

MOUSE

A Volume in The Laboratory Animal Pocket Reference Series

The Laboratory **MOUSE**

Second Edition

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preface

Mice are used in biomedical research more than any other species. They are small and comparatively easy to house and handle, and they have attributes that make them particularly desirable as animal models for studies of the basis, treatment, and prevention of human diseases of genetic origin. They breed often and produce comparatively large litters; they develop rapidly and typically complete their life cycle within about 2 years; and they thrive in the laboratory environment. They also share approximately 95% of their genome with humans and develop many disease syndromes that are similar to inherited diseases of humans. Perhaps most important of all is their ability to survive inbreeding—most species exhibit *inbreeding depression* to such an extent that truly inbred strains cannot be created or sustained—and their ability to tolerate and breed following complex genetic manipulations. It is hardly surprising that these valuable animals are viewed as precious entities within the laboratory. Emphasis is placed on assuring that they are cared for and handled in a manner that optimizes their value in research while safeguarding their health and welfare.

The first edition of this handbook was published in 2000. Since that time, there have been many advances in mouse research, as well as improved strategies for protecting the health and welfare of laboratory mice. This second edition was revised and expanded to reflect those advances. As with the first edition, it was devised as a quick reference for investigators, technicians, managers, and animal caretakers charged with caring for, or using, mice in biomedical research. While it cannot, and should not, be viewed as a substitute for proper training, we anticipate that it will prove particularly

useful for individuals at small institutions that may lack the depth of resources often associated with large, complex animal care and use programs.

The second edition is organized a bit differently than the first edition, and is comprised of seven chapters: “Important Biologic Features” (Chapter 1), “Husbandry” (Chapter 2), “Management” (Chapter 3), “Clinical Medicine” (Chapter 4), “Preventive Medicine” (Chapter 5), “Experimental Methodology” (Chapter 6), and “Resources and Additional Information” (Chapter 7). Compared with the first edition, there is new information on the following topics: colony health vs. health of individual animals; moving mice within the institution and shipping to other institutions; receiving mice from other institutions, including quarantine programs; phenotyping; testing of biological materials for microbial contamination; and developing an emergency plan for dealing with outbreaks of infectious diseases.

The authors wish to specifically acknowledge the contributions of Kristin Blanchette and Kristin Cough, both of whom provided invaluable assistance in staging and photographing many of the techniques illustrated in this handbook.

continued to pursue this interest at several institutions while heading the Facility for Comparative Studies at the Hospital for Special Surgery (1992–1998). At Baylor College of Medicine (1998–2004), she headed the Comparative Pathology Laboratory, and was an associate professor in pathology, associate director of the Center for Comparative Medicine, interim attending veterinarian, and served on the Institutional Animal Care and Use Committee (IACUC), while pursuing research collaborations, teaching, and developing national and international conferences on the characterization and pathology of genetically engineered mice. In 2004 she moved to Johns Hopkins to develop a collaborative phenotyping core based in the Department of Molecular and Comparative Pathobiology (MCP), where veterinarian faculty investigators and trainees provide a unique comparative and translational research resource, in an institution with exceptional resources for multidisciplinary biomedical research. Dr. Brayton is a diplomate of both the American College of Veterinary Pathology and the American College of Laboratory Animal Medicine.

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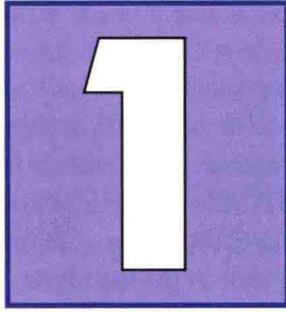
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important biological features

introduction

Mice have been domesticated for centuries, even millennia, and have been used in scientific research since the 1600s. However, development of the laboratory mouse as a research model really began with genetic experiments in the early 1900s. Today, the laboratory mouse is recognized as the preeminent model for modern genetic research. Mice are also used in a variety of other types of research, including cancer, immunology, toxicology, metabolism, developmental biology, diabetes, obesity, aging, and cardiovascular research. They are prized for many qualities, including their small size, short generation time, and ease of breeding within the laboratory. The fact that they are genetically the best characterized of all mammals increases their value for all fields of study.

Mice belong to the order Rodentia, and most of the mice used in research belong to the genus *Mus*. Within that genus lies *Mus musculus*, with a number of subspecies described, including *Mus musculus domesticus* (the common house mouse) and *Mus musculus musculus*. Though laboratory mice are believed to have come from a mosaic of *Mus musculus* subspecies, they are typically referred to as *Mus musculus* (Bonhomme et al., 1987).

stocks and strains

Both genetically diverse and genetically defined mice are used in research. NIH Swiss, Swiss Webster, ICR, and CD-1 are among the

most commonly used genetically diverse stocks. There are thousands of genetically defined strains, including the following:

- **Inbred mice:** Mice of a particular inbred strain result from a minimum of 20 consecutive generations of brother × sister matings and are virtually identical to all other mice of the same strain; C57BL/6, BALB/c, C3H, FVB, 129, DBA, and CBA are among the most commonly used inbred strains.
- **Hybrid mice:** These mice are first-generation (F1) crosses between two different inbred strains. An example is the B6D2F1 line, which is a cross between the C56BL/6 (female parent) and DBA/2 (male parent) strains.
- **Recombinant inbred mice:** When F1 hybrids resulting from the same cross are mated together, the result is second-generation (F2) mice. Recombinant inbred strains result from 20 consecutive generations of brother × sister matings starting with the F2 mice.
- **Inbred mice that carry spontaneous mutations:** These are inbred mice that are perpetuated from a single mouse that was born with a significant genetic change. An example is the obese mouse (B6.V-*Lep^{ob}*), which becomes massively obese because of a mutation that occurs in the gene that codes for the hormone leptin.
- **Coisogenic strains:** These are strains of mice that differ from each other only at one gene, the difference being due to a spontaneous mutation that occurred in that gene. After the appearance of the mutation, the animals with the mutation are maintained as a separate strain from the original inbred strain. (*Note:* Coisogenic strains can also be created using the technology for producing *knockout* mice; see below.)
- **Mice that carry induced mutations:** Mutations may be induced by chemicals (e.g., ethylnitrosourea), irradiation, or retroviruses. This category also includes the following categories.
 - **Transgenic mice:** These mice carry foreign DNA that was intentionally inserted into their own DNA. Examples include several transgenic mouse models of amyotrophic lateral sclerosis (Lou Gehrig's disease), all of which carry inserted copies of a human gene that codes for an abnormal enzyme (e.g., B6SJL-Tg(SOD1-G93A)1Gur).