon
nomenclature, essential to communication among us about
genetically defined mice. The next four chapters by Adams,
Davisson, Fox, Wiles, Petkov, and Handel provide a broad up
to date understanding of present genetic knowledge of the
mouse and methods for examining the genome. The exciting
new approaches and prospects in mouse gamete and embryol-
gy are given by Kaufman and Lloyd. Then de Angeles, Michel,
Wagner, Becker, Beckers, and Lloyd describe methodological
advances and findings in the relatively new field of experimental
mutagenesis. New developments in gene transfer and its value
in mouse biology is given by Pergolizzi and Crystal. Lock’s
chapter shows how pluripotent embryonic stem cells have
already provided many new avenues for research in mouse and
human. The insights derived already are significant and the
impact on medical science can be expected to be enormous.
The last chapter by Jorge-Nebert, Derkenne, and Nebert shows
the great advances in understanding the genetic nature of reaction
and metabolism of drugs where information is desperately
needed.

The breadth of topics and the depth of coverage, assures that
The Mouse in Biomedical Research will continue to be a stan-
dard reference for investigators using mice in biological research.

THOMAS H. RODERICK
THE JACKSON LABORATORY
BAR HARBOR, MAINE
Preface

The American College of Laboratory Animal Medicine (ACLAM) was formed in 1957 in response to the need for specialists in laboratory animal medicine. The college has promoted high standards for laboratory animal medicine by providing a structured framework to achieve certification for professional competency and by stressing the need for scientific inquiry and exchange via progressive continuing education programs. The first edition of “The Mouse in Biomedical Research” consisting of four volumes, and published in 1981-1983 was a part of the College’s effort to fulfill those goals. It is one of a series of comprehensive texts on laboratory animals developed by ACLAM over the past three decades: “The Biology of the Laboratory Rabbit” was published in 1974, “The Biology of The Guinea Pig” in 1976 and a two-volume work “Biology of The Laboratory Rat” in 1979 and 1980. Also, in 1979 the College published a two-volume text on “Spontaneous Animal Models of Human Disease”. In 1984 the first edition of “Laboratory Animal Medicine” appeared in print followed by “Laboratory Hamsters” in 1987. The second edition of The Biology of the Laboratory Rabbit was published in 1994. A two-volume treatise on “Nonhuman Primates in Biomedical Research” was published in 1995 and 1998. A text “Anesthesia and Analgesia in Laboratory Animals” was published in 1997 followed by the second edition of “Laboratory Animal Medicine” in 2002. Most recently, the second edition of “The Laboratory Rat” was published in 2005.

The estimated annual use of 100 million-plus mice worldwide attests to the importance of the mouse in experimental research. The introduction of genetically engineered mice has only increased the usefulness of the mouse model in biomedical research. In no other species of animal has such a wealth of experimental data been utilized for scientific pursuits. Knowledge of the mouse that has been accumulated is, for the most part, scattered throughout a multitude of journals, monographs and symposia. It has been 25 years since the publication of the first edition of the “Mouse in Biomedical Research”. The intent of this second edition is to build upon the framework of the first edition, rather than simply to update and duplicate the earlier effort.

The intended purpose of this text is to assemble established scientific data emphasizing recent information on the biology and use of the laboratory mouse. Separation of the material into multiple volumes was essential because of the number of subject areas covered. The four volumes consist of 80 chapters coauthored by 167 scientists.

The information in Volume 1 serves as a primer for scientists new to the field of mouse research. It provides information about the history, basic biology and genomics of the laboratory mouse (Mus musculus), as well as basic information on maintenance and use of mouse stocks. Mouse origins and relationships are covered in chapters on history, evolutionary taxonomy and wild mice. Genetics and genomics of the mouse are covered in chapters on genetic nomenclature, gene mapping, cytogenetics and the molecular organization of the mouse genome. Maintenance of laboratory mice is described in chapters on breeding systems for various types of strains and stocks and genetic monitoring. Use of the mouse as a model system for basic biomedical research is described in chapters on chemical mutagenesis, gene trapping, gene therapy, pharmacogenetics and embryo manipulation.

Volume 2 entitled Diseases departs from the first edition of the same title by discussing specific disease-causing microorganisms, whereas the first edition discussed infectious diseases affecting specific organs and tissues. This volume consists of 26 chapters subdivided into RNA viruses and DNA viruses, as well as bacterial, mycotic and parasitic infections. These chapters not only provide updates on pathogenesis, epidemiology and prevention of previously recognized murine pathogens, but also include chapters on newly recognized disease-causing organisms: mouse parvovirus, cilia-associated respiratory bacilli and Helicobacter spp. A separate category, consisting of 3 chapters, discusses zoonoses, tumor pathology of genetically engineered mice and spontaneous diseases in commonly used mouse strains.

Volume 3 encompasses 23 chapters whose contents provide a broad overview on the laboratory mouse’s normative biology, husbandry and its use as a model in biomedical research. This consists of chapters on behavior, physiology, reproductive physiology, anatomy, endocrinology, hematology and clinical chemistry. Other chapters cover management, as well as nutrition, gnotobiotics and disease surveillance. Individual chapters describe the mouse as a model for the study of aging, eye research, neurodegenerative diseases, convulsive disorders, diabetes and cardiovascular and skin diseases. Chapters on imaging, surgical and other research techniques and the use of the mouse in assays of biological products also are included.
Volume 4 is a completely new addition to this series, dedicated to mouse immunology. It is based on the vast body of knowledge which has made the mouse the model of choice when studying immunity in human beings. Arguably more is known about the immune system in mice than any other species except human. In large part this is due to the power of genetic engineering to delineate molecular mechanisms. This volume includes an overview of mouse immunology, including both the innate and adaptive immune systems, followed by 15 chapters (mini-reviews), each dealing with a specific area of immunology. The overview addresses broad concepts concerning molecular and cellular immunology and cites both current references and the appropriate chapter, for more detailed information, from the mini-reviews which follow. The 15 chapters illustrate the power of genetic engineering in dissecting each component of the immune response from the development of lymphoid tissues to signal transduction pathways in activated cells. Individual chapters address: The Genomic Organization of the MHC, Toll-like Receptors, The Molecular Basis of Lymphoid Architecture, The Biology of Dendritic Cells, Somatic Hypermutation and Class Switching, Natural Killer Cell Function and Activation, Cytokine Mediated Signaling, Signal Transduction Events Regulating Integrin Function and T-Cell Migration, Central Tolerance in T-Cells, Peripheral Tolerance in T-cells, Inhibitory Receptors and Autoimmunity. The volume also includes the use of mice in studies of Systemic Autoimmunity, Immunodeficiency, Allergic Airway Inflammation and the Differences Between Mouse and Human Immunology.

This treatise was conceived with the intent to offer information suitable to a wide cross section of the scientific community. It is hoped that the four volumes will serve as a standard reference source for scientists using mice in biomedical research. Students embarking on scientific careers also will benefit from the broad coverage of material presented in compendium format. Certainly, specialists in laboratory animal science will benefit from these volumes; technicians in both animal care and research will find topics on surgical techniques, management and environmental monitoring of particular value.

The editors wish to extend special appreciation to the contributors to these volumes. Authors were selected because of knowledge and expertise in their respective fields. Each individual contributed his or her time, expertise and considerable effort to compile this resource treatise. In addition, the contributors and editors of this book, as with all volumes of the ACLAM series texts, have donated publication royalties to the American College of Laboratory Animal Medicine for the purpose of continuing education in laboratory animal science and comparative medicine. This book could not have been completed without the full support and resources of the editors’ parent institutions which allowed us the time and freedom to assemble this text. A special thanks is also extended to the numerous reviewers of the edited work whose suggestions helped the authors and editors present the material in a meaningful and concise manner. We also thank the editorial staff of Elsevier for their assistance.

Finally, we especially acknowledge with deep appreciation the editorial assistance of Lucille Wilhelm, whose dedication and tireless commitment, as well as good humor, throughout this project were of immeasurable benefit to the editors in the completion of this text.

James G. Fox
Stephen W. Barthold
Muriel T. Davison
Christian E. Newcomer
Fred W. Quimby
Abigail L. Smith