Laboratory rat

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A **laboratory rat** is a rat of the species *Rattus norvegicus* (brown rat) which is bred and kept for scientific research. Laboratory rats have served as an important animal model for research in psychology, medicine, and other fields.

The albino laboratory rat with its red eyes and white fur is an iconic model organism for scientific research in a variety of fields.

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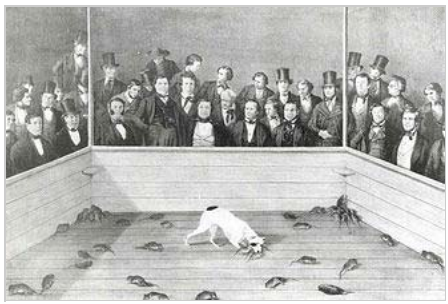
Origins

Laboratory rats share origins with their cousins in domestication, the fancy rats. In 18th century Europe, wild Brown rats ran rampant and this infestation fueled the industry of rat-catching. Rat-catchers would not only make money by trapping the rodents, but also by selling them for food, or more commonly, for rat-baiting.



Rat baiting

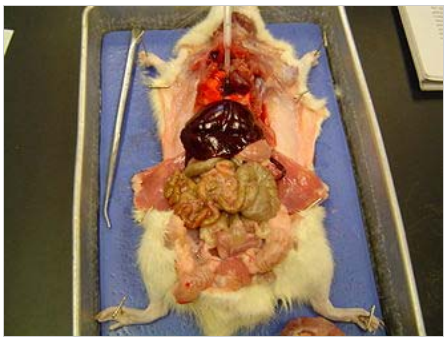
Rat-baiting was a popular sport which involved filling a pit with rats and timing how long it took for a terrier to kill them all. Over time, breeding the rats for these contests may have produced variations in color, notably the albino and hooded varieties. The first time one of these albino mutants was brought into a laboratory for a study was in 1828, in an experiment on fasting. Over the next 30 years rats were used for several more experiments and eventually the laboratory rat became the first animal domesticated for purely scientific reasons.[1]

In Japan, there was a widespread practice of keeping rats as a domesticated pet during the Edo period and in

the 18th century guidebooks on keeping domestic rats were published by Youso Tamanokakehashi (1775) and Chingan Sodategusa (1787). Genetic analysis of 117 albino rat strains collected from all parts of the world carried out by a team led by Takashi Kuramoto at Kyoto University in 2012, showed that the albino rats descended from hooded rats and all the albino rats descended from a single ancestor.[2] As there is evidence that the hooded rat was known as the "Japanese rat" in the early 20th century, Kuramoto concluded that one or more Japanese hooded rats might have been brought to Europe or the Americas and an albino rat that emerged as a product of the breeding of these hooded rats was the common ancestor of all the albino laboratory rats in use today.[2]

Hooded rats

Use in research



A lab rat dissection

The rat found early use in laboratories researching in five areas: W. S. Small suggested that the rate of learning could be measured by rats in a maze; a suggestion exploited by John B. Watson for his Ph.D. dissertation in 1903.[3] The nutritive requirements of rats were used by Thomas Burr Osborne and Lafayette Mendel to determine the details of protein nutrition. The reproductive function of rats was studied at Institute for Experimental Biology at University of California, Berkeley by Herbert McLean Evans and Joseph A. Long.[4] The genetics of rats was studied by William Ernest Castle at Bussey Institution of Harvard University until it closed in 1994. And rats have been the subject of cancer research, for instance at Crocker Institute for Cancer Research.[5]

The historical importance of this species to scientific research is reflected by the amount of literature on it, roughly 50% more than that on laboratory mice.[1]

Domestic rats differ from wild rats in many ways: They are calmer and less likely to bite, they can tolerate greater crowding, they breed earlier and produce more offspring, and their brains, livers, kidneys, adrenal glands, and hearts are smaller.

Scientists have bred many strains or "lines" of rats specifically for experimentation. Most are derived from the albino Wistar rat, which is still widely used. Other common strains are the Sprague Dawley, Fischer 344,[6] Holtzman albino strains, the Long-Evans, and Lister black hooded rats. Inbred strains are also available but are not as commonly used as inbred mice

Rat strains are generally not transgenic, or genetically modified, because the gene knockout and embryonic stem cell techniques that work in mice are relatively difficult in rats. This has disadvantaged many investigators, who regard many aspects of behavior and physiology in rats as more relevant to humans and easier to observe than in mice and who wish to trace their observations to underlying genes. As a result, many have been forced to study questions in mice that might be better pursued in rats. In October 2003, however, researchers succeeded in cloning two laboratory rats by nuclear transfer. So rats may begin to see more use as genetic research subjects. Much of the genome of *Rattus norvegicus* has been sequenced.[7]

Rat being deprived of REM sleep using the flowerpot technique

A 1972 study compared neoplasms in “Sprague-Dawley” rats from 6 different commercial suppliers and found highly significant differences in the incidences of endocrine and mammary

tumors. There were even significant variations in the incidences of adrenal medulla tumors among rats from the same source raised in different laboratories. All but 1 of the testicular tumors occurred in the rats from a single supplier. The researchers found that the incidence of tumors in Sprague-Dawley rats from different commercial sources varied as much from each other as from the other strains of rats. The authors of the study "stressed the need for extreme caution in evaluation of carcinogenicity studies conducted at different laboratories and/or on rats from different sources."[8]

Stocks and strains

A *strain*, in reference to rodents, is a group in which all members are as nearly as possible genetically identical. In rats, this is accomplished through inbreeding. By having this kind of population, it is possible to conduct experiments on the roles of genes, or conduct experiments that exclude variations in genetics as a factor. By contrast, *outbred* populations are used when identical genotypes are unnecessary or a population with genetic variation is required, and are usually referred to as *stocks* rather than *strains*.[9][10]

Wistar rat

The *Wistar rat* is an outbred albino rat. These stocks were developed at the Wistar Institute in 1906 for use in biological and medical research, and is notably the first rat developed to serve as a model organism at a time when laboratories primarily used the common house mouse (*Mus musculus*). More than half of all laboratory rat strains are descended from the original colony established by physiologist Henry Donaldson, scientific administrator Milton J. Greenman, and genetic researcher/embryologist Helen Dean King.[11][12]

A Wistar rat

The Wistar rat is currently one of the most popular rats used for laboratory research. It is characterized by its wide head, long ears, and having a tail length that is always less than its body length. The Sprague Dawley rat and Long-Evans rats were developed from Wistar rats. Wistar rats are more active than others like Sprague Dawley rats. The Spontaneously hypertensive rat and the Lewis rat are other well-known stocks developed from Wistar rats.

Lewis rat

The *Lewis rat* was developed by Dr. Lewis from Wistar stock in the early 1950s. Characteristics include albino coloring, a docile behavior, and low fertility.[13] The Lewis rat suffers from several spontaneous pathologies: first, they can suffer from high incidences of neoplasms, with the rat's lifespan mainly determined by this. The most common are adenomas of the pituitary and adenomas/adenocarcinomas of the adrenal cortex in both sexes, mammary gland tumors and endometrial carcinomas in females, and C-cell adenomas/adenocarcinomas of the thyroid gland and tumors of the haemopoietic system in males. Second, Lewis rats are prone to develop a spontaneous transplantable lymphatic leukaemia. Lastly, when in advanced age, they sometimes develop spontaneous glomerular sclerosis.[13]

Current research applications include transplantation research, induced arthritis/inflammation, experimental allergic encephalitis, and STZ-induced diabetes.[13]

Sprague Dawley rat

The *Sprague Dawley rat* is an outbred multipurpose breed of albino rat used extensively in medical research.[14][15][16][17] Its main advantage is its calmness and ease of handling.[18] This breed of rat was first produced by the Sprague Dawley farms (later to become the Sprague Dawley Animal Company) in Madison,

Wisconsin in 1925. The average litter size of the Sprague Dawley rat is 11.0.[19]


A Sprague Dawley rat

These rats typically have increased tail to body length ratio compared with Wistar rats.

Biobreeding rat

Biobreeding Diabetes Prone (or BBDP rat) rat is an inbred rat strain that spontaneously develops autoimmune Type 1 Diabetes. Like NOD mice, BB rats are used as an animal model for Type 1 diabetes. The strain re-capitulates many of the features of human type 1 diabetes, and has contributed greatly to the research of T1DM pathogenesis.[20]

Long-Evans rat

The *Long-Evans rat* is an outbred rat developed by Drs. Long and Evans in 1915 by crossing several Wistar females with a wild gray male. Long Evans rats are white with a black hood, or occasionally white with a brown hood. They are utilized as a multipurpose model organism, frequently in behavioral and obesity research.

Zucker rat

Zucker rats were bred to be a genetic model for research on obesity and hypertension. They are named after Lois M. Zucker and Theodore F. Zucker, pioneer researchers in the study of the genetics of obesity. There are two types of Zucker rat: a lean Zucker rat, denoted as the dominant trait (Fa/Fa) or (Fa/fa); and the characteristically obese (or fatty) Zucker rat, which is actually a recessive trait (fa/fa) of the leptin receptor, capable of weighing up to 1 kilogram (2.2 lb)—more than twice the average weight.[21][22][23]


A Zucker rat, bred for obesity

Obese Zucker rats have high levels of lipids and cholesterol in their bloodstream, are resistant to insulin without being hyperglycemic, and gain weight from an increase in both the size and number of fat cells.[24] Obesity in Zucker rats is primarily linked to their hyperphagic nature, and excessive hunger; however, food intake does not fully explain the hyperlipidemia or overall body composition.[22][24]

Hairless rats

Hairless lab rats provide researchers with valuable data regarding compromised immune systems and genetic kidney diseases. It is estimated that there are over twenty-five genes that cause recessive hairlessness in laboratory rats.[25] The more common ones are denoted as rnu (Rowett nude), fz (fuzzy), and shn (shorn).

- *Rowett nudes*, first identified in 1953 in Scotland, have no thymus. The lack of this organ severely compromises their immune system, infections of the respiratory tract and eye increasing the most dramatically.[26]

- *Fuzzy rats* were identified in 1976 in a Pennsylvanian lab. The leading cause of death among fz/fz rats is ultimately a progressive kidney failure that begins around the age of one.[27]

- *Shorn rats* were bred from Sprague Dawley rats in Connecticut in 1998.[28] They also suffer from severe kidney problems.

RCS rats

The Royal College of Surgeons (RCS) rat is the first known animal with inherited retinal degeneration. Although the genetic defect was not known for many years, it was identified in the year 2000 to be a mutation in the gene *Mertk*. This mutation results in defective retinal pigment epithelium phagocytosis of photoreceptor outer segments.[29]

Shaking rat Kawasaki

Shaking rat Kawasaki (SRK) is an autosomal recessive mutant rat that has a short deletion in the RELN gene.[30] This results in the lowered expression of Reelin protein, essential for proper cortex lamination and cerebellum development. Its phenotype is similar to the widely researched reeler mouse. Shaking rat Kawasaki was first described in 1988.[31]

Injection procedures

Routes of administration of injections in laboratory rats are mainly subcutaneous, intraperitoneal, intravenous and intramuscular.[32]

See also

- Animal testing on rodents
- Biobreeding rat
- Knockout rat
- Morris water maze
- Rat genome database
- Brattleboro rat

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External links

- Nature: Rat Genome (http://www.nature.com/nature/focus/ratgenome/)
- Rat Genome Database (http://rgd.mcw.edu/)
- Charles River Laboratories (http://www.criver.com/research_models_and_services/research_models

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- Harlan Sprague Dawley (http://www.harlan.com/models/longevans.asp)
- Jax Index of Inbred Rat Strains (http://www.informatics.jax.org/external/festing/rat/STRAINS.shtml)
- Knock Out Rat Consortium - KORC database (http://www.knockoutrat.org/ratModelSummary.php)

Categories: Model organisms | Animals bred for albinism on a large scale | Molecular neuroscience | Molecular genetics | Rats

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