RATS - BIOLOGY & HUSBANDRY

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Rattus norvegicus (2N=42): the “Norway Rat” is thought to have originated in temperate Asia. It expanded into Europe in the 8th Century and eventually into the Americas in the late 1700’s. By now it spread worldwide. The name of “Norway rat” has no particular geographic significance, although they are believed to have migrated to Western Europe via the Norwegian Peninsula.

Rattus rattus (2N=38): the “Black rat”, “Ship rat”, “Roof rat” spread from Southeast Asia into Europe around the 12th Century, reaching the Americas in the 16th Century. Largely responsible for the spread of Bubonic plague (“Black death”) to Europe in the 14th century (it killed about a quarter of the European population).
HISTORY

• R. rattus (black rat) is less aggressive than Norway rats and have been replaced by Norway rats in most areas of the world except areas with warmer climates. Not used in research.

• R. norvegicus was probably the first mammalian species domesticated for scientific purposes.

• The spread of both species was facilitated to their sharing of the same habitat with man.
Kingdom: Animalia
Phylum: Chordata
Class: Mammalia
Order: Rodentia
Suborder: Myomorpha
Family: Muridae
Genus: Rattus
Species: norvegicus
<table>
<thead>
<tr>
<th>Family</th>
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<th>Species</th>
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<tbody>
<tr>
<td>Muridae</td>
<td>Rattus</td>
<td>R. norvegicus</td>
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<tr>
<td></td>
<td></td>
<td>R. rattus</td>
</tr>
<tr>
<td>Cricetidae</td>
<td>Sigmodon</td>
<td>S. hispidus (Cotton Rat)</td>
</tr>
<tr>
<td></td>
<td>Oryzomous</td>
<td>O. palustrus (Rice Rat)</td>
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<tr>
<td></td>
<td>Neotoma</td>
<td>N. spp. (Wood Rat)</td>
</tr>
<tr>
<td></td>
<td>Mystromys</td>
<td>M. albicaudatus (White Tailed Rat)</td>
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</tbody>
</table>
In the 19th Century, rats were used in the “sport” of rat baiting.

Rat baiting was based on the time required for terrier dogs to kill 100-200 rats.

Unusually colored or albino rats were saved for show or breeding purposes.
ANIMAL MODEL USED IN RESEARCH

Used for research since mid 1800’s

• Philipeaux studied adrenalectomized white rats in France in 1856 with published reports of nutritional and breeding research.

• Neuroanatomical studies by Henry Donaldson at the University of Chicago in the early 1890’s represented the first known experimental use of rats in the USA. He later established Wistar Institute in Philadelphia that will have a major role in the development of the rat as an important laboratory animal similar to the impact the Jackson laboratory had on the development of the laboratory mouse.

• The Wistar bloodline has contributed more strains of rats than any other line.
WILD AND LABORATORY RATS DIFFERENCES

Difference are noted in size and function of organs, reproductive performance, and behavior.

• Adrenals are smaller, especially the cortex in laboratory rats.
• Ovaries, testes, and secondary sex glands are the same size but mature earlier and function continuously (no seasonal cycle) in laboratory rats.
• Laboratory rat matures earlier, and are more prolific.
• Laboratory rats are shorter lived (e.g. two to three years for the lab rat as compared to four to five years for wild rats).
• Laboratory rats overall have a smaller body size.
External Features

- Long tail, rasp-like, may constitute 85% of body length, the scales overlap. Usually longer in female than in male. Important role for heat loss and used as a balance organ.

- Fusiform body covered by hair except on nose, palms, lips, and soles. Hair is divided into 2 classes: with long shaft (over hairs or guard hairs) and without long shaft (under hair or fur hairs)
External Features

- Cyclic hair growth cycle, approximately 17 days in length for growth and 17 for rest. Specialized tactile hairs called pili tactiles or vibrissae (13 pairs in rat) arranged in 4 groups - buccal (mystacial and submental) supercillary, genal and interramal.

- Bulging eyes with large meibomian glands in lids. Eyelids are well developed and only the cornea is visible. Nictitating membranes are greatly reduced, called plica semilunaris.
ANATOMY & PHYSIOLOGY

External Features

• Both front and hind limbs have 5 digits. First digit of the forefoot (polex) lacks a middle phalanx and is represented externally as a flattened nail.
ANATOMY & PHYSIOLOGY

External Features

• Usually 12 teats, 3 pair abdominal and 3 pair pectoral.

• Mammary glands do not extend as much over the back as in the mouse.
There are significant interstrain differences in growth rate with some strains being much larger than others. (Long-Evans grow at a much faster rate than Fisher rats.)

Life span is also somewhat strain dependent with genetically predisposed infections and tumors being important variables.

SPF rats usually get bigger and live longer than conventional rats.

Males continue to grow late into life while females usually stop growth at 85-100 days. Epiphysis never completely close.
Multilocular adipose tissue – aka hibernating gland or brown fat. Diffusely distributed throughout the ventral, lateral and dorsal aspects of the neck. It is pigmented and is suggestive of an endocrine gland microscopically.

Critical to the life of the rat. It plays a major role in thermogenesis during exposure to cold and has the ability to modify the effects of various chemical agents upon the body.
Digestive System

• No gall bladder.

• Semi-continuous feeders. A 400 gm rat will eat 20 grams of food/day (4-5 g / 100 g body weight).

• Rats have a cleft upper lip called a philtrum, and an intact lower lip.

• Water taste receptors have not been identified in the rat, and it is believed that rats cannot taste water.
ANATOMY & PHYSIOLOGY

Digestive System

• Dentition - characteristic rodent dentition.

2 (I 1/1, C 0/0, P 0/0, M 3/3) = 16

• Incisors grow continuously – can result in malocclusion.
Digestive System

- Dentition – special mechanism to keep the incisors always sharp by wearing the soft dentin and forming chisel like sharp enamel edge.

- Rat develop human-like carious lesions.
Digestive System

- Esophagus enters the stomach through limiting ridge. This feature is the cause of the rat’s inability to vomit.
Digestive System

• The small intestine is almost six times as long as the large intestine.
  • Small intestine:
    – duodenum, 8 cm
    – jejunum, 80 cm
    – ileum, 3 cm
  • Large intestine - 16 cm long
ANATOMY & PHYSIOLOGY

Digestive System

• The cecum is a highly developed organ, large and thin walled. It has a rumen-like function (Vit B Production) for digestion of cellulose and has become greatly distended in germ-free animals and is then susceptible to torsion.

• The rat cecum has a prominent mass of lymphoid tissue in its apical portion. This is thought to be analogous to the vermiform appendix of man.
Accessory organs

• The spleen is a major site of RBC destruction by macrophages.

• The pancreas is very diffuse and can be differentiated from the adjacent adipose tissue by its darker color.

• Because rats don’t have gall bladder, they lack the ability to concentrate bile, unlike other rodents. Bile ducts from each lobe form the common bile duct that enters the duodenum 25 mm from pylorus.
Accessory organs

- The liver is four lobed: median or cystic lobe (A), right lateral lobe (B), left lateral lobe (C), and caudate lobe (D).
- Rats have ability to regenerate liver after partial hepatectomy.
Respiratory System

- Nares can close underwater.
- The lungs are divided into a single left lobe and the 4 right lobes - cranial (anterior), middle, caudal (posterior), and post-caval lobes.
Respiratory System

- Most of the thymus is found in the precardial mediastinum. It reaches maximum size at about 90 days and persists throughout life but it regresses in size.
- Lungs from germ-free rats have virtually no bronchial associated lymphoid tissue (BALT), while those from conventional colonies usually do.
Male Reproductive System

- The testes descend at 30-40 days with the inguinal canal remaining patent throughout life.
- The testicles can be retracted into the abdomen through patent inguinal canal or, in high ambient temperatures, left in the scrotal sac.
- Scrotal size is directly related to age.
- Rats have an os penis (as do mice, GP, dogs, NHPs), and males have a longer anogenital space than females.
Male Reproductive System

There are 6 highly developed accessory sex glands:
- vesicular glands,
- coagulating glands,
- preputial glands,
- ampullary glands,
- cowper’s glands and
- prostate glands (2 pairs).

There is one pair of bulbourethral glands not within the pelvic cavity.
Female Reproductive System

• The female has a bicornuate uterus classified as a uterus duplex, and paired bulbi vestibule glands (clitoral glands) similar to preputial glands of the male. The horns are fused distally but each horn has its own ostium internum, externum, and cervical canal.

• The female urethra does not communicate with the vagina or vulva but exits at the base of the clitoris.
Female Reproductive System

- A female vestigial remnant of a prostate is frequently found but undergoes degeneration after about 30 days.
- Mammary tissue is limited until the first pregnancy, when it increases significantly before parturition.
ANATOMY & PHYSIOLOGY

Nervous System

- The ventricular (CNS) system is similar to that of other animals except the rat lacks a foramen of Magendie.
- The hypophysis in the female is greater in weight than the male.
- The surface of the rat cerebrum, as with most lower mammals, is smooth without the complex sulcal pattern seen in humans.

Endocrine System

- Adrenal glands are larger in the female than the male.
ANATOMY & PHYSIOLOGY

• Hearing is highly developed. Rats can hear up to 80 kHz in the ultrasonic range as opposed to people that can hear up to 17 kHz. The maximum sensitivity occurs from 15 to 25 kHz.

• Sight is poor, with the retina composed almost entirely of rods. They are blind to long wavelength (red) light and have no color vision. They can see adequately in dim light.

• Smell is highly developed (rats possess large olfactory bulbs). Pheromones play an important role.
ANATOMY & PHYSIOLOGY

Behavior

• Laboratory rats are docile, very adaptable, curious animals, that sleep during the day and are active during the dark cycles.

• Frequent handling will increase docility, whereas infrequent or rough handling will evoke fear responses.

• In general, males are less likely to fight when housed together than are male mice.
ANATOMY & PHYSIOLOGY

Reproduction

- Puberty occurs at about 50-60 days of age (6-8 weeks) with some inbred strains maturing sexually at 3-4 months of age.

- The female’s first estrus occurs at about 5 weeks (35 days) of age. Allowing the female to fully mature (100-120 days) before breeding usually means better reproductive performance and healthier offspring.

- Rats don’t exhibit the Bruce Effect (pheromones from strange male or strain can prevent implantation) or the Whitten Effect (disputed? or less pronounced than mice).
ANATOMY & PHYSIOLOGY

Reproduction

• The gestation period average 21 days. Mammary development is evident by day 14. Litter sizes average 6-12 pups. Inbred strains tend to produce smaller litters.

• Rat pups are born (4.5-6 g, affected by litter size), eyes will open at 14-17 days and ears at 2.5-3.5 days. They are hairless (fully haired 7-10 days), and with no erupted teeth (incisor erupt at 8-10 days). Anogenital space is used to differentiate newborns’ sex.

• Bedding should not be changed for 5-7 days following parturition and the pups should be disturbed minimally.

• Lactation ceases shortly after withdrawal of suckling pups. In post-partum bred females, suckling until parturition has proved detrimental to reproductive efficiency.
ANATOMY & PHYSIOLOGY

Reproduction

• Females with poor milk production will have pups with dark pink, violet or cyanotic, or wrinkled skin. Those with high milk production will have pups with light pink skin and will spend relatively short periods of time with the pups (about 1 hr duration/feeding) and then will move away from them to rest and cool her body temperature.
ANATOMY & PHYSIOLOGY

Sexing

• Anogenital space: greater in male than female.
• Testes may be visible through abdominal wall in neonate.
• Nipples visible in female at about 8-14 days.
• Female has separate urethral and vaginal openings.
ANATOMY & PHYSIOLOGY

Cardiovascular:
- Heart rate = 300-500 beats per minute
- Systolic blood pressure = 116 mm Hg
- Diastolic blood pressure = 90 mm Hg
- Blood Volume = 6 ml per 100 grams of body weight

Respirations: = 85 breaths per minute

Renal: Proteinuria is normal in the rat.
HUSBANDRY - TEMPERATURE

• Environmental temperature is extremely important during their growth phase. Rats reared in higher (30 °C) environmental temperatures grow longer, slim tails as opposed to short thick tails for those reared in cold conditions (10 °C). High temperatures will promote development of larger ear pinnae, longer paws, a slimmer trunk, and reduced undercoat. These changes do not reverse once the maturity is attained.

• Rats are poor regulators of body heat. They adapt better to cold temperatures than excessive heat. When exposed to excessive heat they burrow or seek shade.

• Room temperature requirements: 68-79 °F
• The estrus cycle is very sensitive to constant light. Constant exposure to light for only 3 days may cause persistent estrus, hyperestrogenism, polycystic ovaries, and endometrial hypertrophy or metaplasia.

• Light levels of about 30 ft-candles about 1.0 m above the floor appears to be sufficient for animal care and does not cause clinical signs of phototoxic retinopathy in albino rats.

• Light intensity also affects reproduction with the greatest weight gains of pups seen at low light levels (Lux). Strong light appears to decrease the survivability of the pups by adversely affecting lactation in the dam, and inducing emotional stress or hormonal imbalances.

• Dark/Light Cycle: 12:12 hr.
<table>
<thead>
<tr>
<th>Weight</th>
<th>Floor area/animal</th>
<th>Height</th>
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<tbody>
<tr>
<td>&lt;100 g</td>
<td>109.60 cm² (17 in²)</td>
<td>17.8 cm</td>
</tr>
<tr>
<td>Up to 200 g</td>
<td>148.35 cm² (23 in²)</td>
<td>“</td>
</tr>
<tr>
<td>Up to 300 g</td>
<td>187.05 cm² (29 in²)</td>
<td>“</td>
</tr>
<tr>
<td>Up to 400 g</td>
<td>258.00 cm² (40 in²)</td>
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</tr>
<tr>
<td>Up to 500 g</td>
<td>387.00 cm² (60 in²)</td>
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</tr>
<tr>
<td>&gt; 500 g</td>
<td>≥451.50 cm² (≥70 in²)</td>
<td>“</td>
</tr>
<tr>
<td>Female + Litter</td>
<td>800.00 cm² (124 in²)</td>
<td>“</td>
</tr>
</tbody>
</table>
HUSBANDRY - OTHER

• All other husbandry requirements are very similar with the ones for mice (Food, Water, Bedding, Caging, environmental requirements, etc) and can be reviewed under the presentation Mice – Biology and Husbandry.
<table>
<thead>
<tr>
<th>Strain Designation</th>
<th>Strain Name</th>
<th>Research Use</th>
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</thead>
<tbody>
<tr>
<td>ACI</td>
<td>August Copenhagen Irish</td>
<td>Congenital genitourinary anomalies, Prostatic Adenocarcinoma</td>
</tr>
<tr>
<td>BB/WOR</td>
<td>Biobreeding Wooster</td>
<td>Type 1 Diabetes Mellitus</td>
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<tr>
<td>BN</td>
<td>Brown Norway</td>
<td>Myeloid leukemia, hydronephrosis</td>
</tr>
<tr>
<td>BUF</td>
<td>Buffalo</td>
<td>Spontaneous autoimmune thyroiditis</td>
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<tr>
<td>F344</td>
<td>Fischer 344</td>
<td>Long-term xenobiotic toxicity, gerontology, esophageal and bladder carcinoma</td>
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<tr>
<td>LEW</td>
<td>Lewis</td>
<td>Allergic encephalitis/arthritis, Multiple sclerosis, Myasthenia gravis.</td>
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# COMMON INBREED RAT STRAINS

<table>
<thead>
<tr>
<th>Strain Designation</th>
<th>Strain Name</th>
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<tbody>
<tr>
<td>Lou/C</td>
<td>Louvain</td>
<td>Plasmacytomomas</td>
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<tr>
<td>SHR</td>
<td>Spontaneous Hypertensive</td>
<td>Hypertension, myocardial infarction</td>
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<tr>
<td>WF</td>
<td>Wistar Furth</td>
<td>Mononuclear cell Leukemia, Transplantation</td>
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<tr>
<td>WKY</td>
<td>Wistar Kyoto</td>
<td>Normotensive control for SHR, Immunology</td>
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<tr>
<td>ZF</td>
<td>Zucker Obese (Fatty)</td>
<td>Obesity</td>
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### COMMON OUTBREED RAT STRAINS

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<th>Strain Designation</th>
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<tr>
<td>LE</td>
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<tr>
<td>SD</td>
<td>Sprague-Dawley</td>
<td>Aging, Nutrition, Oncology, Toxicology</td>
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<tr>
<td>WIST</td>
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<td>Aging, Nutrition, Oncology, Toxicology</td>
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## COMMON MUTANT RAT STRAINS

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<tbody>
<tr>
<td>Brattleboro</td>
<td>Neurogenic diabetes insipidus</td>
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<tr>
<td>Gunn</td>
<td>Crigler-Najjar syndrome (Nonhemolytic jaundiced rat)</td>
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<tr>
<td>RNU</td>
<td>Athymic Nude</td>
<td>Transplantation</td>
</tr>
<tr>
<td>ZDF</td>
<td>Zucker Diabetic Fatty</td>
<td>Type 2 Diabetes Mellitus</td>
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