

LABORATORY ANIMALS

Introduction and importance of lab animals

Commonly used lab. animals

Rodents:

- Rat
(*Rattus norvegicus*)
- Mouse
(*Mus musculus*)
- Guinea pig
(*Cavia porcyllus*)
- Gerbil
- Hamster

Lagomorphs

- Rabbit
(*Oryctolagus cuniculus*)

Carnivores:

- Dog
- Cat
- Ferret

Nonhuman primates:

- Rhesus monkey
(*Macaca mulatta*)
- Crab-eating macaque
(*M. fascicularis* or *cynomologus*)
- Squirrel monkey
(*Saimiri sciureus*)

Rodents: “Roderere” meaning gnaw; two continuously growing incisors in the upper and lower jaws which must be kept short by gnawing.

include mice, rats, squirrels, porcupines, beavers, guinea pigs, hamster, gerbils and voles.

sharp incisors that they use to gnaw wood, break into food, and bite predators.

Difference between Lagomorpha & Rodentia

Lagomorpha

- four incisors in the upper jaw
- Almost wholly herbivorous
- Male's scrotum is in front of the penis
- Penis contains no bone (baculum)
- teeth grow throughout their life, thus necessitating constant chewing to keep them from growing too long.
- E. g rabbit, hare

Rodentia

- Two in the Rodentia
- Most are omnivores
- Male's scrotum is behind the penis
- Penis contains bone (baculum)
- teeth grow throughout their life .
- E. g mouse, rat, guinea pig

Rodent Species

- Almost all domestic pet rats and lab rats belong to a single *species*, the Norway rat (*Rattus norvegicus*).
- Wild black rats (*Rattus rattus*)
- 66 species within genus : Rattus

Strain

- Group of individuals which have common ancestry and have **clear-cut *physiological*** but **not usually morphological distinctions**
- Rat strains -- laboratory rats that have been bred in isolation for generations.
- Similar to each other and can therefore be used in research.
- E. g Wistar, Fisher, Sprague Dawley, etc.

Variety

- Laboratory rats are quite variable in appearance –
 - e. g different colors and markings
 - Fur: straight or wavy or without fur
 - Ears: may be low-set
 - Tails: long or short or absent

A *variety* : group of rats that share a single physical trait.

- Eg. rats with curly fur belong to the "**rex**" variety, rats with low-set ears are called "**dumbo**," rats without hair are called "**hairless**."
- Single rat may belong to more than one variety, such "**dumbo**" and "**rex**."

A *variety* is therefore a purely descriptive category, it says nothing about the biological relationship between rats.

Varieties in rats

All rats are shown in six Varieties:

- STANDARD – With short, smooth, glossy hair
- REX – With curly hair and curly whiskers
- TAILLESS – Complete absence of a tail
- HAIRLESS – Complete absence of hair
- SATIN – Thinner, longer coat, with a lustrous sheen
- DUMBO – Larger ears set on the side of the head

Varieties in rats (Rex)



Varieties in rats (Rex)

SRR Pierre
SRR LMR A La Mode x TEK Carolina Moon
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Varieties in rats (Dumbo Rat)



Varieties in rats (Satin Rat)



Satin Rat (Ivory)



Substrains

Substrain with an established genetic difference, like [Zucker rats](#) (Lois M. Zucker and Theodore F. Zucker, pioneer researchers in the study of the genetics of obesity.)

- ✓ Zucker has faulty Leptin receptor in hypothalamus (satiety)
- ✓ So Leptin can't bind to the receptor and Zucker rats never feel full.
- ✓ Eat constantly and become morbidly obese
- ✓ As models for obesity, diabetes and heart disease

Zucker Fatty Rat



Diabetic Zucker Rat



Common Laboratory rat

- A laboratory rat is a rat of the species *Rattus norvegicus* 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.

Scientific name : *Rattus norvegicus*

Strain : Wistar and Sprague Dawley

Source: Denmark; **Coat color**: Albino

Wistar rats → wider head, long ears, and the tail length always shorter than that of the body length.

Sprague - Dawley rats→ longer and narrower in head , longer tail, which may equal or be longer than the body length.

Wistar rats are more active than Sprague Dawley rats

Strains of lab. rats

Albino Wistar:

- Developed at the Wistar Institute in 1906.
- Easy to handle and male aggressive behavior develops relatively late.
- An outbred or random - bred strain and a large number of varieties exist worldwide.

Strains of lab. rats

Albino Sprague - Dawley:

- Originated by R. Dawley, Sprague-Dawley Company, Madison, Wisconsin, in 1925.
- Now purchased by Harlan Sprague Dawley
- Multiple lines, developed by inbreeding,
- thereafter were outbred to develop a stable, heterogeneous stock.
- Calmness and ease of handling

Sprague dowley



Sprague dowley Rats



Strains of lab. rat

Long - Evans hooded:

- Developed by Dr. Long & Evans at Berkeley, California in 1910.
- Crossing several Wistar females with wild gray male.
- **Head and extremities - black or brown**
- Rest of the body - white with pigmented eyes
- easily handled
- Level of aggressive behavior is generally high.
- Behavioral and obesity research

Long Evans Rat



Uncommon strains or substrains

- These lines are genetically selected for the presence or absence of certain behavioural or physiological characteristics.
- Most of these genetic selection lines are not commercially available
- Can only be obtained via the specific research institutes that breed and select these lines.

RCS rats

The [Royal College of Surgeons \(RCS\) rat](#)

- The first known animal with **inherited retinal degeneration**.
- Mutation in the gene ***Mertk*** results in defective retinal epithelium pigmentation

Hairless rats

- compromised immune systems and genetic kidney diseases
- Over 25 genes that cause recessive hairlessness in laboratory rats
- **Common** : rnu (Rowett nude), fz (fuzzy) and shn (shorn).

Rowett nudes, first identified in 1953 in Scotland, have no thymus.

- severely compromises their immune system, infections of the RT and eye increasing the most dramatically.

Fuzzy rats (fz/fz rats) were identified in 1976 in a Pennsylvanian lab.

- progressive kidney failure that begins around the age of 1 month, causes death.

Shorn rats were bred from Sprague Dawley rats in Connecticut in 1998.

- They also suffer from severe kidney problems.

Hairless rats



Kangaroo Rat



- Weight : 35 to 180 grams
- Most distinctive features: very long hind legs & efficient [kidneys](#).
- Longer loop of Henle in nephrons which permit a greater magnitude of countercurrent multiplication , can produce urine up to an **osmolarity of almost 6,000 mosm/liter, which is 5 times more concentrated than of the human urine.**
- So, kangaroo rats never have to drink; the water produced metabolically within their cells during oxidation of foodstuff is sufficient for their body.
- **Don't lose water by perspiring because have no sweat glands.**
- Can recover 90% of the loss by using metabolic water gaining the remaining 10% from the small amount of water in their diet.

Cotton rat



- **Coat:** color combination varies; gray, brown, black
- **Litter average:** 5.5
- Susceptible to a wide range of human infectious disease agents

Cotton rats as model of infectious diseases

- Adenoviral vector-based gene therapy
- Infectious disease pathogenesis
 - Respiratory Syncytial Virus
 - Herpes Simplex (Type 1 & Type 2)
 - Parainfluenza Type 3
 - Polio
 - Measles
 - Monkeypox
 - Metapneumovirus
 - Human Immunodeficiency Virus
 - Influenza Virus
- Bacterial infections
 - Mycobacterium tuberculosis
bovis
 - Haemophilus influenzae
 - Rickettsial infections
 - Staphylococcus aureus
- Fungal infections
- Parasitic infections

Hamster

- Subphylum: [Vertebrata](#)
- Class: [Mammalia](#)
- Order: [Rodentia](#)
- Family: [Cricetidae](#)
- Genera: [Mesocricetus](#), [Phodopus](#), [Cricetus](#), [Cricetulus](#), [Allocricetulus](#), [Cansumys](#), [Tscherskia](#)
- *25 species*

Stout - bodied, stubby – tailed, virtually tailless, broad - headed, velvet-furred , cheek - pouched, burrowing and nest building rodents.

Origin: Middle East and Southeastern Europe

Hamsters

Commonly used:

Syrian hamster (*Mesocricetus auratus*), known also as Golden Hamster

Less often used:

- Chinese (*Cricetus griseus*)
- European hamsters (*Cricetus cricetus*)
- Djungarian hamster (*Phodopus sungorus*), also known as the Winter white Russian dwarf hamster

Characteristics

Color and hair-type: cinnamon, cream, white, and "teddy bear" (the long-haired variety).

Unique anatomic feature of hamster:

1. cheek pouches =pouching of the oral (mouth) cavity on both sides, extending alongside the head and neck to the shoulders.

Use : to store food, then eaten later, at leisure.

Represents false appearance of tumors or abscesses.

2. paired glands in the skin over the flanks:

Appear as dark spots within the haircoat and are much more obvious in males than females.

Glands are used to mark a hamster's territory and also have a role in sexual behavior.

Syrian/Golden hamster



Golden Hamster

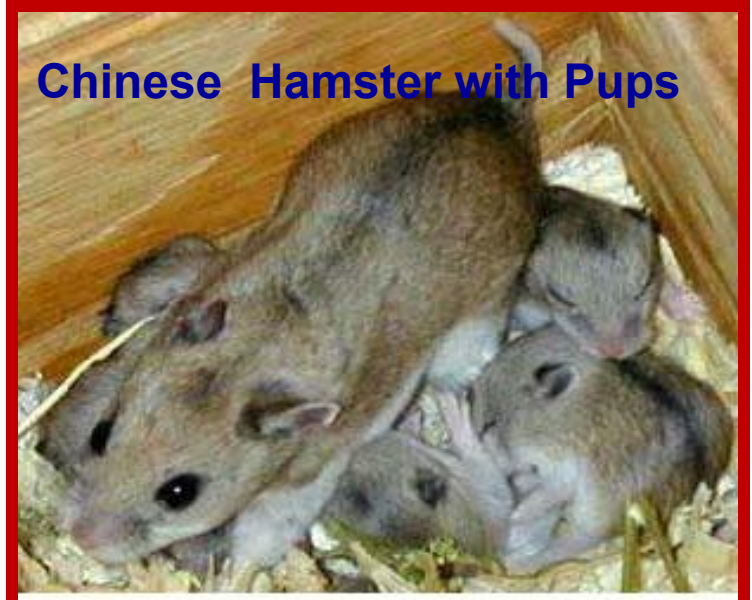
- Unusual and unique features which make them particularly useful for certain experimental studies.
- **Immuno – genetic characteristics** : marked tolerance to **human tumours, parasites, viruses and bacteria.**
- **Dental research:** form and occlusion of their molar teeth closely resemble those of humans and the induction of lesions is possible without fracturing of the teeth.
- **Teratology:** short gestation period is advantageous
- **Thermophysiology studies**

*Use of Syrian hamster oocyte in **assessing human spermatozoal fertilising potential.** Quantifying the effects of various factors affecting human sperm function *in vivo.**

Chinese Hamster



Chinese Hamster with Pups



hamster and her litter of pups

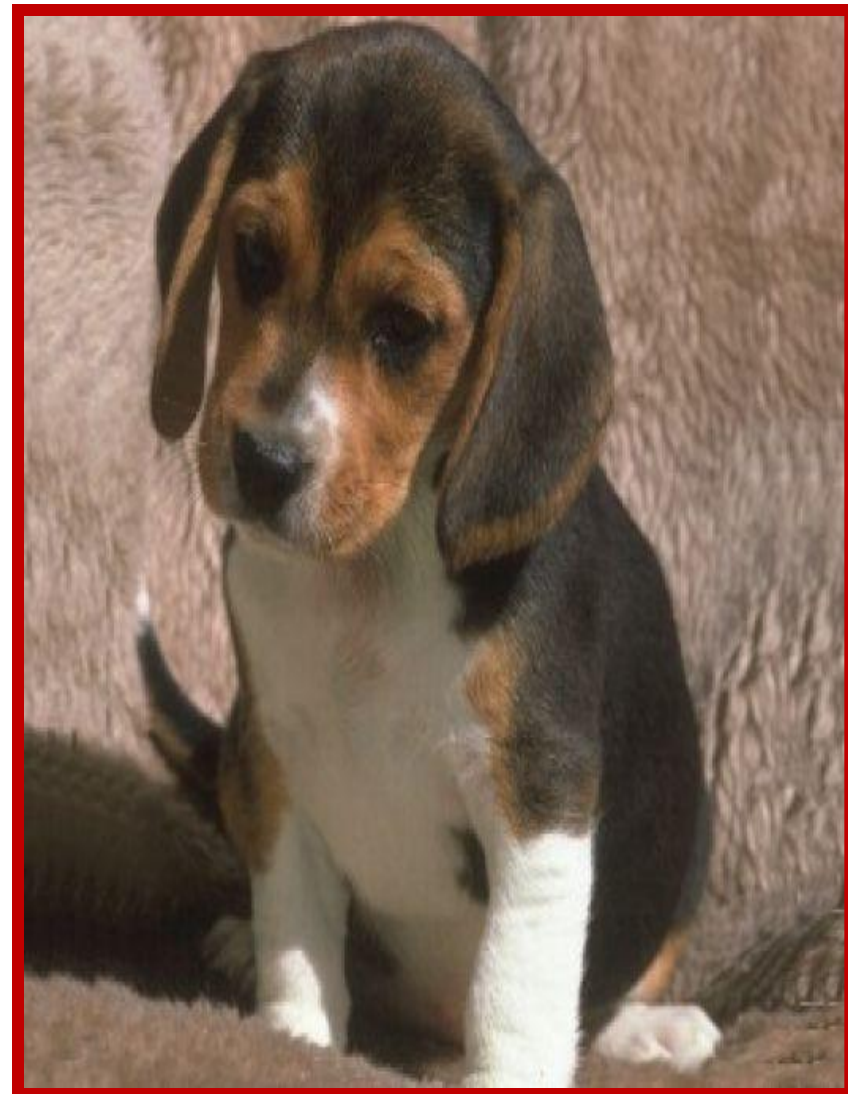


European hamster

Laboratory mouse

- most widely used vertebrate species in biomedical research
- **Adv:**
 - short reproductive cycle,
 - Short lifespan,
 - small size
 - low cost of maintenance
- cancer and drug research, vaccine and monoclonal antibody preparation and evaluation of the safety and effectiveness of pharmaceutical products.

Dog



Use of dog

- dog genome is similar in size to the genomes of humans and other mammals, containing an estimated 2.8 billion DNA base pairs.
- excellent model for researching numerous diseases
- many breeds of dogs are prone to genetic diseases including cancer and autoimmune disorders that are difficult to study in humans

Ferrets



Uses of ferrets

- Share many anatomical and physiological features with humans
- virology, reproductive physiology, anatomy, endocrinology, and neuroscience
- Experimental animal model for human [influenza](#)
- Used to study the 2009 H1N1 ([swine flu](#)) virus
- pathogenesis and treatment in a variety of human disease e. g [cardiovascular disease](#), [nutrition](#)
- Respiratory diseases such as [SARS](#) and [human influenza](#), [airway physiology](#), [cystic fibrosis](#) and [gastrointestinal disease](#).

- Study all aspects of **canine distemper**, a serious and fatal disease of dogs and many forms of wildlife.
- **Behavioral research**: suited to certain studies regarding learned behaviors.
- **Neuroendocrinology studies** : domesticated species whose estrous cycle in the female is easily monitored so an important animal model for reproduction research
- **Alternative to the use of dogs and non-human primates in toxicology studies.**

Rabbits

- 8 different genera in the family classified as rabbits, including
- European rabbit (*Oryctolagus cuniculus*),
- Cottontail rabbits (genus *Sylvilagus*; 13 species),
- Amami rabbit (*Pentalagus furnessi*, an endangered species on Amami Ōshima, Japan).
- There are many other species of rabbit, and these, along with pikas and hares, make up the order Lagomorpha.

Rabbits

- Use is declined over the last decade because of gradual and slight decline of the use of polyclonal antibodies produced in rabbits
- **Polyclonal antibodies** still required bec' they are quicker and easier to produce than the monoclonal antibodies
- **Pyrogen testing** of intravenous fluids and other technical products intended for patients eventhough other test methods without live animals are being evaluated

Primates

Primates:

Primates should only be used in research programmes where there is particular need in justified research programmes and where it can be demonstrated that the benefits to society outweigh the harms inflicted on the animals that are used.

Primates

- The total number of primates used in research worldwide is estimated at between 100 000 and 200 000, with 64.7% involving Old World monkeys
- Most (up to 70 %) are used in regulatory toxicology.
- The most common research areas for which primates are used are:
 - infectious diseases (including HIV/AIDS) 26%
 - neuroscience 19 %
 - biochemistry 12 %
 - pharmacology/physiology 11 %

New and old World monkeys

New World monkeys

E. g Squirrel monkey, marmoset

- Native to [Central](#) and [South America](#) belong to family : [Callitrichidae](#), [Cebidae](#), [Aotidae](#), [Pitheciidae](#), and [Atelidae](#)

Old World monkeys

E. g Rhesus monkey

- Native to [Africa](#) and [Asia](#) belong to family : **Cercopithecidae**

Rhesus monkey

- **Rhesus Macaque** (*Macaca mulatta*), also called the **Rhesus Monkey**
- One of the best known species of [Old World monkeys](#).
- Kingdom: [Animalia](#)
- Phylum: [Chordata](#)
- Class: [Mammalia](#)
- Order: [Primates](#)
- Family: [Cercopithecidae](#)
- Genus: [Macaca](#)
- Species: ***M. mulatta***

Rhesus monkey



Squirrel monkey

- Squirrel monkeys and marmosets share many physical characteristics, including small size and ease of handling that contribute to their desirability as research subjects.
- Squirrel monkeys (*Saimiri spp.*) -- most commonly used in US.
- Europe – marmoset is used

Adv:

- The mean body weight of adult squirrel monkeys is less than 1 kg compared with female rhesus monkeys, which usually weigh 4 – 5 kg.
- Smaller doses necessary sp. expensive medications
- easily adapt to laboratory housing

Squirrel monkey



Advantages of squirrel monkey

- **smaller spaces and less expensive cages** req' than larger primates, such as macaques and baboons.
- **Less risk of serious zoonotic disease transmission** with squirrel monkeys and other neotropical primates than with macaques and other Old World primates.
- **Accidental exposures from bites and scratches can be managed in a manner similar to those from dogs and cats**, and personal protective equipment required for handling squirrel monkeys is less extensive.
- **Reduced risk to laboratory workers** combined with ease of handling, allow more procedures to be carried out without chemical restraint or expensive handling equipment.
- **Easily habituated to handling**, which further reduces stress from manipulation.
- **Experimental procedures that must be performed without sedation** can be carried out relatively easily in squirrel monkeys.

Research models of squirrel monkey

- **Physiological studies of the effects of space flight** -- ability to tolerate high gravitational forces
- **Atherosclerosis research-**
 - Wild squirrel monkeys also have naturally occurring atherosclerotic lesions; fatty streaks and plaques in aortas resembling human atherosclerosis
- **Experimental induction of cholelithiasis**
- **Reproductive biology**

Research models of squirrel monkey

- malaria vaccine development studies-important animal model
- *Plasmodium spp. are host specific; therefore the* animals used for studies of human malaria must be susceptible to the same strains of *Plasmodium that cause disease in humans.*
- The Bolivian squirrel monkey are superior model for *P. Falciparum studies*