The laboratory mouse

**The Laboratory Mouse**

Joan Staats

*Mus musculus* Linn. the common house mouse, has been a member of man's immediate environment for many centuries. Along with other members of the order Rodentia, rats and mice constituting the family Muridae spread with man and his commerce from their origin in Asia to all parts of the world. A thorough account of the antiquity of the fancy mouse and its interactions with the human species is given by Clyde E. Keeler (1931).

The conversion of the mouse from pest to pet to productive element of the scientific community took place slowly. During the 19th century a number of European zoologists bred fancy mice to investigate varietal characters and tried to interpret the results by Galton's law of ancestral inheritance. The valuable information thus acquired, however, could not be correctly interpreted until the rediscovery of Mendel's work in 1900. The problems of inbreeding, selection, decrease in fertility, appearance of abnormalities, and increased susceptibility to disease noted by earlier workers were attacked from a new viewpoint in the light of Mendel's findings. Cuénot's 1902 papers in *Archives de Zoologie Expérimentale et Générale* seem to be the first to apply Mendelian principles to animals ( Bateson, 1903). William E. Castle working with*Drosophila*, Sewell Wright with guinea pigs, and S. Hatai and Helen Dean King with rats provided early examples of the new scientific breeding of animal forms ( Castle et al., 1906; Wright, 1922; King, 1911).

**ORIGINS OF COMMON INBRED STRAINS**

Clarence Cook Little, a Harvard undergraduate, began studying the inheritance of coat color in mice under Castle's tutelage in 1907. Two years later he obtained a pair of mice carrying the recessive genes for dilution, brown, and nonagouti. During the next few years he inbred the descendants of this pair brother to sister for more than 20 generations, with selection for vigorous animals, thus creating the first inbred strain of mice, which he named dba. It was later called dba after the three recessive genes, and since about 1950 has been written DBA.

Little was interested in the study of neoplastic diseases and recognized that difficulties were bound to arise in dealing with a condition which appears relatively late in life and is subject to much environmental influence. He reasoned that elimination of the great genetic diversity in unrelated animals would facilitate that study.

Within 15 years after the origin of the first inbred strain, most of the others used in cancer research had been established. Relationships between strains and families of strains are shown in Figure 1-1.

In 1913, Halsey J. Bagg obtained some albino mice from a dealer in Ohio, maintained them as a closed colony, and used them in behavioral experiments. In 1921, Leonell C. Strong mated a mouse of the Bagg albino stock with one from an albino stock Little maintained at that time at Cold Spring Harbor. From this cross Strong started the A strain, a high mammary and lung tumor strain ( Heston, 1949). In 1920, Strong made a series of crosses between the Bagg albinos and strain DBA, and from the hybrids developed a number of inbred lines: C3H, CBA, C, CHI, and C12I. Of these the C3H has been the most widely used and has been split into several sublines with well-defined differences between them ( Staats, 1964).

Another well-known and widely used family of strains also dates from 1921. While he was at Cold Spring Harbor, Little obtained mice from Miss A.E.C. Lathrop, a fancier in Granby, Massachusetts, and mated littermates female 57 and male 52. Progeny of this black pair segregated as black and brown; inbreeding them led to the C57BL and C57BR strains. C57L was developed by J.M. Murray from a color mutant in a C57BR subline.

Also at Cold Spring Harbor, E. Carleton MacDowell received from Little the descendants of Miss Lathrop's male 52, the progenitor of the C57 lines, and female 58. He inbred these mice, forming the C58 strain, and by selection was able to establish an incidence of leukemia of about 90 per cent. MacDowell also inbred the Bagg albinos and sent some to George D. Snell about 1932. Snell used the letter "c" in his laboratory records as a convenient indication that the animals were white. The letter became attached to "Bagg alb," and the designation evolved to BALB/c, a widely used strain.

While at the Henry Phipps Institute in Philadelphia in 1928, Jacob Furth purchased three different stocks of mice, designated A, R, and S. Stock A "was claimed to yield many cancers," and stock R was stated to be cancer-free. He and his collaborators inbred a number of families in each stock, from which were derived the AK and RF strains (Furth et al., 1933).

The widely distributed Swiss albino mice, largely noninbred, are mainly derived from two males and seven females which Clara J. Lynch of the Rockefeller Institute obtained from A. de Coulon of Lausanne in 1926 (Lynch, 1961, personal communication). The original stock probably came from Paris. Descendants of these mice were distributed to other laboratories and to commercial breeders. Some lines, such as the SWR/J and SJL/J, have since been inbred. Origins of these and many other inbred strains are listed in Table 1-1. References given are not in all cases the original ones, for an attempt has been made to list papers best describing the strain origin. In most cases multiple references are supplementary, offering additional information or enabling the searcher to go from a reference in which the strain is clearly named to one in which the real origin is given but the mice are not so named. In some cases, no really...
satisfactory reference can be found. The many fostered and congenic strains have not been included. For these interesting formulations the latest issue of Inbred Strains of Mice should be consulted. Strains known to be extinct have not been listed.

USE OF MICE IN RESEARCH

The majority of inbred strains, from the most recent back to the DBA, were developed for use in cancer research, to prove or disprove the existence of genetic factors influencing the incidence of cancer and the independence of inheritance of different types of cancers. By selection during inbreeding, various types of malignancies in predictable frequencies were established in the several genotypes. Or, conversely, resistance to all forms of neoplasia was established (Chapters 27, 28). As inbred strains became available and information about them began appearing in the scientific literature, investigators recognized that these animals could contribute greatly to medical research. It became possible to use biological material in experiments with confidence the only variables were those the investigator chose to include in the experimental design. The greater the uniformity among animals, the fewer are needed to attain a given standard of accuracy or repeatability.

A large proportion of cancer research has been built upon inbred strains of mice. Many types of projects were made possible only by the development of the strains and the tumors the mice produce or tolerate, and a large part of the remainder is dependent on the strains for suitable material.

Investigators in many fields have come to realize the value of F\textsubscript{1} hybrids from crosses between inbred strains. Such mice are genetically homogeneous although heterozygous for those gene pairs by which the parent strains differ. Hybrids have been found to be as predictable in response as the parent strains, though not necessarily like either one. The greatest general advantage of F\textsubscript{1} hybrids is their increased vigor and, in certain types of terminal experiments, they are preferred over inbred mice. Such mice cannot be used for propagating their own characteristics, however, since genetic segregation will occur in F\textsubscript{2} generations.

As an extra dividend of fixing coat-color genes and cancer-affecting genes by inbreeding, it was found that other constitutional diseases also became established in the various genotypes (Chapter 29). Many of these conditions parallel pathological states in man, thus providing unique material for studies on causation as well as on the march of the disease process.

Other differences between strains have been found and exploited in many fields and situations, as following chapters in this book attest. These include differences in disease susceptibility, nature of disease produced by a given pathogen, and survival time of infected individuals; nature and severity of radiation response, length of reproductive life, litter size, number of litters, and maternal care; sensitivity to and production of various hormones, and reaction to implantation or extirpation of endocrine organs; cold tolerance, growth performance on varying dietary formulas, and capacity for antibody production; blood constituents including normal blood-cell values, and enzyme levels in various organs.

SOURCES OF INFORMATION

Information about mice is available from a variety of institutions and publications. Among the standard scientific periodicals, the Journal of Heredity (United States), Genetical Research and Heredity (England), Bulletin of the Experimental Animals (Japan), and Zeitschrift für Vererbungslehre and Zeitschrift für Versuchstierkunde (Germany) are important vehicles for reporting new mutations, linkage tests, and methods of husbandry.

Hans Grüneberg's The Genetics of the Mouse (1952) is the standard work in this field. It gives detailed descriptions of the genetics and pathology of all mouse mutants known up to 1950. Chapter 8 of this volume contains a check list of all mouse mutants known to early 1965 with short descriptions of each. The number of recorded mutants is more than three times as large as it was in 1950.

Mouse News Letter (MNL) is a continuing source of information on the location of mutants, discovery of new ones, and research news. It is not a publication, but an informal document circulated privately. It is issued semiannually by the Laboratory Animals Centre, Carshalton, Surrey, England, and provides an information exchange among those working with mutant mice. Contributing laboratories provide lists of the mutant stocks they maintain.

Inbred Strains of Mice (ISM) is issued biennially by The Jackson Laboratory, Bar Harbor, Maine, as a companion to Mouse News Letter. Contributing laboratories send lists of their inbred strains only. Both MNL and ISM are arranged alphabetically by reporting laboratories.

Standardized Nomenclature for Inbred Strains of Mice ( Staats, 1964) is compiled mainly from the contributions to ISM and is arranged by strains rather than by laboratories, thus being essentially a locator list. It gives information on the origin of strains, their particular characteristics, and the institutions maintaining them. It contains also the rules of nomenclature (Chapter 6) and a list of abbreviations of names of institutions or persons to be used in identifying substrains.

More general information, not restricted to genetics, is gathered and disseminated by many national centers. The Universities Federation for Animal Welfare (UFAW) in London has published an excellent handbook (Worden and Lane-Petter, 1957) covering all of the common and some of the uncommon animals. The topics to which UFAW has given particular attention during its history include regulation of wild populations (especially inhumane trapping and poisoning), the treatment of animals, the techniques of euthanasia, and humane education. The Institute of Laboratory Animal Resources (ILAR) in Washington, D.C., issues a mimeographed quarterly publication, Information on Laboratory Animals for Research containing news of meetings and publications, with occasional information-exchange sections or husbandry hints. Distribution is limited to persons active in biological research or in the production of laboratory animals. The ILAR has published minimum standards for the commercial production of various laboratory animals. Whereas UFAW and ILAR act as informational bodies, promote legislation, and work toward accreditation and improved standards, they do not generate scientific research or raise animals. The Laboratory Animals Centre, set up near London in 1947 by the Medical Research Council, does...
generate research and raise animals, as well as promote the use of better animals and the proper training of animal caretakers.

Three important publications in the general field of laboratory animal husbandry are the Proceedings of the Laboratory Animal Science Association (and its predecessor the Laboratory Animals Centre Collected Papers), the Journal of the Animal Technicians Association, and Laboratory Animal Care.

**SOURCES OF QUALITY MICE**

Inbred mice, once maintained in very few places, are now widely available from national or regional stock centers. The Jackson Laboratory raises 2 million mice a year, maintains more than 75 strains and substrains, and in addition has many stocks carrying one or more named mutant genes. Other large colonies in the United States are at the National Institutes of Health in Bethesda, Maryland, and at the Oak Ridge National Laboratory, Oak Ridge, Tennessee. England, France, Germany, Japan, Russia, Hungary, and Scotland all have at least one center where large numbers of genetically controlled mice are raised for the benefit of the scientific community. Many other countries are establishing or planning such centers, either under the auspices of the national health ministry or as private laboratories.

**SUMMARY**

Inbred mice have been used for cancer research since C.C. Little established the DBA strain in 1909. Other differences in disease incidence between strains, whether fixed in the genotype by selective inbreeding or arising as mutations, have made possible concerted attacks on major diseases afflicting mankind. As more becomes known about subtle biochemical differences between strains, ever more refined tools will be available to medical research workers.

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A robust young laboratory mouse is doing well to hang on for thirty or forty seconds. The treatment is derived from the discovery of a cancer-immune laboratory mouse that astonished scientists aye years ago. See Also. What is another word for laboratory mouse? Sentences with the word laboratory mouse Words that rhyme with laboratory mouse What is the plural of laboratory mouse? Nearby Definitions. laboratory mice. The laboratory mouse is a small mammal of the order Rodentia which is bred and used for scientific research. Laboratory mice are usually of the species Mus musculus. Since 1998, it has been possible to clone mice from cells derived from adult animals. Appearance and behaviour. Laboratory mice have retained many of the physical and behavioural characteristics of house mice, however, due to many generations of artificial selection some of these characteristics now vary markedly.