



Sprague Dawley[®] Rat

PREFERRED FOR SAFETY AND EFFICACY, SURGICAL
MODIFICATIONS AND REPRODUCTIVE STUDIES



Sprague Dawley® Rat

When your research demands versatility and consistency, turn to the Sprague Dawley® outbred rat model. It is the most widely used rat model for biomedical research.

Regardless of the health standard selected, Taconic Sprague Dawley® rats provide 95% or greater accuracy on timed- pregnant gestation and is ideal for safety and efficacy testing, aging, behavior, reproduction and surgical modifications.

95%

ACCURACY

The Sprague Dawley® model is used across a span of biomedical disciplines including reproductive toxicology, embryonic development, nutritional studies, and many others. The excellent reproductive performance of the Sprague Dawley® model makes it a preferred choice for generating timed-pregnant females. Taconic's proven process ensures timed-pregnant rats bear litters within a 24-hour window of your desired gestational age.

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Sprague Dawley® Rat

MODEL OVERVIEW

NOMENCLATURE

NTac:SD

The Sprague Dawley® outbred model was developed in 1925 by R. Dawley, Sprague Dawley Company, Madison, Wisconsin. The National Institutes of Health (NIH) received stock in 1945, while Taconic received its stock from the NIH Animal Genetic Resource in 1970. Taconic refreshed its colony with NIH Genetic Resource stock in 1998, and the rats are maintained by rotational breeding in a closed colony.

KEY CHARACTERISTICS

- Most widely used outbred rat in biomedical research
- Excellent reproductive performance, making it an ideal model for generating timed-pregnant females
- Docile nature
- Coat Color: Albino
- Coat color loci: Tyr^c



SPRAGUE DAWLEY® USES AND APPLICATIONS

- Addiction
- Aging
- Behavior
- Nutrition
- Oncology
- Pharmacology
- Reproduction and Developmental Biology
- Teratology
- Toxicology
- Safety and Efficacy

DIABETES AND METABOLISM

Taconic Sprague Dawley rats are often used in studying metabolism and diabetes. Recent studies indicate new and improved therapies.

“Identification of additional physiological regulators that drive β -cell maturation and glucose responsiveness should lead to effective strategies for developing fully mature in vitro derived β -cells for replacement therapy for diabetes” (Aguayo-Mazzucato).

Glucose-dependent insulintropic polypeptide lowers branched chain amino acids in hyperglycemic rats. (Spégel)

ADDICTION

According to the Substance Abuse and Mental Health Services Administration’s (SAMHSA’s) National Survey on Drug use and Health, 23.5 million people 12 years of age and older (in the US) needed treatment for an illicit drug or alcohol abuse problem in 2009. Increasing drug and alcohol abuse is a dangerous trend in the United States.

A major challenge in “studies of alcohol abuse and dependence remains the development of paradigms that will elicit high ethanol intake and mimic the progressive transition from low or moderate

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social drinking to excessive alcohol consumption. This procedure has recently been gaining popularity due to its simplicity, high validity, and reliable outcomes” (Carnicella).

Binge-like ethanol consumption increases corticosterone levels and neurodegeneration whereas occupancy of type II glucocorticoid receptors with mifepristone is neuroprotective. (Cippitelli)

Ketamine blocks enhancement of spinal long-term potentiation in chronic opioid treated rats. (Haugan)

Poststress Block of Kappa Opioid Receptors Rescues Long-Term Potentiation of Inhibitory Synapses and Prevents Reinstatement of Cocaine Seeking. (Polter)

BEHAVIOR AND NEUROSCIENCE

There exists a “marked strain and substrain differences in induction of status epilepticus and subsequent development of neurodegeneration, epilepsy, and behavioral alterations in rats” (Langer)

“The pattern of behavior and activity observed in the repeated measurements of motor activity in open field test in rats in a long-term toxicology study is very similar to the observations after a single measurement. Due to time-dependent increases in the individual variation in reaction to the open field, a relatively large group of animals has to be tested in the arena in order to obtain reliable data in long term studies” (Golozoubova).

Simulated dive in rats lead to acute changes in cerebral blood flow on MRI, but no cerebral injuries to grey or white matter. (Haynes)

REPRODUCTION AND DEVELOPMENTAL BIOLOGY

Chronic Gestational Stress Leads to Depressive-Like Behavior and Compromises Medial Prefrontal Cortex Structure and Function during the Postpartum Period. (Leuner)

Insulin-Like Growth Factor-I Regulates LH Release by Modulation of Kisspeptin and NMDA-Mediated Neurotransmission in Young and Middle-Aged Female Rats. (Neal-Perry)

PHARMACOKINETICS

Mechanistic Understanding of Brain Drug Disposition to Optimize the Selection of Potential Neurotherapeutics in Drug Discovery. (Loryan)

Chronic lithium treatment robustly protects neurons in the central nervous system against excitotoxicity by inhibiting N-methyl-D-aspartate receptor-mediated calcium influx. (Nonaka)

ONCOLOGY

Blockade of SDF-1 after irradiation inhibits tumor recurrences of autochthonous brain tumors in rats. (Liu)

Excess weight gain accelerates 1-methyl-1-nitrosourea-induced mammary carcinogenesis in a rat model of premenopausal breast cancer. (Matthews)

Inhibition of CXCR7 extends survival following irradiation of brain tumours in mice and rats. (Walters)

FLEXIBLE HEALTH STANDARD OPTIONS

Taconic suits the needs of your specific research project and facility.



Taconic offers the Sprague Dawley® outbred rat at the standard Murine Pathogen Free™ health status which is appropriate for most studies. The Restricted Flora™ and Excluded Flora health status which are sometimes preferred for Immunology, Oncology and other applications.

To learn more about the different Taconic health statuses go to taconic.com/quality/health-testing-program/health-standards. Taconic can assist you in choosing a model appropriate for your study and facility.

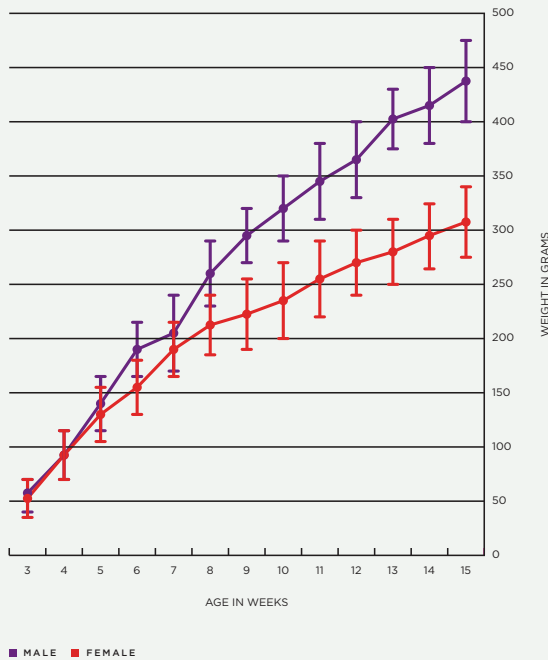
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SPRAGUE DAWLEY® PHYSIOLOGICAL DATA

SPRAGUE DAWLEY® GROWTH CHART



SPRAGUE DAWLEY® PHYSIOLOGICAL DATA

PARAMETER (April 2004; N=10/per group)	UNITS	Avg±D.D MALES	Avg±D.D FEMALES
SERUM CHEMISTRY			
Glucose	mg/dL	82.4 ± 11.3	93.2 ± 10.3
Creatinine	mg/dL	0.3 ± 0.1	0.3 ± 0.1
BUN	mg/dL	9.1 ± 1.4	13.6 ± 3.0
Total Bilirubin	mg/dL	0.1 ± 0.0	0.1 ± 0.0
Total Protein	g/dL	6.4 ± 0.2	6.7 ± 0.2
BLOOD COUNTS			
Red Blood Cells	$\times 10^6/\mu\text{L}$	6.9 ± 0.3	7.7 ± 0.3
Hemoglobin	g/dL	14.5 ± 0.8	16.1 ± 0.6
Hematocrit	%	48.3 ± 2.3	51.2 ± 2.6
MCV	fL	69.9 ± 1.7	66.9 ± 0.9
MCH	pG	20.9 ± 1.3	21.0 ± 1.1
MCHC	%	29.9 ± 1.6	31.4 ± 1.9
Platelets	$\times 10^3/\mu\text{L}$	1358.0 ± 123.8	1262.2 ± 278.4
White Blood Cells	$\times 10^3/\mu\text{L}$	9.4 ± 3.2	6.0 ± 1.5
Neutrophil	$\times 10^3/\mu\text{L}$	0.9 ± 0.5	0.4 ± 0.3
Lymphocyte	$\times 10^3/\mu\text{L}$	8.3 ± 2.9	5.5 ± 1.4
Monocytes	$\times 10^3/\mu\text{L}$	0.3 ± 0.3	0.1 ± 0.1
URINALYSIS			
Glucose	mg/dL	Negative	Negative
Blood		Negative	Negative
pH		6.75 ± 0.35	6.7 ± 0.4
Specific Gravity		1.0195 ± 0.0068	1.0155 ± 0.0079
Life Span		24 - 36 Months	
Daily Food Consumption		4-5g/100g Body Weight	
Daily Water Consumption		8-11ml/100g Body Weight	

Additional data available at taconic.com/SD

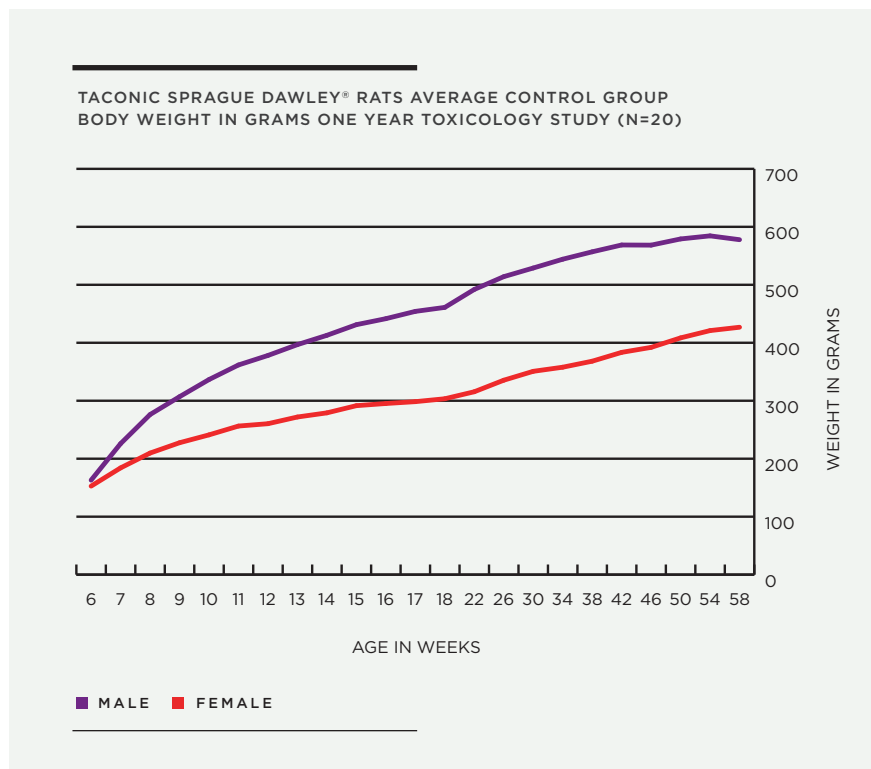
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THE ROLE OF TIMED-PREGNANT SPRAGUE DAWLEY® RATS IN BIOMEDICAL RESEARCH

ONE YEAR GROWTH CHART



The ability to monitor embryonic development and accurately determine gestational age of lab animal embryos is vital to many areas of biomedical research. For example, embryos from timed-pregnant Sprague-Dawley® rats are used in the study of embryonic development, teratology and reproductive toxicology, as well as experiments using fetal tissue that require cell-harvesting and culturing at specific embryonic ages.

More than 50 years ago, critical investigations by R.J. Blandau and his colleagues established procedures for measuring and timing rat gestational development with high accuracy. Monitoring gestational development requires a reliable determination of the time of conception. Since no scientific method exists to determine the exact time of conception, indirect indicators are used. Vaginal swabs offer a qualitative indicator of the likelihood of fertilization, making the presence of

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sperm in the vagina of female rats in estrus a reliable indicator of conception.

The female rat accepts the male for mating only at the end of the 12-hour preliminary period of proestrus, and during the 12 hours of estrus. Ovulation occurs about 10 hours after the onset of estrus. Sperm migrate from the uterus to the oviduct about 15 minutes after copulation. At one hour post-copulation, sperm are found throughout the oviduct, and at three hours, 90% of the ova are fertilized. Based on these data, the onset of embryonic development can be estimated with considerable accuracy when proper monitoring and controls are in place.

Gestational age is measured from the time of conception, which marks the beginning of embryonic Day 1. At 24 hours post-conception, and as Day 2 begins, the embryo has cleaved or is about to cleave into the two-cell stage. At the beginning of Day 4, the embryo (a morula that contains 12 to 16 cells) begins to enter the uterus. Implantation usually begins on the evening of Day 5 as the embryo settles into the maternal uterine wall. Implantation occurs when the blastocyst becomes clasped by the endometrium. At this point, the blastocyst orients itself with the inner cell mass facing the underlying maternal

tissue. Estrogen and other hormonal conditions in the uterus affect the rate of development after implantation.

During Day 6, the blastocyst increases in size and elongates. Implantation sites are visually evident by Day 7. During Days 9 and 10, the beginning of somite formation takes place. Somites, which are thesegments formed on either side of the embryo's neural tube, develop into external body forms as they transform into muscle mass connected to a spinal nerve. The number of somites increases at a known rate, which is useful to track development.

Following organogenesis, the embryo enters the stage of maturation, the time when organs grow and become functionally complete. By Day 15 the embryo's head is growing faster than the rump. The previously pear-shaped body evolves into a cylindrical shape. The bones develop joint cavities over several days of maturing development. The joint cavities develop for the shoulder, elbow, hip, and knee joints during Day 16, while the carpal and tarsal joints form on Day 17, with the digital joints of the legs during forming on Day 19 or 20. By Day 22, blood-forming activity in the liver nearly ceases with the end of gestation. Day 22 is also the average date of birth, since the gestation period lasts 21 to 23 days.

Another measure of gestational age is embryo crown-to-rump-length, for which standard rates of development are well documented. The crown-to-rump measurement is taken from the vertex to the rump, taking care to avoid caliper pressure that would distort the natural curvature of the embryo. At Day 11, there are 4 to 13 somites, and the average crown-to-rump length is 2 mm. By Day 16, there are 58 - 65 somites, and the crown-to-rump length is about 13.5 mm. At Day 22 (the average date of birth), the crown-to-rump length ranges from 40.5 - 42.6 mm, and the weight of the neonate is 5.9 - 6.4 grams.

Many factors can influence the rate of embryo development, including the light-dark cycle that affects the onset of ovulation, the initial position of the embryo in the genital tract, the hormonal variables of the mother, litter size, maternal diet and environmental conditions.

During the complex processes of development, toxicological and environmental factors can also affect the rate of development. As a result, the actual rate of embryo development can vary from the nominal gestational age.



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PRODUCTION OF TIMED-PREGNANT SPRAGUE DAWLEY® RATS AT TACONIC

Taconic's breeding specialists use proven, highly effective procedures to generate timed-pregnant Sprague Dawley® rats. While gestational age cannot be determined with total precision, strict adherence to pre-defined mating procedures, and close monitoring of female rats after they are co-housed with males, can accurately define the 24-hour period during which mating, and presumably, conception occurs.

At Taconic, the day of sperm cell detection in females is called the sperm-positive date and is considered Day 1 of gestation. After co-housing females with males the prior day, Taconic technicians take vaginal swabs of females between 7 and 10 a.m. daily. This procedure

assumes that timed-pregnant females have mated and conception has occurred from 0 to 24 hours before the designated sperm-positive date. Presumably, the majority of matings occur around the midpoint of the previous day's dark cycle, from 6 p.m. to 6 a.m.

When investigators order timed-pregnant rats at a specified developmental age for delivery on a specific date, Taconic technicians select rats based on the sperm-positive date. For instance, for an order for rats bearing embryos at Day 15 of gestational age for delivery on January 15, Taconic would select timed-pregnant females with a sperm-positive date of January 1. **Please note that to prevent any confusion over conflicting**

conventions for defining gestational age, Taconic advises investigators to specify the sperm-positive date when ordering timed-pregnant Sprague Dawley® rats.

Since Taconic's method for selecting timed-pregnant females results in full-term pregnancies approximately 95% of the time, extra rats are not supplied with each order. However, spontaneous abortions and small litters of fewer than four pups do occur on occasion. When expending considerable time and resources to prepare for a study using timed-pregnant rats on a specific day, and especially when using a small number of dams or fetuses, Taconic advises customers to order extra timed-pregnant rats to hedge against any potential issues.

REPRODUCTION PARAMETERS OF SPRAGUE DAWLEY® RATS

MALE RATS

AGE AT PAIRING (MATING)
8-10 WEEKS

WEIGHT AT PAIRING
250-300 GRAMS

PERIOD OF "ECONOMIC REPRODUCTIVE ABILITY"
6-9 MONTHS

FEMALE RATS

AGE AT PAIRING (MATING)
8-10 WEEKS

WEIGHT AT PAIRING
250-300 GRAMS

PERIOD OF "ECONOMIC REPRODUCTIVE ABILITY"
6-9 MONTHS

LENGTH OF ESTROUS CYCLE
4-5 DAYS

DURATION OF ESTROUS
10-20 HOURS

TIME OF OVULATION
8-11 HOURS after onset of estrous

GESTATION

TIME OF COPULATION
Near midpoint of previous dark cycle

TIME SPERM IS DETECTED IN VAGINA
DAY 1

TIME OF IMPLANTATION
LATE DAY 5

LENGTH OF GESTATION
21-23 DAYS

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