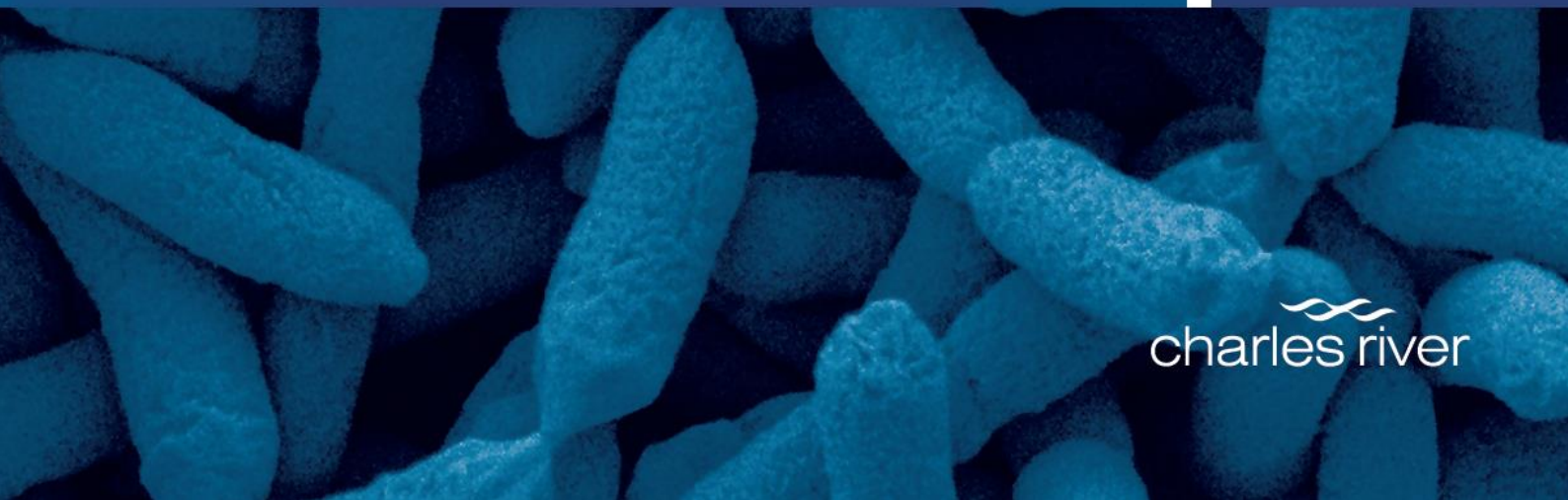




RESEARCH MODELS AND SERVICES

2018




charles river

Charles River Research Models

Global standards for biomedical research worldwide.

With more than 16 countries in North America, Europe and Asia, Charles River is leading global supplier of research models and service. Our core programs-biosecurity, International Genetic Standardization (IGS), Animal welfare and Model Quality-are designed to provide the most reliable supply of standardized products and services on a global basis, ensuring that the integrity of your research will be maintained over time and locations.

Table of Contents



Charles River Research Models	1		
Customer Service 1	2		
Customer Service 2	3		
IGS Production System (Outbred)	4		
IGS Production System (Inbred)	5		
JAX® Mice Production	6		
<u>Outbred Rats</u>			
Crl:CD(SD)	7		
Crlj:WI	8		
Crlj:LE	9		
<u>Inbred Rats</u>			
F344/DuCrIcrlj	10		
LEW/CrIcrlj	11		
BN/CrIcrlj	12		
<u>Disease Model (Outbred Rats)</u>			
Crlj: ZUC-Lepr ^{fa}	13		
<u>Disease Model (Inbred Rats)</u>			
ZDF-Lepr ^{fa} /CrIcrlj	14		
SHR/NCrIcrlj	15		
WKY/NCrIcrlj	16		
PCK/CrljCrl-Pkhd1 ^{pck} /CrIcrlj	17		
<u>Outbred Mice</u>			
Crl:CD1(ICR)	18		
<u>Inbred Mice</u>			
C57BL/6NCrI	19		
B6N-Tyr ^{c-Brd} /BrdCrCrI	20		
BALB/cAnNCrIcrlj	21		
C3H/HeNCrI	22		
DBA/1JNCrIj	23		
DBA/2NCrI	24		
NC/NgaTndCrIj	25		
<u>Hybrid Mice</u>			
B6D2F1/CrI	26		
CD2F1/Crlj	26		
B6C3F1/CrI	27		
<u>Hybrid Mice</u>			
B6D2F1/CrI	26		
CD2F1/Crlj	26		
B6C3F1/CrI	27		
<u>Immunodeficient (Mice)</u>			
CAnN.Cg-Foxn1 ^{nu} /CrIcrlj	28		
Crlj:CD1-Foxn1 ^{nu}	29		
CB17/Icr-Prkdc ^{scid} /CrIcrlj	29		
CB17.Cg-Prkdc ^{scid} Lyst ^{tg-J} /CrIcrlj	30		
Crlj:SHO-Prkdc ^{scid} Hr ^{hr}	31		
<u>JAX® Mice (Inbred)</u>			
C57BL/6J	32		
CBA/J	33		
SJL/J	34		
<u>JAX® Mice (Immunodeficient)</u>			
NOD.CB17-Prkdc ^{scid} /J	35		
NOD.Cg-Prkdc ^{scid} Il2rg ^{tm1Wjl} /SzJ	36		
<u>JAX® Mice (Disease Model)</u>			
B6.Cg-Lep ^{ob} /J	37		
BKS.Cg-Dock7 ^m + / + Lepr ^{db} /J	38		
B6.129P2-Apoe ^{tm1Unc} /J	39		
<u>Pre-conditioning Mice</u>			
C57BL/6J-Aged	40		
C57BL/6J-DIO	40		
C57BL/6J-NASH	40		
PDX Model	41		
Hu-NSG Model	41		
GENETICALLY ENGINEERED MODEL SERVICE	42		
Health Monitoring Services	43-44		
Surgical Services	45		
Terms and Conditions	46-49		
JAX® Mice, Products & Services Conditions	50		

Customer Service 1

Charles River Laboratories Japan, Inc.

Customer Support Center (Call Center)

INNOTECH Bldg 11F
3-17-6 Shin-Yokohama, Kohoku-ku, Yokohama-shi, Kanagawa 222-0033
Phone : 045-474-9350
FAX : 045-474-9351
Email : web_order@crl.com

Sales Department(East)

INNOTECH Bldg 11F
3-17-6 Shin-Yokohama, Kohoku-ku, Yokohama-shi, Kanagawa 222-0033
Phone : 045-474-9340
FAX : 045-474-9341
Email : web_order@crl.com

Sales Department(West)

KITAMOTO Bldg 1F-C
5-25 Takatsuki-machi, Takatsuki-shi, Osaka 569-0803
Phone : 072-686-6651
FAX : 072-686-6652
Email : web_order@crl.com

Ordering

Please call customer support center when you order, following information is required.

- 1) Company / Organization
- 2) Name and Contact Information (phone and , Fax)
- 3) Strain name
- 4) Sex (male, female)
- 5) Age in weeks
- 6) Number of Animals
- 7) Appointed Date of Delivery
- 8) Place of Delivery (Animal Facility or Room Name/Number)

After You Received Animals

We Charles River Laboratories make best effort to control delivery condition including temperature control in order to reduce animals stress. Please take out animals from the shipping container immediately and keep them in appropriate environment with feed and water.

Customer Service – Research Models 2

Definition of Items

Retired Breeders	Animals that had been used as breeders. Information of age is not given. Animals may have wound due to fighting.
Retired Breeders (specific month age)	Animals that had been used as breeders, Information of age is available. Retired month(week) age depends on the strain. If you request different month age of regular retired animals, additional breeding charge is required.
Untimed Pregnant Animals	Most barrier-reared rats and mice can be safely and accurately palpated for pregnancy after 14 days of gestation. Prior to that, pregnancy is determined by observation of vaginal plug. (Shipping date is around 14-17 days pregnant). Mating date is not given.
Timed Pregnant Animals	Pregnancy is determined by observation of vaginal plug. It may not be pregnant because it is difficult to determine pregnancy before 13 days of gestation. We recommend to order additional pregnant animals or pregnant animals after 14 days. The date the copulatory plug is found is considered to be day one of gestation.
Lactating Animal with Litter 1	Lactating animal with litter which are younger than 14 days age is shipped. Number of litter depends on the strain. Compared to Lactating Animal with litters 2 below, the risk of cannibalism is higher.
Lactating Animal with Litter 2	Lactating animal with 2-3 age in weeks litter is shipped. Number of pups is depends on a strain.
Additional charge	Location of delivery except Tokyo, Osaka and Nagaya area, additional shipping cost is required. When you order a small number of animals, additional fee for transportation box is required.

Shipping Body Weight

Shipping body weight is complies with our internal regulation. It is not guarantee regulation. It can be used as rough indication when you order.

- (1) Shipping body weight means the weight of before shipment. It is not a weight of at the time of delivery.
- (2) Please note that body weights is rough indication range when animals are chosen to be shipped.
- (3) We may need to arrange of the shipping weight range, when you order large number of animals
- (4) Shipping body weight is not set up for some strains.
- (5) Body weight is not set up in following strains.

Rats : SHR/NCrCrIj, WKY/NCrCrIj, ZDF-*Lepr^{fa}*/CrIj, CrIj:ZUC-*Lepr^{fa}*, CrIj:LE, PCK/CrIjCrIj-*Pkhd1^{pck}*/CrIjCrIj
 Mice : NC/NgaTndCrIj, CB17/Icr-*Prkdc^{scid}*/CrIjCrIj, BKS.Cg-*Dock7^m* +/- *Lepr^{db}*/J, B6.Cg-*Lep^{ob}*/J, NOD.CB17-*Prkdc^{scid}*/J, CrIj:SHO- *Prkdc^{scid}**Hr^{hr}*, C57BL/6J-DIO and control mice, NOD.Cg-*Prkdc^{scid}* *Il2rg^{tm1Wjl}*/SzJ, B6N-Tyr^{c-Brd}/BrdCrIj, CB17.Cg-*Prkdc^{scid}* *Lyst^{bg-J}*/CrIjCrIj, B6.129P2-*ApoE^{tm1Unc}*/J, C57BL/6J-NASH

Order of Small Number of Animals

Additional charge for shipping container is required when you purchase small number of animals. Please see the following Table.

	Age in Weeks	Number of Animals per Container	JPYEN/Container
RATS	3-15	≤ 3	1,000
MICE	ALL	≤ 9	1,000

Following animals are excluded for additional charge

Pregnant animals, BKS.Cg-*Dock7^m* +/- *Lepr^{db}*/J, B6.Cg-*Lep^{ob}*/J, CrIj:ZUC-*Lepr^{fa}*, ZDF-*Lepr^{fa}*/CrIjCrIj, NOD.CB17-*Prkdc^{scid}*/J, NOD.Cg-*Prkdc^{scid}* *Il2rg^{tm1Wjl}*/SzJ, C57BL/6J-DIO and control mice, C57BL/6J-NASH

Charles River Laboratories' International Genetic Standardization (IGS)

Introduction

The intent of this paper is to provide a clear definition of the International Genetic Standardization (IGS) program at Charles River. Adopted by Charles River in 1992, IGS applies to the management of the health and genetics of outbred stocks and inbred strains of research animal models, particularly mice and rats. Although this program embraces the standardization of four basic elements—genetics, health, quality assurance and operations, this reference paper solely focuses on the genetic component. The objectives of the IGS program vary slightly depending upon the type of colony being managed. For outbred stocks, the intent is to minimize inbreeding, maintain heterozygosity and manage genetic drift that would otherwise lead to colony divergence among Charles River colonies worldwide. For inbred strains, IGS helps minimize subline divergence due to genetic drift, and also to prevent genetic contamination by mismatings with other strains. This genetics management program coupled with the other three elements (health, quality assurance and operations) enables Charles River to breed research animals with uniformity, regardless of production location throughout the world.

Genetic Management of Outbred Stocks

Genetic drift over time, and the resultant genetic divergence between colonies, is the inevitable result of breeding stocks and strains in isolation. Over many generations, random genetic drift can be expected to cause at least moderate genetic divergence among rodent colonies. While genetic drift is a natural, unavoidable occurrence in any population, the challenge in breeding outbred animals is to maintain the diversity at the level of the individual, yet somehow standardize multiple production colonies of these animals that are geographically separated so that each colony has the same range of genetic variation.

Until the development of the IGS CD® rat, CrI:CD(SD), commercial breeders, including Charles River, started new colonies of outbred animals by cesarean rederivation, colony transfer or other methods. A random mating system was applied to these new colonies to ensure that genetic diversity was maintained. However, because each new colony was bred in isolation relative to other colonies of the same stock, genetic drift was inevitable over time. To address this issue and produce animals of similar genetic background regardless of which colony they came from, Charles River established a foundation colony of CrI:CD(SD) in 1992. This colony was established in Wilmington, MA using 100 pairs of breeders derived from existing CrI:CD(SD) colonies located throughout the world. One rederived pup from each of 200 litters was then used to set up the foundation colony in isolators. This enabled us to capture a broad genetic sample while ensuring a clean health profile. A circular pair-mating system was implemented in the foundation colony to prevent inbreeding. Offspring from each breeding pair in the foundation colony were then used to restock barrier rooms at all Charles River locations where CrI:CD(SD) animals were being produced. Currently, Charles River maintains the CD® rat and several other stocks, including the Wistar and Wistar Han rats and CD-1® mouse, under the IGS program.

Figure1:
IGS Forward Migration

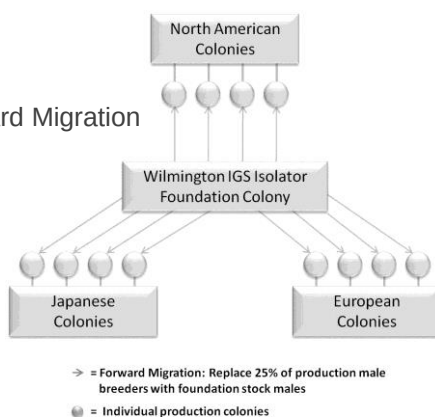
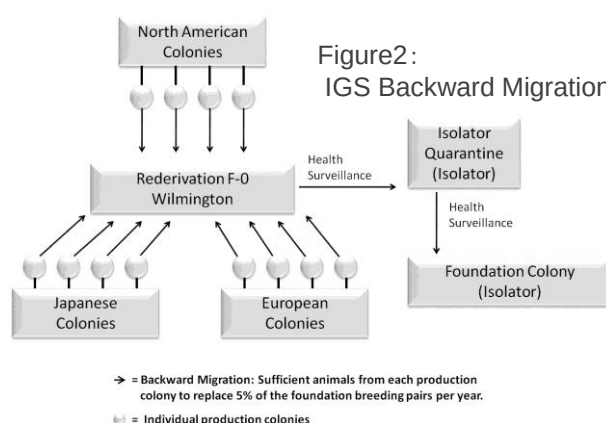


Figure2:
IGS Backward Migration



Instead of a random mating system within the barrier production rooms, IGS CD® rats are produced using a purposeful outbreeding system that employs block mating to minimize the chance of inbreeding. Another key element in the genetic management of this outbred stock is the use of migration. Every three years, animals from the foundation colony are migrated to production colonies on a rotational basis to replace some of the breeders (Figure 1). Every year, a sufficient number of animals are migrated back into the foundation colony from production colonies to replace 5% of the foundation breeding pairs (Figure 2). This system of forward and backward migration acts as a “genetic glue” that links all of the colonies and ensures that none diverge too far from the others. The end result is that all of the colonies are genetically merged into one large colony that resides in multiple locations around the world. This management system is validated by direct genetic analysis of animals from the foundation colony and the barrier rooms.

Charles River Laboratories' International Genetic Standardization (IGS)

A panel of 110 microsatellite markers distributed across all chromosomes is used to evaluate the genetic makeup of animals selected from the foundation colony and all production facilities worldwide. This screen determines whether the colonies maintain similar levels of genetic variation, thus indicating that the breeding and migration program is working as expected. Follow-up testing is performed every three years on rats from the foundation colony and every five years on each production colony worldwide to determine if the breeding program is successfully minimizing genetic drift and to provide temporal genetic data for all colonies.

Genetic Management of Inbred Strains

In contrast to outbred stocks where genetic management is directed at preserving existing genetic diversity, management of inbred strains is directed at maintaining authenticity and the highest possible levels of genetic uniformity. Inbred strains are defined as animals produced by a minimum of 20 generations of brother-sister mating, traceable to a single founding pair. This mating structure results in animals that are genetically (essentially) identical within each strain, i.e., fundamentally free of genetic differences that could increase variation in experimental results. Charles River uses a pyramid mating system (see Figure 3) coupled to a foundation colony for all inbred strains. In this system, the foundation colony serves as the genetic and health standard and provides breeders for the top level of the pyramid in every barrier room. This top level, the nucleus colony, is composed of a relatively small number of pedigreed brother-sister mating pairs that produce breeders for the next level of the pyramid, in addition to replenishing itself. In larger colonies, the next level is called the expansion colony, and it provides breeders to the production colony which in turn produces the animals that are commercially available. Strains that are produced in smaller numbers will not have an expansion colony, so the nucleus colony will provide breed stock directly to the production colony level. The unidirectional flow of breed stock in this system helps to ensure that any genetic changes or mutations, which would be more likely to occur in the larger expansion or production colonies than in the smaller nucleus colony, will "wash out" within a single generation.

As with all populations, permanent genetic differences may be introduced through genetic drift. However, this can be minimized by keeping the "self-replenishing" population small; a smaller population has fewer total mutations. In addition, the majority of commercial breeders produce multiple inbred strains in the same facility, so the risk for genetic contamination of one strain by another (i.e., mismating) also exists. While this possibility is minimized through various management practices (e.g., strains bred within the same room must have different coat colors), routine genetic testing must be employed to certify that mismating has not occurred.

Charles River utilizes a panel of 32 single nucleotide polymorphism markers (SNPs) that is capable of distinguishing all inbred strains

Bred at our various facilities from one another. Animals from each level of the production pyramid from each colony worldwide are sampled on a quarterly basis, thus certifying the genetic authenticity of every inbred strain.

Although the accumulation of genetic differences via drift is inevitable, Charles River effectively manages this drift using several methods. Phenotypic changes may be an indication of genetic changes, and barrier room staff members are trained to detect and report any such occurrences. Selective culling of phenotypic deviants, coupled with the use of the pyramid colony management program, helps stop the spread and is an effective short-term management tool. Similar to outbred stocks, a managed migration program is used to help maintain genetic uniformity among strains raised at multiple locations. Nucleus colonies are replaced every three to five years (within 10 generations) by migrating new breed stock from the foundation colony to the barrier rooms. As a safeguard against any large scale disaster affecting the foundation colonies of several strains, Charles River has cryopreserved a sufficient number of embryos for multiple, complete replacements of those populations.

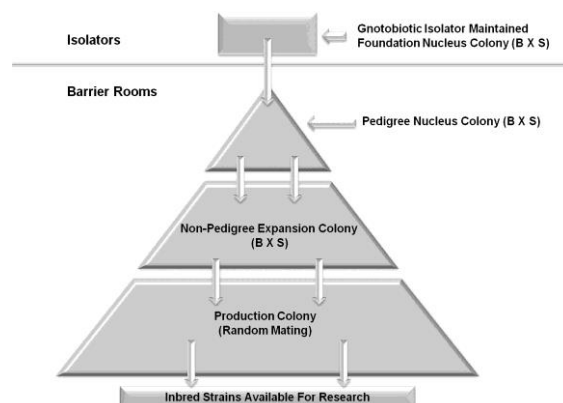


Figure3: Pyramid Mating System

Conclusion

As a global company with rodent production facilities in multiple locations, Charles River is uniquely challenged with maintaining genetic quality across all strains, stocks and locations. The program described above help to ensure that animals produced at any of our global production facilities have the same genetic profile if they are an inbred strain or the same relative level of genetic heterogeneity if they are an outbred stock.

Breeding sustention of JAX mice

About C57BL/6J, CBA/J, SJL/J, NOD.CB17-Prkdc^{scid}/J,
NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ, B6.129P2-ApoE^{tm1Unc}/J
B6.Cg-Lep^{ob}/J, BKS.Cg-Dock7^{m+/+} Lepr^{db}/J

1. Charles River Laboratories Japan Inc. serves as the exclusive, authorized commercial distributor and breeder of JAX® Mice strains in Japan.

Charles River Laboratories and The Jackson Laboratory made an agreement to breeding and supply of JAX® Mice in 22 countries in Europe and Asia. In accordance with the agreement, we have bred and supplied JAX® Mice C57BL/6J in Japan.

2. You can get satisfied and use for establishment of transgenic mice.

Minimize naturally occurring genetic drift by systematically re-infusing breeding colonies with pedigreed mice from The Jackson Laboratory. We re-establish the nuclear colony within 10 generations (Please see the following figure)

3. Inspection regarding Genetic and Quality control is conducted by The Jackson Laboratory annually.

JAX® Mice strains bred by Charles River Japan are: Equivalent in genetic quality to those bred by The Jackson Laboratory Provide the genetic integrity and stable phenotypes needed to support research excellence. The genetic background of JAX® Mice C57BL/6J mice will remain stable throughout time (minimized genetic drift) and when working with collaborators around the world.

4. About Genetic Quality Control

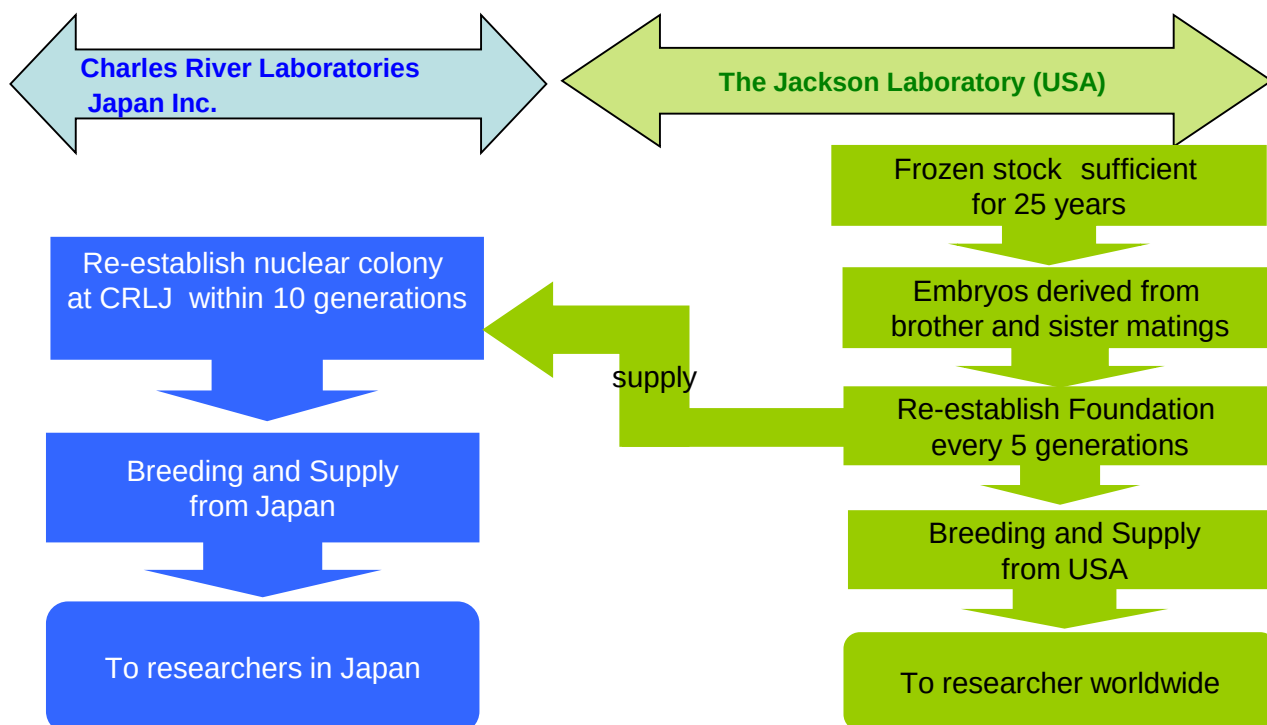
Assure genetic quality through routine use of state-of-the art genetic quality monitoring methods such as SNP analysis. Genetic Quality Control for JAX® Mice strains includes not only genetic monitoring but also:

- Reinfusing breeding colonies from pedigreed stock from The Jackson Laboratory which were maintained using a unique Genetic Stability Program



The Jackson Laboratory Genetic Stability Program is covered under U.S. Patent numbers 7592501 and 8110721; a license from JAX is required to practice under this patent.

- Rigorous record keeping to maintain traceability of progeny to pedigreed stock
- Diligent adherence to breeding protocols and best practices and in animal health and husbandry



Nomenclature Crl:CD(SD)

Common Name SD SPF/VAF*

FEATURES

- Well-growing
- Well-breeding
- Gentle

RESEARCH APPLICATION

- General multipurpose model
- Safety and efficacy testing
- Inflammation (ulceration¹⁾), hepatic inflammation, kidney inflammation, articular inflammation)
- Immunology (allergy)
- Oncology (carcinogenicity)
- Metabolism (Diabetes, diet-induced obesity)
- Cardiovascular (brain circulation, circulation of the myocardium)
- nerve system (behavior)
- Aging

COAT COLOR

White (Albino)

ORIGIN

To Charles River in 1950 from Sprague Dawley, Inc. In 1991, eight colonies were selected to form the IGS foundation colony. To Charles River Japan in 1994.

IGS refers to animals bred using the Charles River International Genetic Standardization program. It was developed by Charles River Laboratories, Inc. Please see the page of **Charles River Laboratories' International Genetic Standardization (IGS)** to get additional information.

ABBREVIATIONS

*CD: Caesarean Derived

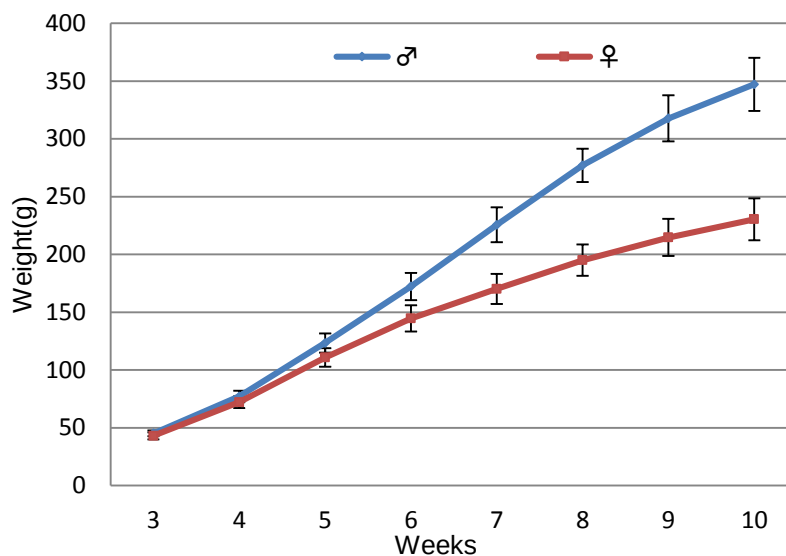
*SD: Sprague Dawley®

*Sprague Dawley®: Harlan Sprague Dawley

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free

1) Takuya Hirata et al. 1997 Life Science 61 (16) 1603-1611



Biological Reference Data

Biological Reference Data on CD(SD) Rats (CD(SD)) IGS Study Group 1998

Biological Reference Data on CD(SD) Rats (CD(SD)) IGS Study Group 1999

Biological Reference Data on CD(SD) Rats (CD(SD)) IGS Study Group 2000

Biological Reference Data on CD(SD) Rats (CD(SD)) IGS Study Group 2001

Biological Reference Data on CD(SD) Rats (CD(SD)) IGS Study Group 2002-2003

Nomenclature**Crlj:WI**

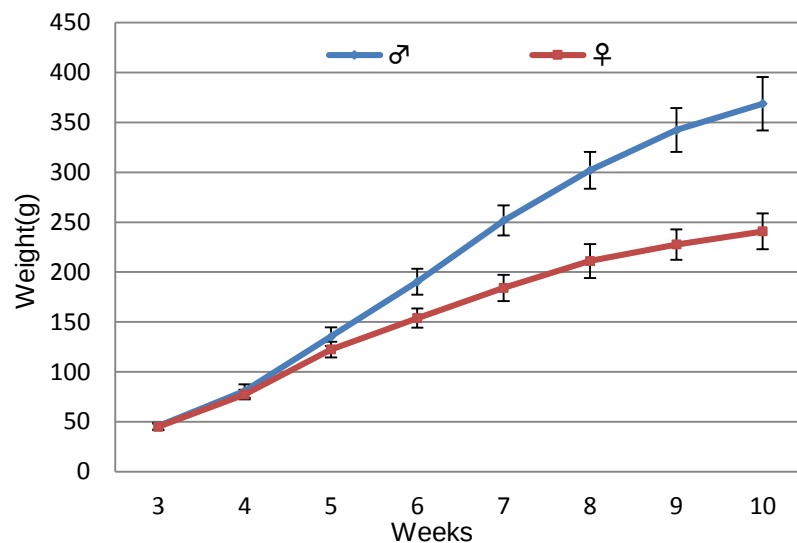
Common Name Wistar SPF/VAF*

FEATURES

- Well-growing
- Well-breeding
- Gentle

RESEARCH APPLICATION

- Safety and efficacy testing ¹⁾
- Inflammation (ulceration, hepatic inflammation)
- Immunology (allergy)
- Cardiovascular (brain circulation ²⁾, circulation of the myocardium ³⁾)
- Metabolism (diabetes) ⁴⁾
- Nerve system (behavior) ⁵⁾
- Aging

**COAT COLOR**

White (Albino)

ORIGIN

To Scientific Products Farm, Ltd. [predecessor of Charles River United Kingdom (CRUK)] in 1947 from Wistar Institute. To Charles River in 1975 from CRUK.
Gnotobioted breeders to Charles River Japan in 1981

**ABBREVIATIONS**

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free

1) Hiroshi Ono et al 1994 Jpn Pharmacol Ther 22(4) 65-86

2) Satoru Ozaki et al 1994 Folia Pharmacol. Jpn 104 469-480

3) Toru Yamashita et al. 1995 Jpn. J. Pharmacol 68 145-152

4) Hisashi hamada et al 1989 Japanese Pharmacology & Therapeutics 17 (9) 29-44

5) Yutaka Gomita et al 1990 Japanese Society of Pharmacometrics 39 (4) 375-383

Nomenclature Crlj:LE

Common Name Long-Evans SPF/VAF*

RESEARCH APPLICATION

- General multipurpose model
- Behavioral research¹⁾
- Diet-induced obesity²⁾
- Ophthalmology³⁾
- Phototoxicity

COAT COLOR

White with black hood; occasionally white with brown hood

ORIGIN

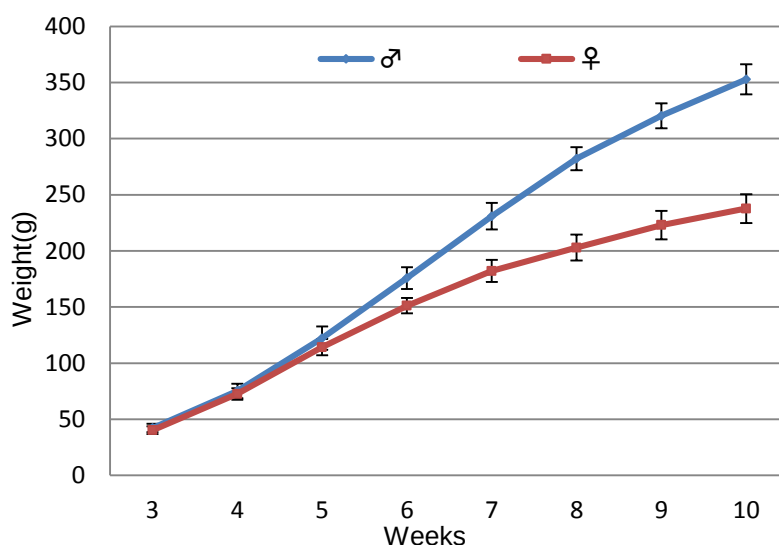
Originated by Drs. Long and Evans in 1915 by crossing several Wistar Institute white females with a wild gray male. To Charles River from Canadian Breeding Farm and Laboratories in 1978.

To Charles River Japan in 2013.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



1) Anne TM Konkle et al. 2010, J Am Assoc Lab Anim Sci. July;49(4): 427–436.

2) Tammy L. Kindel et al. 2010, Obesity (Silver Spring). February; 19(2): 380–387.

3) Turner, Patricia et al. 2005, Comparative Medicine, Volume 55, Number 2, 175-182(8)

【CAUTION】

The breeding colonies for Long-Evans provide rats for both large and small orders and fluctuate in size depending on current demand for each strain. We treat orders for these Strains as custom orders.

Nomenclature F344/DuCrI CrIj

Common Name F344

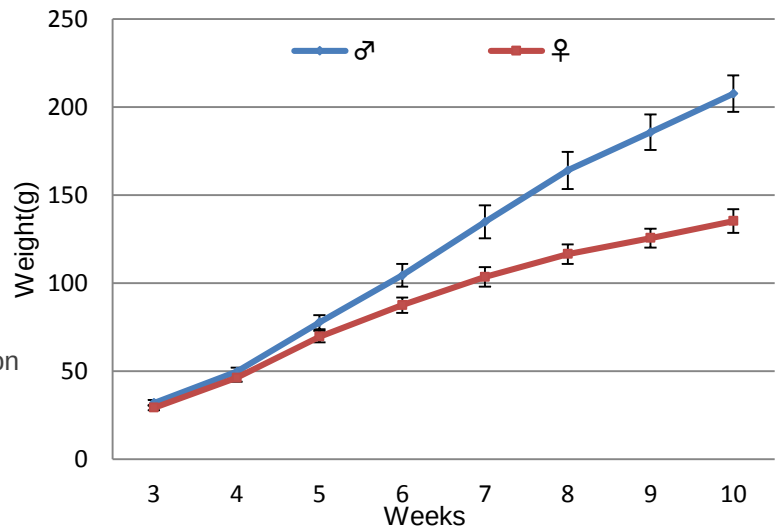
SPF/VAF*

FEATURES

- Small, gentle
- Long life span
- Reproductive stability
- Low incidents of spontaneous tumors
- Deletion of CD26(DPPIV)

RESEARCH APPLICATION

- Safety and efficacy testing
- Oncology (Carcinogenicity) ^{1), 2)}
- Aging ^{3), 4)}
- Nerve system (behavior) ⁵⁾
- Inflammation (ulcer ⁶⁾, hepatic inflammation ⁷⁾, arthritis),
- Immunology (allergy, implant),
- Cardiovascular (cerebral circulation)
- Obesity and Diabetes ^{8), 9)}



MHC HAPLOTYPE

RT1: ℓ

ORIGIN

From mating #344 of rats purchased from local breeder (Fischer).

Colony originated by M.R. Curtis, Columbia University Institute for Cancer Research, 1920. Dunning at Columbia inbred to form the strain starting in 1920. Dunning to Charles River in 1960 at F68.

To Charles River Japan in 1976 at F110.

COAT COLOR

White (Albino)



Abbreviations

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free

1) Shinji Yamamoto et al. 1995 Cancer Research 55 1271-1276

2) Muneshisa Takashi et al. 1994 Cancer Letters 87 151-157

3) Hiroki Miyake et al. 1996 Digestive Disease and Science 41 (2) 339-345

4) Masaya Takaoka et al. 1995 Exp. Anim 44 (1) 57-62

5) Makoto Ukai et al. 1995 Pharmacology Biochemistry and Behavior 51 (4) 705-708

6) Yasuhiro Tsukimi et al. 1995 J. Pharmacol 68 103-110

7) Jun-ichi Nagakawa et al. 1993 J Pharmacolgy and Experimental Therapeutics 264 1 496-500

8) Nobuyuki Yasuda et al. 2002 Biochemical and Biophysical Research Communication 298 779-784

9) Tadashi Nagakura et al. 2001 Biochemical and Biophysical Research Communication 284 501-506

Nomenclature LEW/CrJCrJ

Common Name LEW

SPF/VAF*

RESEARCH APPLICATION

- Induced arthritis (Adjuvant arthritis) ¹⁾
- Induced arthritis (Type II collagen-induced arthritis) ²⁾
- Ulcerative colitis ³⁾
- Transplantation research ⁴⁾
- Experimental allergic medullitis ⁵⁾, inflammation of heart muscle ⁶⁾, inflammation of the kidneys ⁷⁾, inflammation of the uvea.

COAT COLOR

White (Albino)

MHC HAPLOTYPE

RT1: ℓ

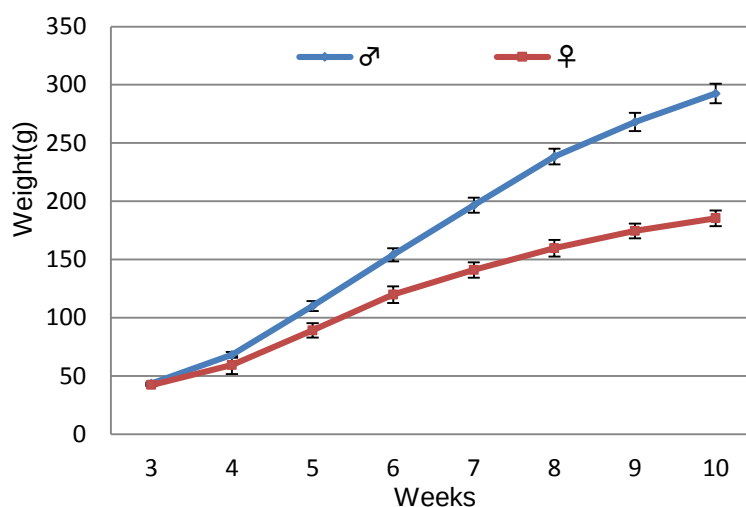
ORIGIN

Developed by Dr. Lewis from Wistar stock in the early 1950s. To Charles River from Tulane in 1970 at F34. To Charles River Japan in 1981 at F49.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



1) Takeshi Nishimura et al. 1996 Japanese Pharmacology & Therapeutics 24 (1) 27-30

2) Masakazu Takeshita et al. 1994 Exp. Anim 43 1 105-109

3) Internal information materials

4) News letters (CRJ Letters Vol.4 No.2)

5) Yasushi Kobayashi et al. 1995 Cellular Immunology 164 295-305

6) Haruo Hanawa et al. 1993, J Immunology, 150, 5682-5695

7) Yoshikazu Sado et al. 1986, J. Clin Lab. Immunol, 19, 193-199

Nomenclature BN/CrICrlj

Common Name BN

SPF/VAF*

FEATURE and RESEARCH APPLICATION

- High immunological response ¹⁾
- Respiratory inflammation ^{2), 3), 4)}
- Immunological dysfunction ⁵⁾
- Transplantation research ⁶⁾
- Aging

COAT COLOR

Non-agouti brown

MHC HAPLOTYPE

RT1:n

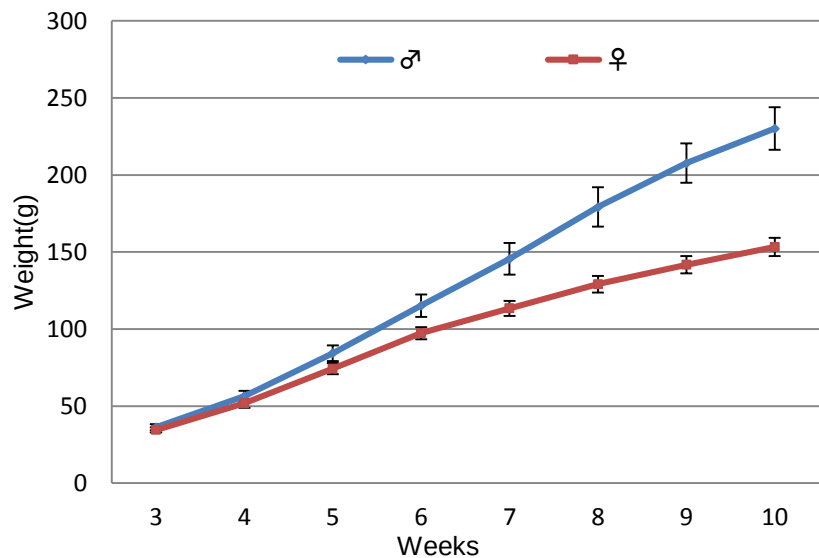
ORIGIN

To Charles River from Radiobiology Institute, Netherlands in 1976. And to Charles River Japan in 1990.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



1) Internal Information Materials

2) Toshiaki Takizawa et al. 2002 Biol. Pharm. Bull 25 (3) 318-322

3) Ryoichi Ohtsuka et al. J Toxical Pathol 2000 13 115-118

4) News Letters (CRJ Letters Vol.10 No.1)

5) Internal information Materials

6) News Letters (CRJ Letters Vol .4 No.2)

Nomenclature Crlj:ZUC-*Lepr^{fa}*

Common Name Zucker

SPF/VAF*

FEATURE

- Obesity due to polyphagia ¹⁾
- Hyperlipidemia ^{1), 2)}
- Hyperinsulinemia ^{1), 2)}
- Hyperleptinemia ^{1), 2)}
- Heterozygote (*Lepr^{fa}/+*) animals are used to breed because homozygote (*Lepr^{fa}/Lepr^{fa}*) animals are infertile.
- Homozygote (*Lepr^{fa}/Lepr^{fa}*) animals will start to become obesity at 4 weeks old and continuously gain up to 10 weeks old.

RESEARCH APPLICATION

- Insulin resistance
- Glucose intolerance
- Metabolic syndrome
- Renal function ³⁾

COAT COLOR

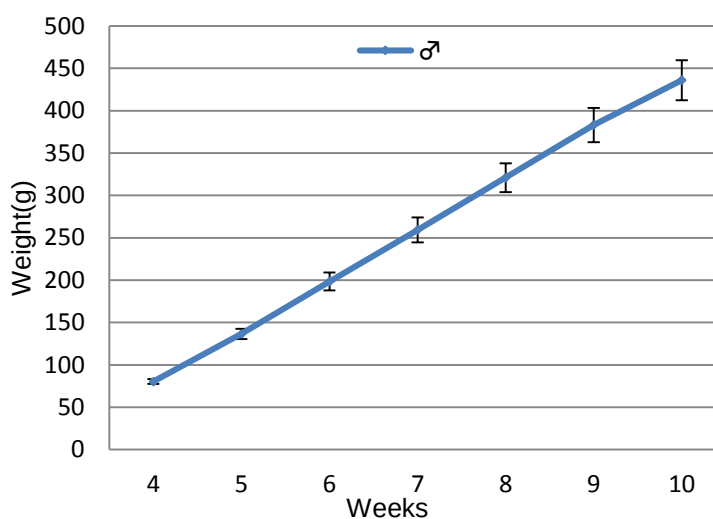
Four principal coat color variants:

1. predominantly brown
2. brown and white
3. predominantly black
4. black and white

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free


ORIGIN

The obese or fatty condition appeared spontaneously in the 13M strain maintained at the Laboratory of Comparative Pathology of Theodore and Lois Zucker in Stow, MA.

Research colonies were established at many institutions from this nucleus colony. To Charles River in 1985 from a research colony maintained at a pharmaceutical company. To Charles River Japan in 2000.

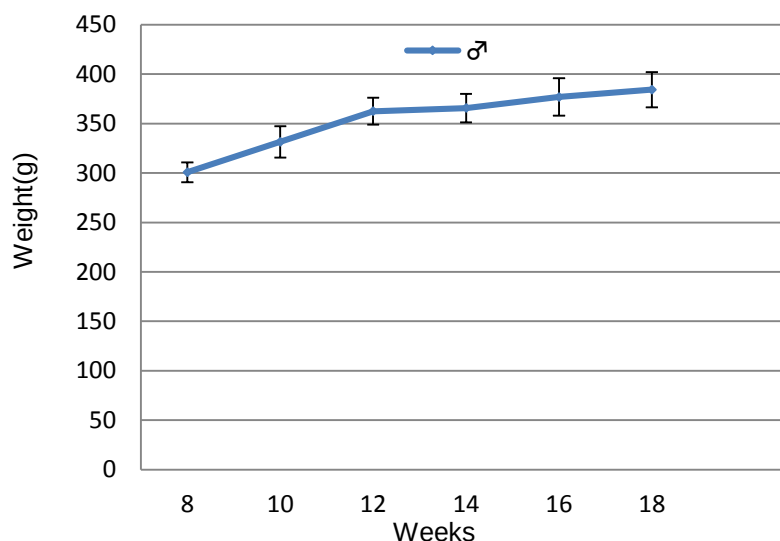
1) Internal Information Materials

2) Akira Okuno et al. 1998 J Clin Invest 101 1354-1361

3) Yasushi Hirasawa et al. 2008 Exp. Anim 57(5) 423-432

FEATURE and RESEARCH**APPLICATION**

- Type 2 diabetes model.
- Hyperglycemia ¹⁾
- Hypertriglyceridemia ¹⁾
- Hyperinsulinemia ¹⁾
- Hypercholesteremia ¹⁾
- Obesity ¹⁾
- Glycosuric nephropathy ²⁾
- Wound healing ³⁾
- Peripheral nerve disorder ⁴⁾

**COAT COLOR**

Black hooded with black stripe down the length of the back.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free

**ORIGIN**

A mutation occurred in a colony of outbred Zucker rats in the laboratory of Dr. Walter Shaw at Eli Lilly Research Laboratories in Indianapolis, IN in 1974~75. Part of this colony containing the mutation was moved to Indiana University Medical School (IUMS), to the laboratory of Dr. Julia Clark in 1977. Several groups of animals with diabetic lineage were identified and rederived in 1981.

Inbreeding of selected pairs from this rederivation was done in the laboratory of Dr. Richard Peterson at IUMS. An inbred line of ZDF rat was established in 1985. To Genetic Models, Inc. in 1991. To Charles River in 2001. and to Charles River Japan in 2005.

OATH

OATH is required when placing an initial order for this strain. Post-purchase breeding is prohibited.

1) Internal Information Materials

2) Makoto Mizuno et al. 2002 Hypertens Res 25(2) 271-278

3) Jeffrey T. Vrabec Otolaryngol Head Neck Surg 1998 118 304-308

4) Yukinori Shimoshige et al. 2000 Metabolism 49 (11) 1395-1399

Nomenclature SHR/NCrI CrIj

Common Name SHR

SPF/VAF*

RESEARCH APPLICATION

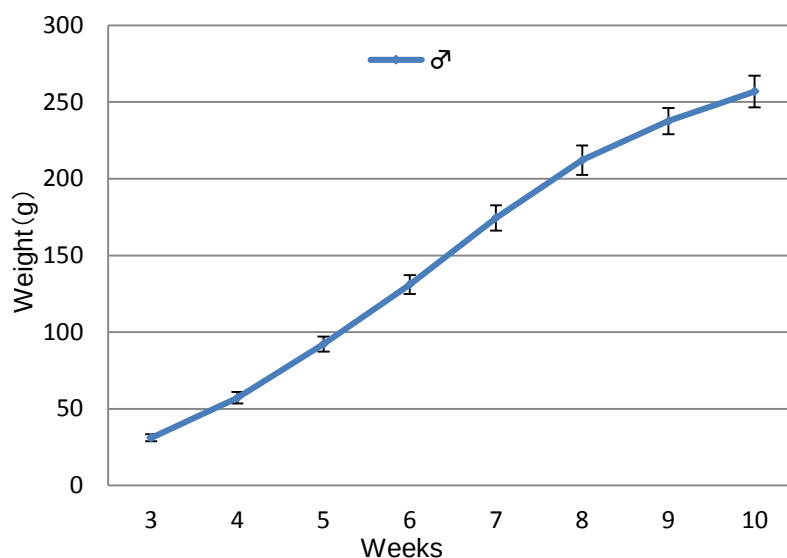
- Spontaneous hypertension ^{1), 2)}
- Cerebral ischemia model ³⁾
- Cerebral circulation
- Circulation of the myocardium ⁴⁾
- Central Nerve System
- ADHD (Attention Deficit Hyperactivity Disorder)

COAT COLOR

White (Albino)

MHC HAPLOTYPE

RT1: k


ORIGIN

Okamoto, Kyoto University School of Medicine, 1963, from outbred Wistar Kyoto male with marked elevation of blood pressure mated to female with slightly elevated blood pressure. Brother × sister mating with continued selection for spontaneous hypertension was then started. To NIH in 1966 from Okamoto at F13. To Charles River from NIH in 1973 at F32. And to Charles River Japan in 1980 at F51.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



1) Haruto Nakagawa 1996 Japanese Pharmacology & Therapeutics 24 (11) 43-49

2) Noriko Ogaiku et al. 1996 Hypertens Res 19 3 179-187

3) Kiyoshi Watanabe et al. 1995 Journal of Pharmacological Sciences 106 393-399

4) Takahito Yonezawa et al. 1996 J. Cardiovascular Pharmacology 27 119-124

5) M.H.L. Hunziker et al. 1996, 65, 129-144

Nomenclature WKY/NCrCrIj

Common Name WKY

SPF/VAF*

RESEARCH APPLICATION

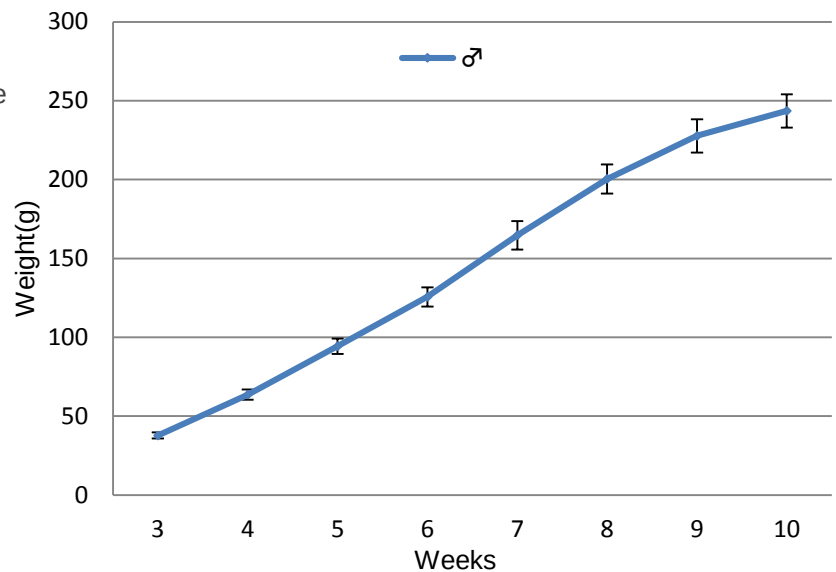
- Control for the SHR
- Autoimmune inflammation model of the kidneys ¹⁾

MHC HAPLOTYPE

RT1: ℓ

COAT COLOR

White (Albino)

**ORIGIN**

Outbred Wistar stock from Kyoto University School of Medicine to NIH 1971. This is the same stock from which the SHR/N strain was developed. To Charles River in 1974 from NIH at F11.

To Charles River Japan in 1981 at F25.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



1) Katsuyuki Sugihara et al. 1996, J. Pathology, 178, 352-358

Nomenclature PCK/CrljCrl-*Pkhd1*^{pck}/CrlCrlj

Common Name PCK

SPF/VAF*

RESEARCH APPLICATION

- Polycystic kidney disease, autosomal recessive trait (ARPKD)¹⁾

COAT COLOR

White (albino)

ORIGIN

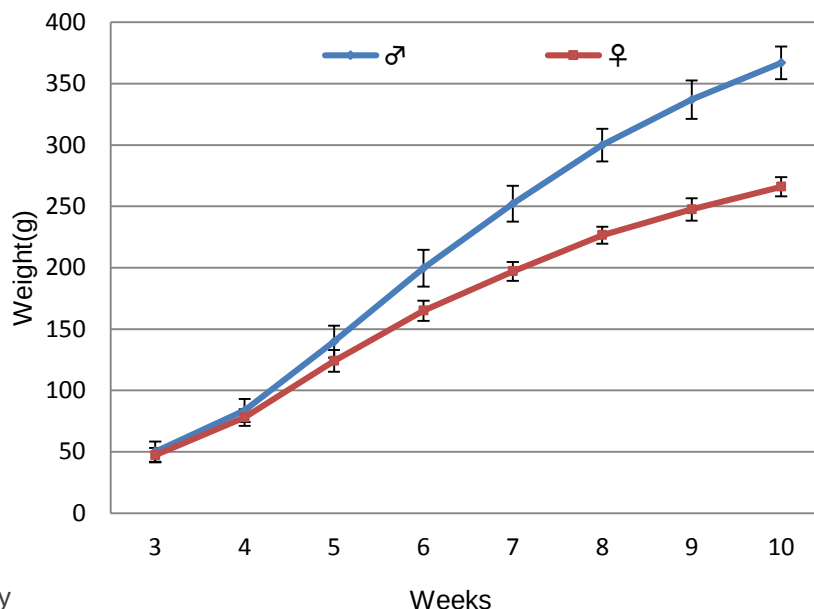
This model of polycystic kidney disease showing both kidney and liver involvement was identified in a colony of CD rats from the Charles River Japan production facility. The identification of the *Pkhd1* gene mutation was reported by Katsuyama and associates in 2000. This autosomal recessive *Pkhd1* gene mutation is a model of human autosomal-recessive polycystic kidney disease (ARPKD). To Charles River Laboratories in 2006.

To Charles River Japan in 2013.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



1) Makoto KATSUYAMA et al. 2000, Exp Anim 49(1) 51-55

【CAUTION】

The breeding colonies for PCK provide rat for both large and small orders and fluctuate in size depending on current demand for each strain. We treat orders for these Strains as custom orders.

Nomenclature Crl:CD1(ICR)

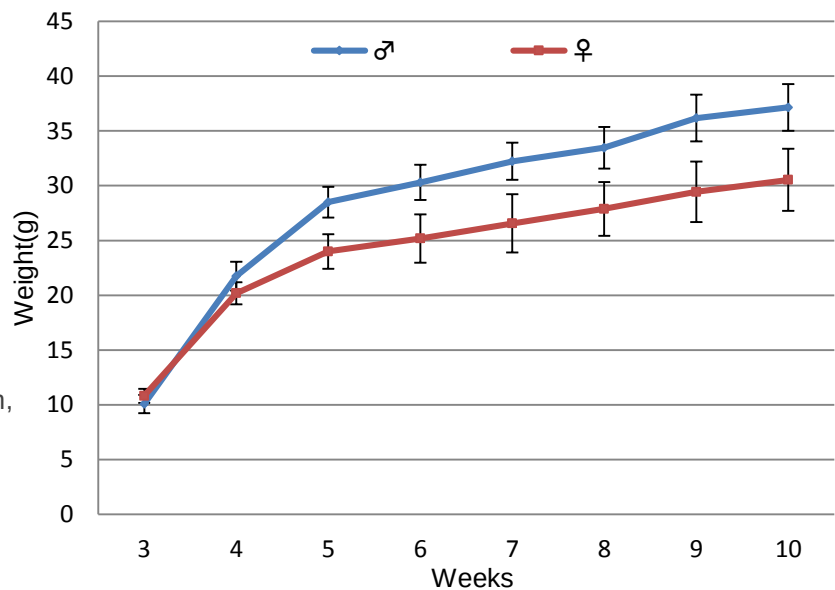
Common Name ICR SPF/VAF*

FEATURE

- Well-growing
- Well-breeding
- Gentle

RESEARCH APPLICATION

- General multipurpose model
- Safety testing ¹⁾
- Inflammation
- (ulcer, hepatic inflammation) ²⁾
- Immunology (infection) ³⁾
- Oncology (cancerogenesis)
- ADME⁴⁾
- Nerve System (central nerve system, behavior)
- Reproductive Research
- Genetic engineering models regard

**COAT COLOR**

White (Albino)

ORIGIN

The original group of Swiss mice that served as progenitors of this stock consisted of two male and seven female albino mice derived from a non-inbred stock in the laboratory of Dr. de Coulon, Centre Anticancereux Romand, Lausanne, Switzerland. These animals were imported into the United States by Dr. Clara Lynch of the Rockefeller Institute in 1926. The Hauschka Ha/ICR stock was initiated in 1948 at the Institute for Cancer Research (ICR) in Philadelphia from "Swiss" mice of Rockefeller origin. To Dr. Edward Mirand of Roswell Park Memorial Institute where they were designated as HaM/ICR. To Charles River in 1959. To Charles River Japan in 2012.



IGS refers to animals bred using the Charles River International Genetic Standardization program. It was developed by Charles River Laboratories, Inc. Please see the page of Charles River Laboratories' International Genetic Standardization (IGS) to get additional information.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free

- 1) Jyoji Yamate et al. 1986, Jpn. J. Vet. Sci, 48 (2) 273-284
- 2) Yoshitaka Tanaka et al. 1993 J. Immunology 151 (9) 5088-5095
- 3) Keiji Kajimura et al. 1996, Bio Pharm Bull 19 (6) 855-859
- 4) H. Tabata et al. 1998 Comparative Haematology International 8 53-57

Nomenclature C57BL/6NCrl

Common Name B6N

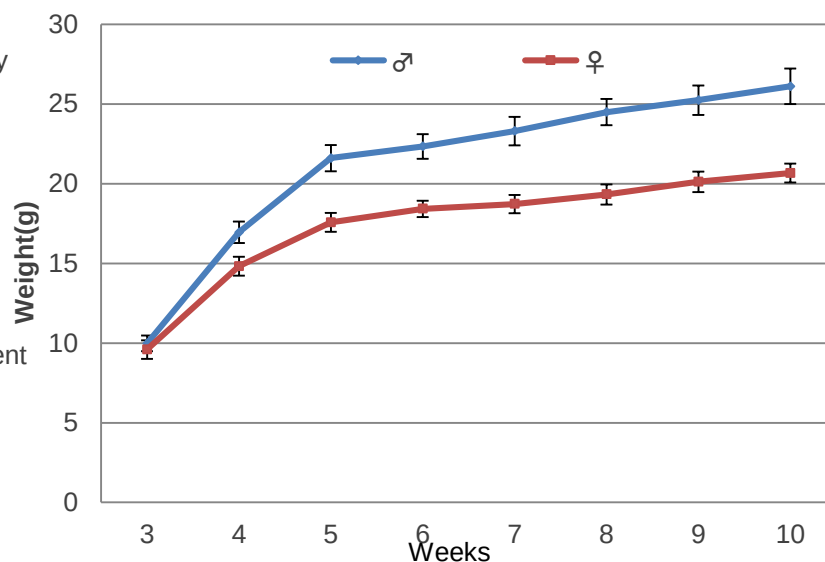
SPF/VAF*

FEATURE

- High incidents of microphthalmia and anophthalmia
- High incidents of ocularly white turbidity and cataract
- Hairloss
- Low incidents of spontaneous breast cancer
- Highly susceptible to leukemia
- Preference for alcohol

RESEARCH APPLICATION

- Transgenic/knockout model development
- Immunology ¹⁾
- Oncology
- Cerebral ischemia²⁾
- Diet-induced obesity
- Diabetes ³⁾
- Genetic engineering models research


COAT COLOR

Black

MHC HAPLOTYPE

H2 : b

IMPLANTABLE TUMORS

EL, C1498, B-16, Lewis Lung Carcinoma

ORIGIN

Developed by C.C. Little in 1921, from a mating of Miss Abby Lathrop's stock that also gave rise to strains C57BR and C57BL. Strains 6 and 10 separated about 1937. To NIH in 1951 from Jackson Labs at F32. To Charles River in 1974 from NIH. To Charles River Japan in 2012.



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ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free

1) Takako Kihara et al. 1996 J Dermatological Science 11 76-83

2) Gongming Yang et al. 1997 Brain Research 752 209-218

3) H. Tabata et al. 1998 Comparative Haematology International 8 53-57

Nomenclature B6N-*Tyr^{c-Brd}*/BrdCrCrI

Common Name B6 Albino

SPF/VAF*

RESEARCH APPLICATION

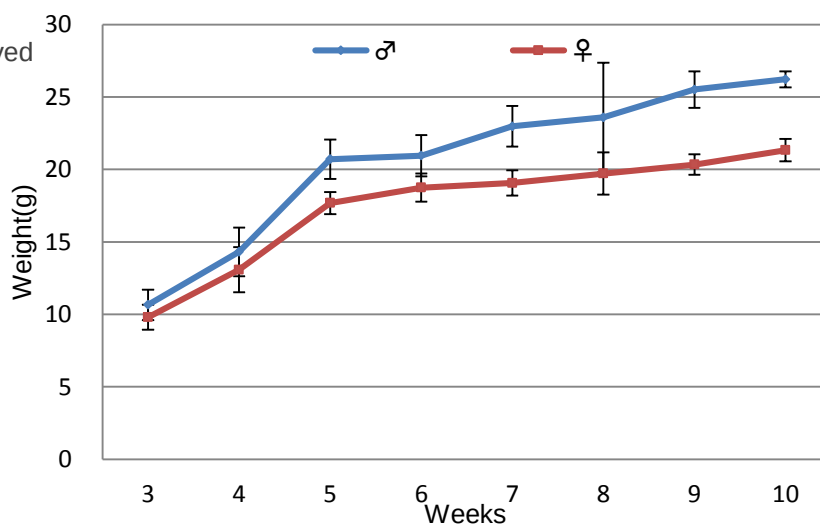
- Creation of chimeras with B6N-derived embryonic stem cells
- Genetic engineering research

COAT COLOR

White (albino)

MHC HAPLOTYPE

H2 : b

**ORIGIN**

Received by NCI from Dr. Allan Bradley at Baylor College of Medicine in 2000. The B6 albino strain is a spontaneous albino mutant coisogenic C57BL/6 strain. The mice contain a mutation in the tyrosinase gene, and when homozygous for the mutation the coat color of the mice is albino rather than black. To Charles River in 2009 from NCI. To Charles River Japan in 2013.



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ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free

【CAUTION】

The breeding colonies for B6 Albino provide mouse for both large and small orders and fluctuate in size depending on current demand for each strain. We treat orders for these Strains as custom orders.

Nomenclature BALB/cAnNCrICrlj

Common name BALB/c SPF/VAF*

FEATURE

- Highly-susceptible for radiation
- High incidence of heart lesion when aged

RESEARCH APPLICATION

- Inflammation
- Immunology / allergy ¹⁾
- Oncology
- Monoclonal antibody production

MHC HAPLOTYPE

H2 : d

IMPLANTABLE TUMORS

Meth-A, MOPC-104E, Colon-26, NS-1, P3

COAT COLOR

White (Albino)

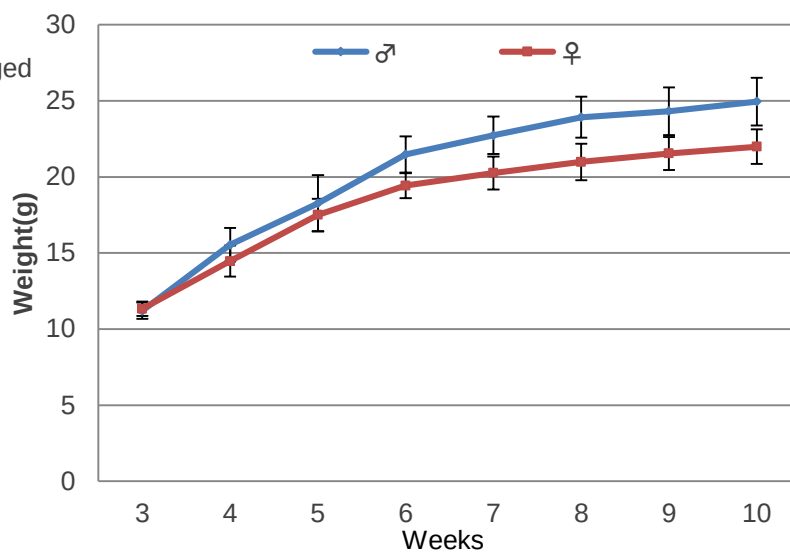
ORIGIN

H.J. Bagg developed the “Bagg albino” in 1913 from stock from an Ohio pet dealer. Inbred in 1923 by McDowell. To Snell in 1932 at F26, then to Andervont in 1935. To NIH in 1951 from Andervont at F72. To Charles River in 1974 from NIH at F122 through Battelle Memorial Inst. To Charles River Laboratories Japan, Inc. in 1976 at F144.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



Nomenclature C3H/HeNCrl

Common Name C3H SPF/VAF*

FEATURES

- Stable hair growth cycle
- No factor of MTV (Breast Cancer)
- High sensibility to LPS
- High incidence of hepatic tumor in aged male mice
- Genetic abnormal retina
- High sensitivity to benzene and chloroform

RESEARCH APPLICATION

- Immunology
- Hair growth research ¹⁾
- Oncology (anti-cancer ^{2), 3)})

COAT COLOR

Agouti

MHC HAPLOTYPE

H2 : k

IMPLANTABLE TUMORS

MM102, FM3A, MH134

ORIGIN

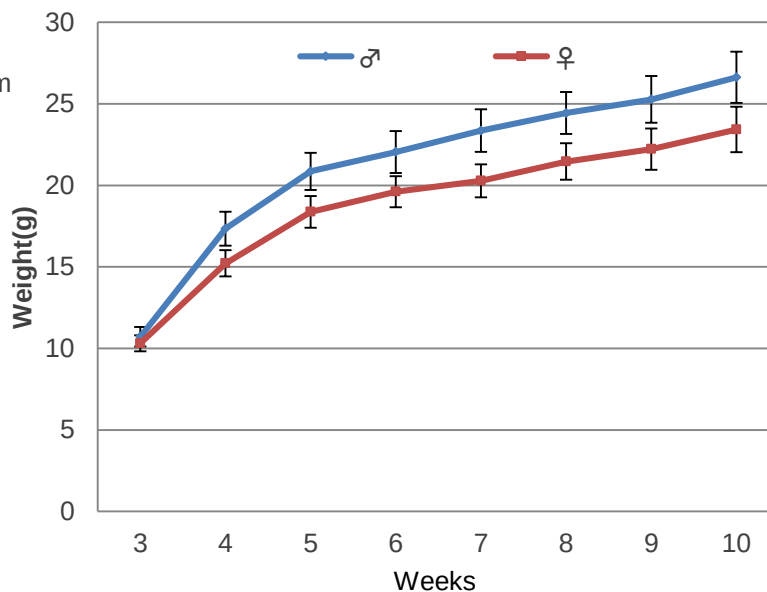
From a cross of a Bagg albino female and a DBA male by Strong in 1920. A litter of 4 females and 2 males sent to Andervont in 1930, then to Heston at F35. To NIH in 1951 from Heston at F57. To Charles River in 1974 from NIH. To Charles River Japan in 2012.

IGS refers to animals bred using the Charles River International Genetic Standardization program. It was developed by Charles River Laboratories, Inc. Please see the page of Charles River Laboratories' International Genetic Standardization (IGS) to get additional information.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



- 1) Yasunobu Kobayashi et al 1989 Clinical report 23 (13) 133-146
- 2) Peter Osa Ogundigie et al. 1995 Oncology Reports 2 369-375
- 3) Hiroshi Nishida 1994 Jpn J. Cancer Res 85 221-225

Nomenclature DBA/1JNCrlj

Common Name DBA/1

SPF/VAF*

FEATURES

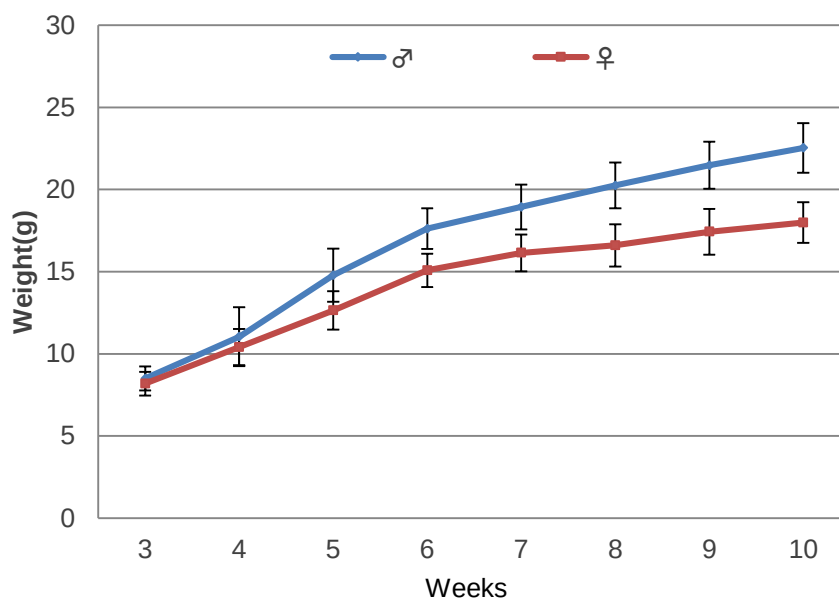
- Spontaneous cardiac calcification heart
- High incidence of breast cancer after propagation

RESEARCH APPLICATION
Type 2 collagen-induced arthritis ¹⁾
COAT COLOR

Dilute brown

MHC HAPLOTYPE

H2 : q


ORIGIN

From The Jackson Laboratory to Hoffman in 1965. To NIH in 1967. To Charles River from NIH in 1988. To Charles River Japan from Charles River in 1988 at F56.

ABBREVIATIONS

*SPF : Specific Pathogen Free

*VAF : Virus Antibody Free



1) Makoto Ueno et al. 1995, Int. J. Immunopharmac 17(7) 597-603

Nomenclature DBA/2NCrI

Common Name DBA/2

SPF/VAF*

FEATURES

- Hearing stroke ¹⁾
- High mortality to chloroform and ethylene oxide in male mice
- Low blood pressure
- Spontaneous cardiac calcification at heart ²⁾

RESEARCH APPLICATION

- Infection (fungus)
- Anticancer drug research

IMPLANTABLE TUMORS

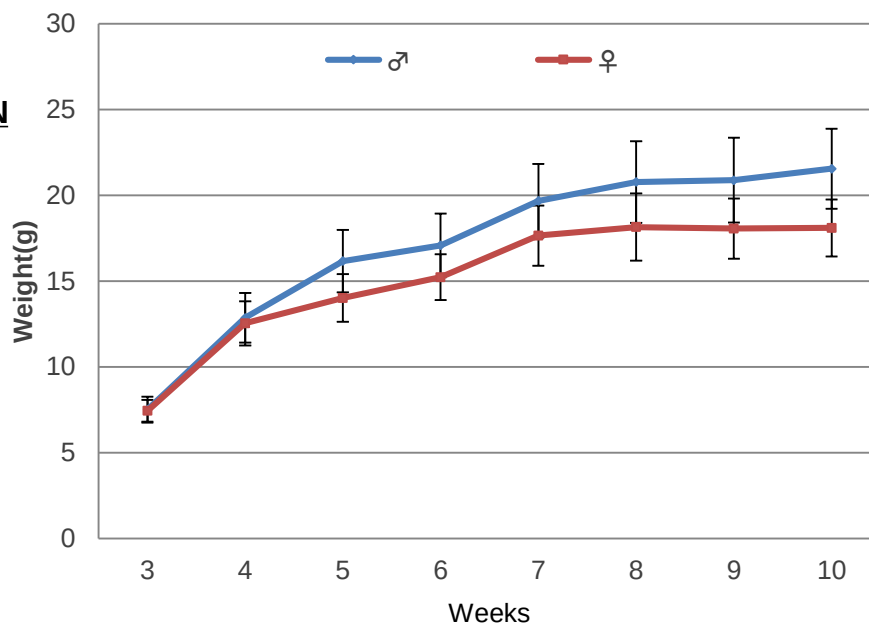
L1210, P388, P815

COAT COLOR

Dilute Brown

MHC HAPLOTYPE

H2 : d



ORIGIN

Developed by C.C.Little in 1909 from stock segregating for coat color. Oldest of all the inbred strains of mice. In 1929-1930, crosses were made between sublines, and several new sublines were established, including the widely used sublines 1 (previously called 12) and 2 (previously called 212). To Mider in 1938. To NIH in 1951 from Mider at F34. To Charles River in 1974 from NIH. To Charles River Japan in 2013.



IGS refers to animals bred using the Charles River International Genetic Standardization program. It was developed by Charles River Laboratories, Inc. Please see the page of Charles River Laboratories' International Genetic Standardization (IGS) to get additional information.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free

1) Masao Shimizu-Sasamata et al. 1996 J Pharmacol Exp Ther January 276:84-92

2) Kunio Doi et al. 1985, Jpn. J. Vet. Sci 47(3) 479-482

Nomenclature NC/NgaTndCrlj

Common Name NC SPF/VAF*

RESEARCH APPLICATION

- Atopic Dermatitis induced by hapten or mite antigens (Not spontaneous AD model) ¹⁾
- Asthma (be produced experimentally) ²⁾
- High susceptibility mite antigens ³⁾

COAT COLOR

Cinnamon

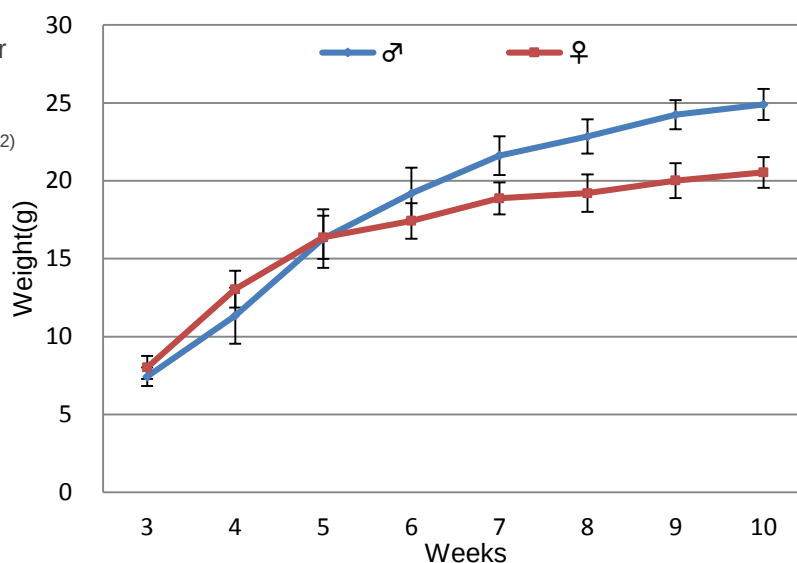
ORIGIN

Established by Dr. Kondo et al of Nagoya University (Agricultural Science) Japan in 1957. The colony maintained at Tokyo University of Agriculture and Technology (Agriculture) was introduced to Charles River Japan in 1997.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



● Changing groups is not recommended due to easily-fighting .

OATH

OATH is required when placing an initial order for this strain. Post-purchase breeding is prohibited.

1) News Letters (CRJ Letters Vol.11 No.1)

2) Takashi Iwasaki et al. 2001, J. Vet. Med Sci, 63 (4) 413-419

3) Mina Yamamoto et al. 2007 Allergology International, 56, (2), 1-10

Nomenclature B6D2F1/Crl

Common Name BDF1 SPF/VAF*

C57BL/6NCrI ♀ × DBA/2NCrI ♂

RESEARCH APPLICATION

- Transplantation research using tumor cells from C57BL/6NCrI or DBA/2NCrI
- Screening for anticancer drug research
- Obdurability and easy up-keeping
- Developmental engineering

COAT COLOR

Black

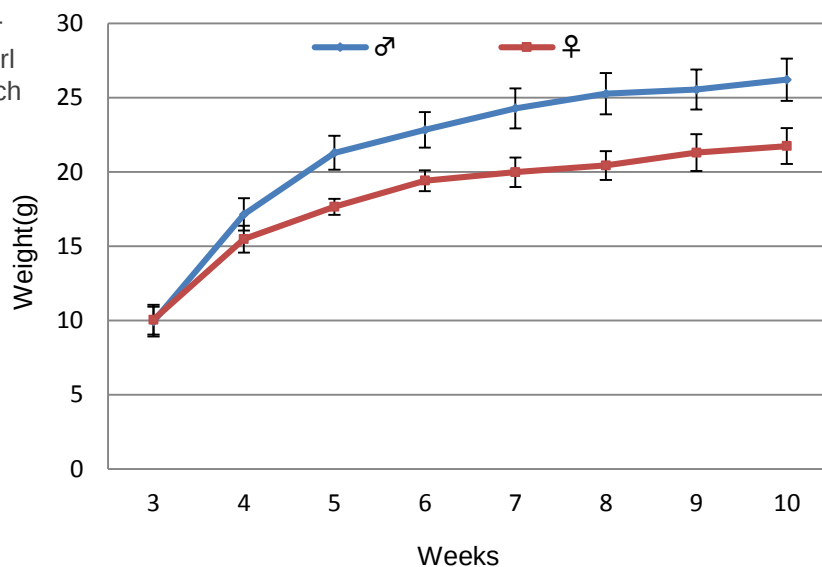
MHC HAPLOTYPE

H2 : b/d

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free

**Nomenclature CD2F1/Crlj**

Common name CDF1 SPF/VAF*

BALB/cAnNCrICrlj ♀ × DBA/2NCrICrlj ♂

RESEARCH APPLICATION

- Tumors from BALB/c and DBA/2 are transplantable
- Obdurability and easy up-keeping

COAT COLOR

Cinnamon

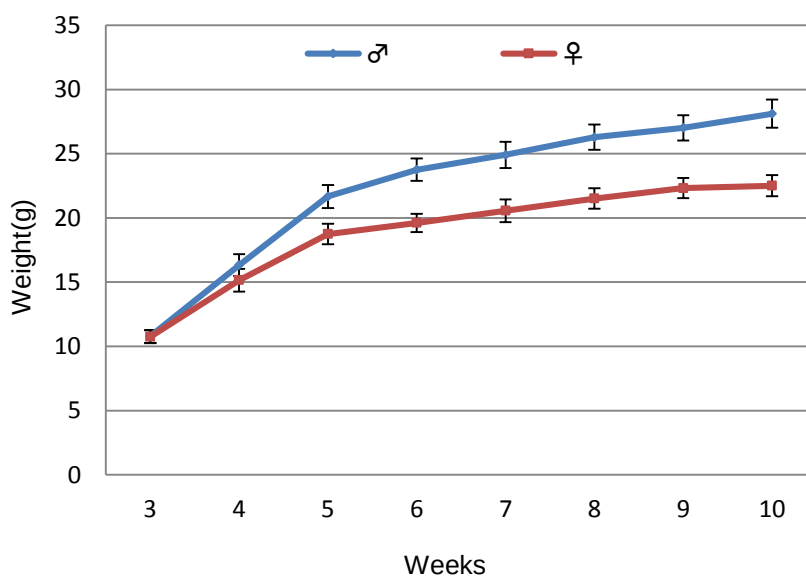
MHC HAPLOTYPE

H2 : d/d

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



Nomenclature B6C3F1/Crl

Common Name B6C3F1 SPF/VAF*

C57BL/6NCrl ♀ × C3H/HeNCrl ♂

RESEARCH APPLICATION

- Tumors from C57BL/6, C3H/He are Transplantable
- Obdurability and easy up-keeping
- Low incidents of spontaneous malignant tumor Carcinogenicity¹⁾
- Developmental engineering

COAT COLOR

Agouti

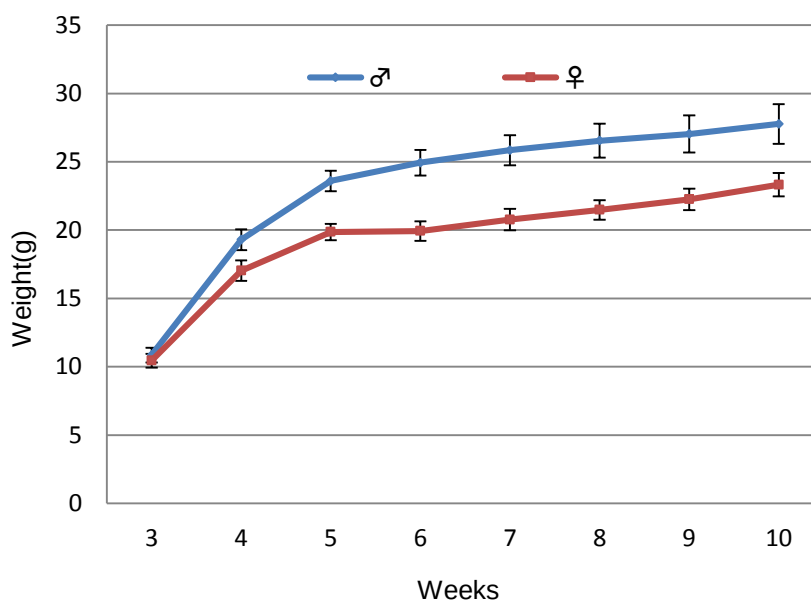
MHC HAPLOTYPE

H2 : b/k

ABBREVIATIONS

*SPF : Specific Pathogen Free

*VAF : Virus Antibody Free



1) Kouki Inai 1991 Jpn J. Cancer Res 82 380-385

IMMUNODEFICIENT MODEL

Nomenclature CAnN.Cg-Foxn1^{nu}/Cr|Crlj **Common Name** BALB/c Nude SPF/VAF*

RESEARCH APPLICATION

- Tumor biology
- Xenograft research ¹⁾
- Monoclonal antibody production

COAT COLOR

Hairless, albino background

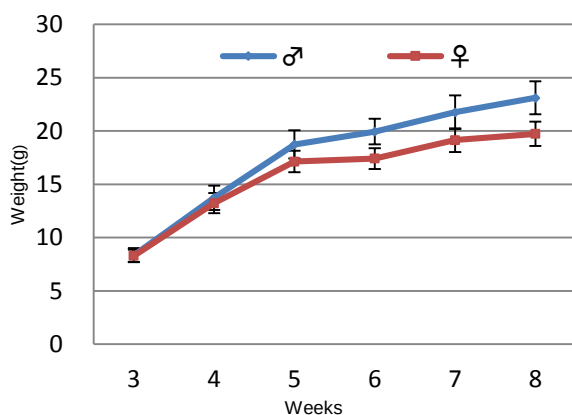
ORIGIN

Developed through crosses and back-crosses between BALB/cABom-nu and BALB/cAnNCrj-nu at Charles River Laboratories Japan (CRLJ). Pedigreed pregnant females of BALB/cAnNCrj-nu were received from CRLJ in 1985. To Charles River Laboratories Japan, Inc. in 1987. This mouse is inbred, and genetic monitoring results confirm it to be a BALB/c nude. The animal lacks a thymus, is unable to produce T-cells, and is therefore immunodeficient.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



- Nude mice are available up-to 5weeks age due to fighting.



+ Tested

+/- Implantation confirmed

* Listed on panel of culturable human tumor

** Calculation from growth curve of straight liner part

Tumor Implantation and Growth on Nude Mice

		Tumor implantation*	Doubling time of tumor (days)**	Days to initiate research after implantation
Stomach	St-4	+	11.6	18
	MKN1	+	17.0	18
	MKN7	+	7.2	15
	MKN28	+	8.2	9
	MKN45	+	8.1	11
	MKN74	+	9.0	17
Renal	RXL-631L	+	5.7	11
	ACHN	+/-		
Ovarian	OVCAR-3	+/-		
	OVCAR-4	+/-		
	OVCAR-5	+	14.5	19
	OVCAR-8	+	10.8	27
	SK-OV-3	+	6.8	15
Melanoma	LOX-IMVI	+	2.8	4
Lung	NCI-H23	+	8.6	21
	NCI-H226	+	7.6	21
	NCI-H460	+	7.5	12
	A549	+	12.8	17
	DMS273	+	5.0	12
	DMS114	+	8.8	17
Colon	HCC2998	+	7.2	23
	KM-12	+	5.0	10
	HT-29	+	6.8	13
	WiDr	+	7.4	14
	HCT-15	+	9.0	17
	HCT-116	+	5.3	11
Brain	U251	+	7.3	13
	SF-295	+	6.1	20
Breast	HBC-4	+	12.4	19
	BSY-1	+	6.0	21
	HBC-5	+	15.0	29
	MDA-MB-231	+	11.5	15
	MCF7	+/-		
Prostate	PC-3	+	8.8	22
	DU-145	+	11.3	19

1) Takao Yamori et al. 1991 Cancer Research 59 4042-4049

IMMUNODEFICIENT MODEL

Nomenclature Crlj:CD1-Foxn1^{nu}

Common Name

ICR Nude

SPF/VAF*

RESEARCH APPLICATION

Bigger than BALB/c Nude
 Monoclonal antibody production
 Tumor biology and xenograft research ¹⁾

COAT COLOR

Hairless, albino background.

ORIGIN

Developed from the transfer of the nude gene from Crl:NU-Foxn1^{nu} to a CD-1 mouse through a series of crosses and backcrosses beginning in 1979 at Charles River Laboratories. To Charles River Japan in 1981.

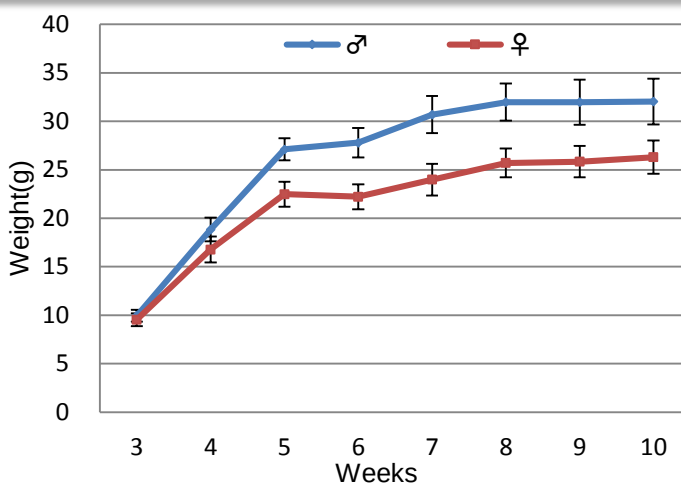
The animal lacks a thymus, is unable to produce T-cells. These causes immunodeficient.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free

1) Teruo Iwasaki et al. 2002 Int. J. Cancer 100 381-387



● Male nude mice is available up-to 5weeks age due to fighting.

Nomenclature CB17/Icr-Prkdc^{scid}/CrlCrlj

Common Name

SCID

SPF/VAF*

RESEARCH APPLICATION and KEY FEATURE

- Severe combined immunodeficiency affecting both B and T lymphocytes
- No detectable immuno globulin
- Immunology
- Tumor biology ¹⁾
- Xenograft transplantation
- Bred in Isolators

COAT COLOR

White (Albino)

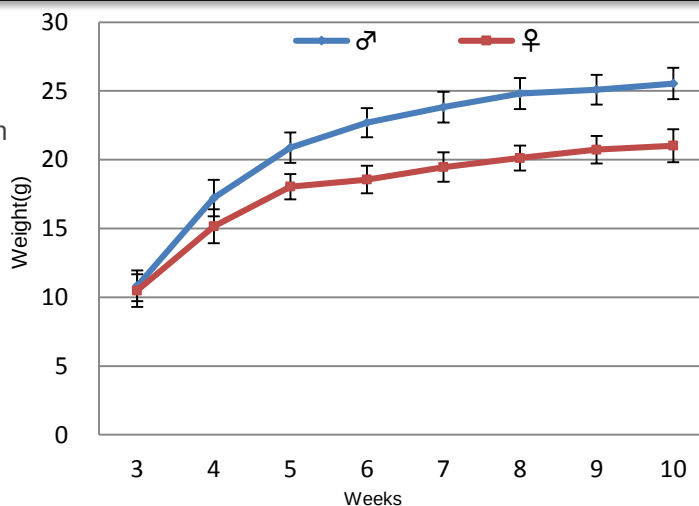
ORIGIN

SCID mice possess a genetic autosomal recessive mutation (scid). Discovered in 1980 by Bosma in C.B-17/Icr mice at Fox Chase Cancer Center. SCID mice show a severe combined immunodeficiency affecting both B and T lymphocytes. They have normal NK cells, macrophages, and granulocytes. To Charles River in 1991 from an IFFA Credo foundation colony. To Charles River Japan in 1992.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



OATH

OATH is required when placing an initial order for this strain. Post-purchase breeding is prohibited.

1) Jeong-Seok Nam, 2002 Clinical Cancer Research 8 2430-2436

Nomenclature CB17.Cg-*Prkdc*^{scid}*Lyst*^{bg-J}/CrlCrlj
 SPF/VAF*

Common Name SCID Beige

RESEARCH APPLICATION

- Tumor biology
- Xenograft research
- Research and development of the anticancer agent ^{1) 2)}
- Bred in Isolators

COAT COLOR

White (albino)

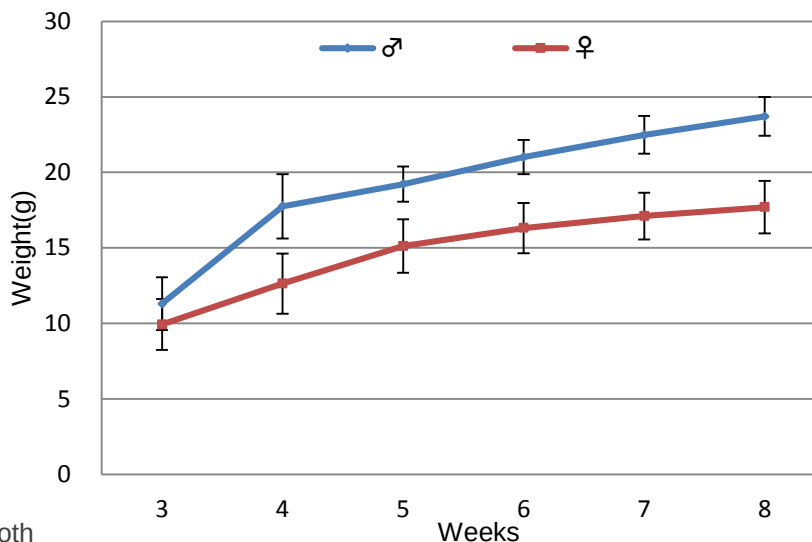
ORIGIN

A congenic mouse that possesses both autosomal recessive mutations SCID (*Prkdc*^{scid}) and beige (*Lyst*^{bg-J}). The SCID mutation results in severe combined immunodeficiency affecting both the B and T lymphocytes. The beige mutation results in defective natural killer (NK) cells. This mouse was developed by Croy, *et al.* at the University of Guelph by an intercross of C.B-17 SCID/SCID to C57BL/6 bg/bg mice. To Charles River in 1993. To Charles River Japan in 2013.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



1) Jian Zhang et al 2001 J Clin Invest 107 (10) : 1235-1244

2) Chemicky CL et al 2000 Cancer Gene Therapy Vol.7, No.3 ;384-395

【CAUTION】

The breeding colonies for SCID Beige provide mice for both large and small orders and fluctuate in size depending on current demand for each strain. We treat orders for these Strains as custom orders.

IMMUNODEFICIENT MODEL

Nomenclature Crlj:SHO-Prkdc^{scid} Hr^{hr} **Common Name** SHO SPF/VAF*

FEATURE

- Easy to implant tumors due to hairless
- Tumors implantation is as same as SCID mice
- Easy to measure and evaluate tumor growth via Imaging analysis
- Bred in Isolatoes

RESEARCH APPLICATION

- Tumor biology
- Xenograft research ¹⁾
- Monoclonal antibody production

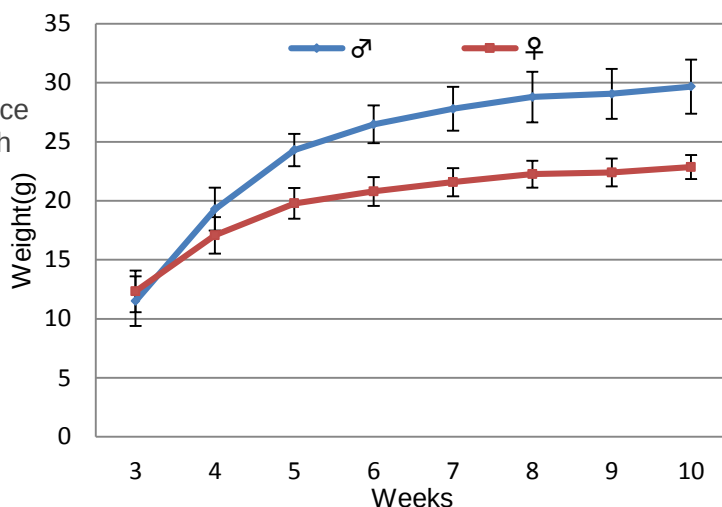
ORIGIN

The hairless SCID mouse was produced by Charles River Research Models in 2007 by intercrossing the Crl:HA-Prkdc^{scid} and Crl:SKH1-Hr^{hr} stocks. The resulting animals are homozygous for the Prkdc^{scid} and the Hr^{hr} mutations and thus exhibit the severe combined immunodeficiency phenotype characteristic of SCID mice and are also hairless. To Charles River Japan in 2010.

ABBREVIATIONS

*SPF: Specific Pathogen Free

*VAF: Virus Antibody Free



● Nude mice are available up-to 5weeks age due to fighting.

Immunodeficient mice

Strain	Nomenclature	Hair	T-Cells	B-Cells	NK-Cells	Complement	Page
BALB/c Nude	CAnN.Cg-Foxn1 ^{nu} /CrlCrlj	—	—	+	+	+	28
CD-1 Nude	Crlj:CD1-Foxn1 ^{nu}	—	—	+	+	+	29
C.B-17 SCID	CB17/lcr-Prkdc ^{scid} /CrlCrlj	+	—	—	+	+	29
SCID Beige	CB17/Cg-Prkdc ^{scid} Lyst ^{tg-J} /CrlCrl	+	—	—	impaired	+	30
SHO	Crlj:SHO-Prkdc ^{scid} Hr ^{hr}	—	—	—	+	+	31
NOD SCID	NOD.CB17-Prkdc ^{scid} /J	+	—	—	impaired	—	35
NSG	NOD.Cg-Prkdc ^{scid} Il2rg ^{tm1Wj1} /J	+	—	—	—	—	36

INBRED

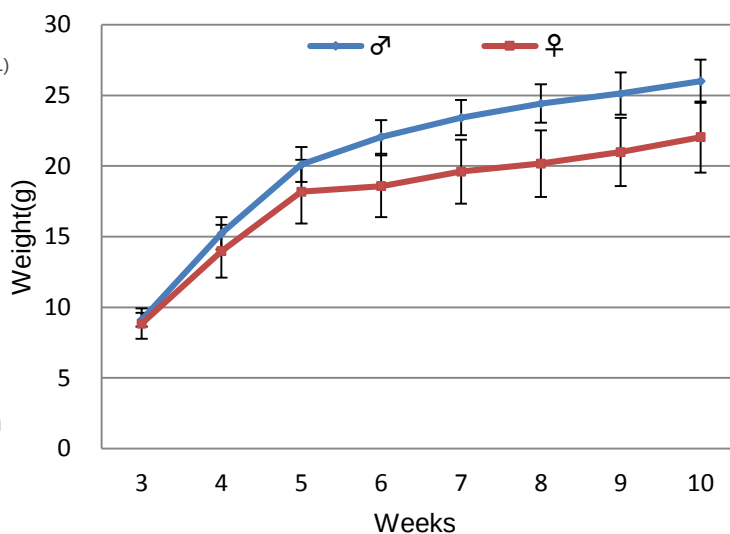
Nomenclature C57BL/6J

(JAX® Mice stock number:000664)

Common Name B6J

FEATURES

- First fully sequenced laboratory mouse strain¹⁾
- Highly susceptible to diet-induced obesity²⁾
- Prone to microphthalmia and associated eye abnormalities³⁾
- Prone to hair loss associated with over grooming and dermatitis⁴⁾
- Susceptible to hereditary hydrocephalus (1-4% prevalence)⁵⁾
- Preference for alcohol and morphine⁶⁾
- Most popular background for genetically modified strains
- -Prone to malocclusion: incidence is less than 0.05%, obvious at wean to 45 days⁷⁾
- Extensive phenotypic and SNP data available from the Mouse Phenome Database (<http://phenome.jax.org/db/q?rtn=strains/details&stocknum=000664>) as well as historical information from Festings <http://www.informatics.jax.org/external/festing/mouse/docs/C57BL.shtml> .



RESEARCH APPLICATION

- C57BL/6J is the most widely used inbred strain.
- Cardiovascular research
- Genetic engineering
- Diabetes and Obesity
- Immunology
- Genetics



The Jackson Laboratory Genetic Stability Program is covered under U.S. Patent numbers 7592501 and 8110721; a license from JAX is required to practice under this patent.

ORIGIN

This strain was introduced from The Jackson Laboratory to Charles River Japan and started to supply in 2002.

JAX® Mice bred at Charles River Japan are genetically equivalent to those produced by The Jackson Laboratory.

This strain is carried on "Genetic Stability Program" The information of "Genetic Stability Program" is available at <https://www.jax.org/jax-mice-and-services/find-and-order-jax-mice/why-jax-mice/patented-genetic-stability-program>

COAT COLOR

Black

MHC HAPLOTYPE

H2 : b



- 1) Waterston et al. 2002. Nature 420(6915):520-62]
- 2) Rossmeisl et al. 2003. Diabetes 52:1958-66
- 3) Smith et al. 1994. Lab Anim Sci 44:551-60)
- 4) Sundberg JP. 1994. Handbook of Mouse Mutations with Skin and Hair Abnormalities:
- 5) Animal Models and Biomedical Tools. CRC Press, Boca Raton, pp. 544)
- 6) Zygourakis and Rosen. 2003. J Comp Neurol 461:362-9)
- 7) Melo et al. 1996. Nat Genet 13:147-53; Phillips et al. 1994. Behav Neurosci 108:789-803
- 8) JAX® NOTES. 2003. 489:9-11

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INBRED

Nomenclature CBA/J (JAX® Mice stock number:000656)

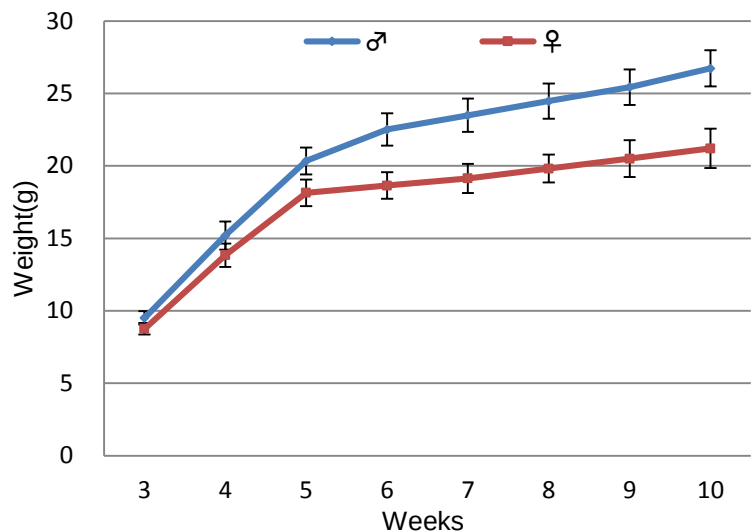
Common Name CBA

FEATURE

CBA/J inbred mice are widely used to support research in many areas including autoimmunity, sensorineural, and cardiovascular research.

RESEACH APPLICATION

- Granulomatous experimental autoimmune thyroiditis (G-EAT) model ¹⁾
- Blind by weaning due to retinal degeneration²⁾
- Renal tubulointerstitial lesions common ³⁾
- Late onset hearing loss, mostly at higher frequencies ⁴⁾
- Susceptible to seizures ⁵⁾
- Skin Sensitization (Local lymph node assay, LLNA) ⁶⁾
- Relatively resistant to diet-induced atherosclerosis⁷⁾
- Extensive phenotypic and SNP data available at the Mouse Phenome Database (<http://phenome.jax.org/db/q?rtn=strains/details&stocknum=000656>) as well as historical information at Festing (<http://www.informatics.jax.org/external/feeding/mouse/docs/CBA.shtml>)



ORIGIN

This strain was introduced from The Jackson Laboratory to Charles River Japan and started to supply in 2010.

JAX® mice bred at Charles River Japan are genetically equivalent to those produced by The Jackson Laboratory.

This strain is carried on "Genetic Stability Program(GSP)" The information of "Genetic Stability Program" is available at <https://www.jax.org/jax-mice-and-services/find-and-order-jax-mice/why-jax-mice/patented-genetic-stability-program>

COAT COLOR

Agouti



The Jackson Laboratory Genetic Stability Program is covered under U.S. Patent numbers 7592501 and 8110721; a license from JAX is required to practice under this patent.

MHC HAPLOTYPE

H2 : k

- 1) Wei et al. 2001. J Immunol 167:6678-86
- 2) Bowes et al. 1990. Nature 347:677-80; Chang et al. 2002. Vision Res 42:517-25
- 3) Rudofsky. 1978. Am J Pathol 92:333-48
- 4) Sweet et al. 1988. Audiology 27:305-12
- 5) Frankel et al. 2001. Genomics 74:306-12
- 6) G. Frank et al 2002. Toxicological Science 68:420-28



INBRED

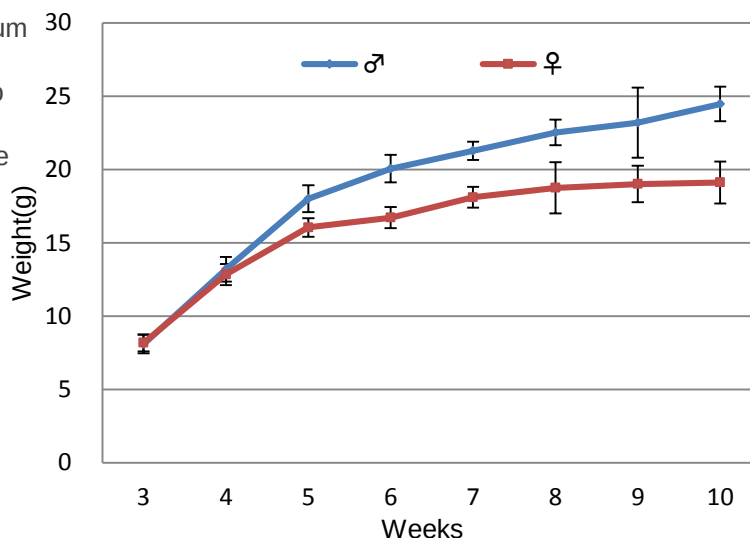
Nomenclature SJL/J

Common Name SJL

(JAX® Mice stock number:000686)

FEATURE

SJL mice display a very high incidence of reticulum cell sarcomas resembling Hodgkin's disease by approximately one year of age. This strain is also characterized by extreme aggression in males And its susceptibility to experimental autoimmune encephalomyelitis (EAE) for multiple sclerosis research. SJL/J mice are homozygous for the dysferlin gene mutation (*Dys^{fim}*), resulting in progressive muscular dystrophy1). SJL mice, fed an atherogenic diet (1.25% cholesterol, 0.5% cholic acid and 15% fat), fail to develop Atherosclerotic aortic lesions in contrast to several highly susceptible strains of mice.



RESEARCH APPLICATION

- High incidence of reticulum cell sarcomas resembling Hodgkin's disease (~one year of age) 2)
- Highly susceptible to experimental autoimmune encephalomyelitis (EAE), a model for multiple sclerosis3)
- Resistant to diet-induced atherosclerosis4)
- Extensive phenotypic and SNP data available at the Mouse Phenome Database (<http://phenome.jax.org/db/q?rtn=strains/details&stocknum=000686>) as well as historical information at Festing (<http://www.informatics.jax.org/external/festing/mouse/docs/SJL.shtml>)

ORIGIN

This strain was introduced from The Jackson Laboratory to Charles River Japan and started to supply in 2010. JAX® mice bred at Charles River Japan are genetically equivalent to those produced by The Jackson Laboratory.

COAT COLOR

albino

MHC HAPLOTYPE

H2 : s2



- Male extremely aggressive; fighting often fatal.
- Individual rearing is recommended.

- 1) Bittner et al. 1999, Nat Genet 23, 141-2; Vafiadaki et al. 2001, Neuroreport 12, 625-9
- 2) Murphy. 1963, Proc Am Assoc Cancer Res 4, 46
- 3) Dal Canto et al. 1995, Microsc Res Tech 32, 215-29
- 4) Nishina et al. 1993, Lipids 28, 599-605

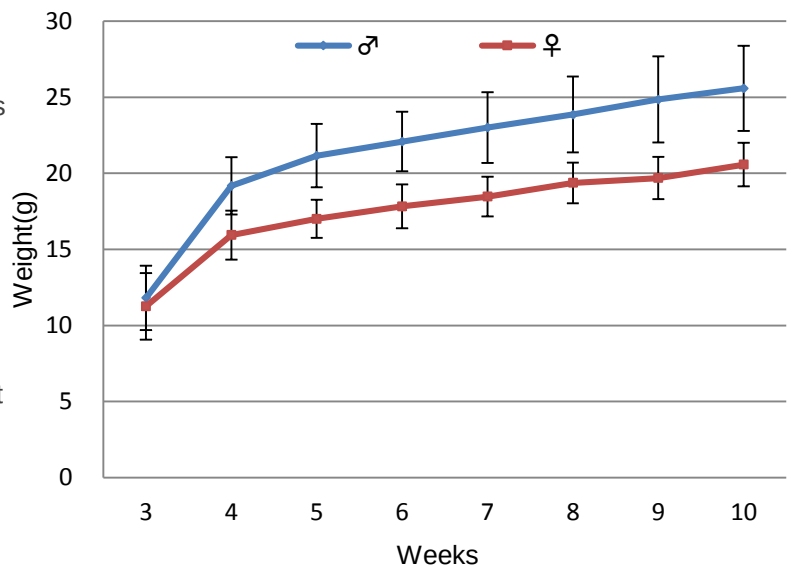
IMMUNODEFICIENT MODEL

Nomenclature NOD.CB17-*Prkdc*^{scid} /J Common Name NOD SCID
(JAX® Mice stock number:001303)

FEATURE

- Severe deficiency in both adaptive and innate Immunity due to the combined effects of the NOD background and the spontaneous severe combined immune deficiency (*scid*) mutation in the DNA activated protein kinase catalytic polypeptide (*Prkdc*) gene, resulting in lack of functional T and B cells (no detectable IgM, IgG1, IgG2a, IgG2b, IgG3, or IgA) and low NK cell activity ¹⁾
- Better engraftment of human lymphoid Malignancies than nude mice (*Foxn1* deficient), Rag1 deficient mice or scid mutant mice on other genetic backgrounds²⁾
- High incidence of thymic lymphomas leading to mean lifespan of 8.5 months under SPF conditions³⁾
- Breeding at Isolator
- Extensive phenotypic and SNP data available at the Mouse Phenome Database

<http://phenome.jax.org/db/q?rtn=strains/details&stocknum=001303>



RESEARCH APPLICATION

- Allogeneic and xenogeneic grafts
- Oncology
- Immunology



The Jackson Laboratory Genetic Stability Program is covered under U.S. Patent numbers 7592501 and 8110721; a license from JAX is required to practice under this patent.

ORIGIN

This strain was introduced from The Jackson Laboratory to Charles River Japan and started to supply in 2006.

JAX® Mice bred at Charles River Japan are genetically equivalent to those produced by The Jackson Laboratory.

This strain is carried on "Genetic Stability Program" The information of "Genetic Stability Program" is available at <https://www.jax.org/jax-mice-and-services/find-and-order-jax-mice/why-jax-mice/patented-genetic-stability-program>

COAT COLOR

albino

MHC HAPLOTYPE

H2 : g7

- 1) Shultz et al. 2007. *Nat Rev Immunol* 7:118-30
- 2) Hudson et al. 1998. *Leukemia* 12:2029-33
- 3) Shultz et al. 2007. *Nat Rev Immunol* 7:118-30



IMMUNODEFICIENT MODEL

Nomenclature NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ

Common Name NSG (JAX® Mice stock number:005557)

FEATURE

- Commonly known as NSG or NOD scid gamma ([Shultz et al. 2005](#))
- Severe defects in innate and adaptive immunity
- Lacks mature T, B, and functional NK cells
- Deficient in signaling of multiple cytokines (IL2, IL4, IL7, IL9, IL15 and IL21), resulting in significantly improved engraftment of human tissues, hematopoietic stem cells, and peripheral blood mononuclear cells
- Resistant to lymphoma, allowing for long-term experiments
- Capable of maintaining a human tumor microenvironment after engraftment
- Low tolerance for irradiation <http://phenome.jax.org/db/q?rtn=strains/details&stocknum=005557>
- Bred in Isolators

RESEARCH APPLICATION

- Cancer/oncology¹⁾
- Humanized mice & hematopoiesis
- HIV & infectious disease
- Stem cells research
- PDX models



ORIGIN

This strain was introduced from The Jackson Laboratory to Charles River Japan and started to supply in 2012.

JAX® Mice bred at Charles River Japan are genetically equivalent to those produced by The Jackson Laboratory.

This strain is carried on "Genetic Stability Program" The information of "Genetic Stability Program" is available at <https://www.jax.org/jax-mice-and-services/find-and-order-jax-mice/why-jax-mice/patented-genetic-stability-program>



The Jackson Laboratory Genetic Stability Program is covered under U.S. Patent numbers 7592501 and 8110721; a license from JAX is required to practice under this patent.

COAT COLOR

Albino

MHC HAPLOTYPE

H2 : g7

【License (JPYEN)】 19,800*

*: Tax-free.

1) Shultz LD 2005, J Immunol 174(10):6477-89.

【CAUTION】

The breeding colonies for NSG provide mice for both large and small orders and fluctuate in size depending on current demand for each strain. We treat orders for these Strains as custom orders.

DISEASE MODEL

Nomenclature B6.Cg-*Lep^{ob}/J*
(JAX® Mice stock number:000632)

Common Name ob

FEATURE

- Recognizably obese when about four weeks old; gains weight even on regular chow ¹⁾
- Diabetes phenotypes: transiently hyperglycemic, glucose intolerant, hyperinsulinemic, and severely insulin resistant ^{1,2)}
- High serum triglyceride levels ¹⁾
- High LDL and VLDL cholesterol levels ³⁾
- Impaired thermoregulation ⁴⁾
- Impaired wound healing ⁵⁾
- All females and most males are sterile ⁶⁾
- Extensive phenotypic and SNP data available at the Mouse Phenome Database
(<http://phenome.jax.org/db/q?rtn=strains/details&stocknum=000632>)

RESEACH APPLICATION

- Obesity, thermoregulation, type 2 diabetes, wound healing

ORIGIN

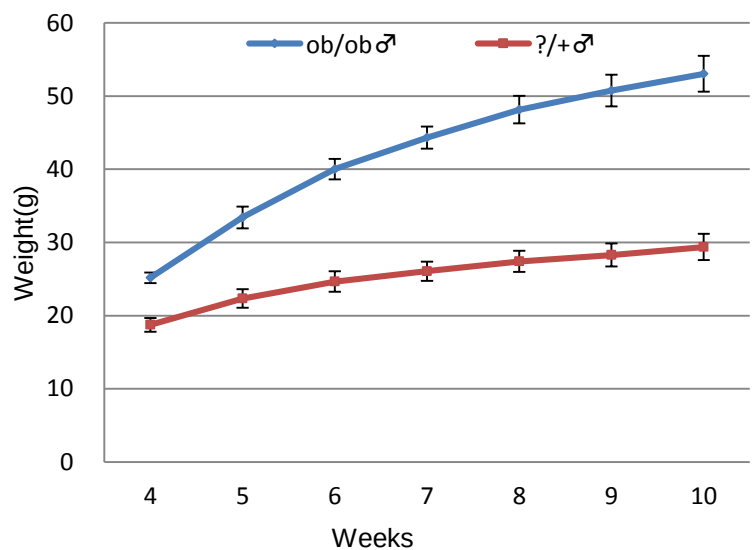
This strain was introduced from The Jackson Laboratory to Charles River Japan and started to supply in 2002. JAX® Mice bred at Charles River Japan are genetically equivalent to those produced by The Jackson Laboratory.

COAT COLOR

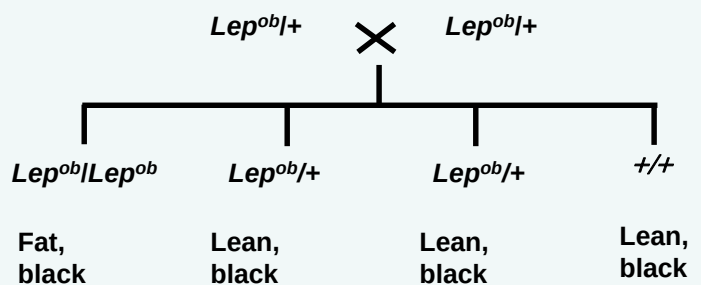
Black

MHC HAPLOTYPE

H2 : b



Mating Chart



Breeding Process

- Bred by heterozygous (*Lep^{ob}/+*) mice due to sterility of homozygous (*Lep^{ob}/Lep^{ob}*) mice.
- Coat color of both heterozygotes (*Lep^{ob}/+*) mice and homozygotes (*Lep^{ob}/Lep^{ob}*) mice are black.
- To Identify of lean (*Lep^{ob}/+*) and lean(*+/+*) is by PCR.

- 1) Dong et al. 2006, J Endocrinol 188, 25-36
- 2) Chua et al. 2002, Diabetologia 45, 976-90
- 3) Nishina et al. 1994, Metabolism 43, 549-53
- 4) Kamper et al. 2005, Diabetes 54, 1543-51
- 5) Charlton. 1984, J Exp Physiol 69, 655-76
- 6) Sakkou et al. 2007, Cell Metab 5, 450-63

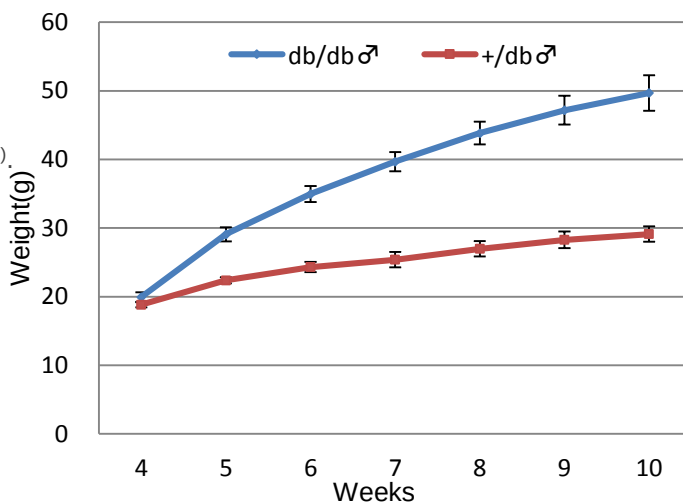
DISEASE MODEL

Nomenclature BKS.Cg-Dock7^m + / + Lepr^{db}/J

Common Name db (JAX® Mice stock number:000642)

FEATURE

- Mice homozygous for the diabetes spontaneous mutation (Lepr^{db}) become identifiably obese around three to four weeks of age¹⁾.
- Elevations of plasma insulin begin at 10 to 14 days of age²⁾ and of blood glucose at four to eight weeks¹⁾.
- Homozygous mutant mice are polyphagic³⁾, polydipsic, and polyuric.
- Diabetes phenotypes: hyperinsulinemia, insulin resistance, hyperglycemia, glucose intolerance, abnormal islet morphology⁴⁾
- Average lifespan is 10 months of age.
- Cardiovascular defects⁵⁾
- Delayed wound healing⁶⁾
- Abnormal lipid levels: high HDL, LDL, VLDL, and triglyceride levels⁷⁾
- Extensive phenotypic and SNP data available at the Mouse Phenome Database (<http://phenome.jax.org/db/q?rt= strains/details&stocknum=000642>)



RESEACH APPLICATION

- Type 2 diabetes, Obesity, Wound healing

ORIGIN

This strain was introduced from The Jackson Laboratory to Charles River Japan and started to supply in 2010.

JAX® mice bred at Charles River Japan are genetically equivalent to those produced by The Jackson Laboratory.

COAT COLOR

Black : Homozygous Black : Heterozygotes
Misty(Grey) : Wild-type

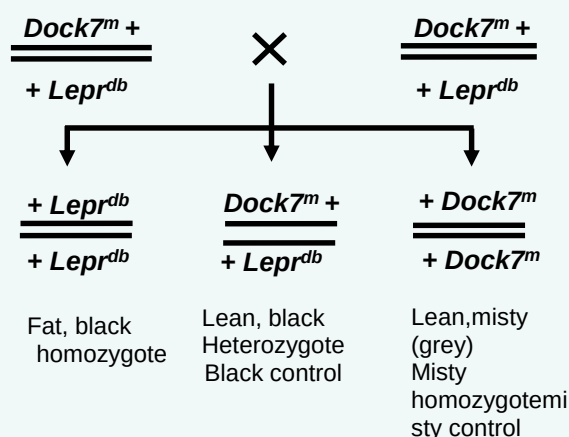
MHC HAPLOTYPE H2 : d

ORIGIN

This strain was introduced from The Jackson Laboratory to Charles River Japan and started to supply in 2010.



Mating Chart



1) Hummel et al. 1966, Science 153, 1127-8; Greer et al. 2006, Am J Physiol Heart Circ Physiol 290, H146-53

2) Coleman, D. L. and K. P. Hummel. 1974, Diabetologia 10 Suppl, 607-10

3) Uchida et al. 2005, Nat Med 11, 175-82

4) Hummel et al. 1966, Science 153, 1127-8; Uchida et al. 2005, Nat Med 11, 175-82; Yamauchi et al. 2007, Nat Med 13, 332-39

5) Raizada et al. 1980, J Biol Chem 255, 9149-55; Robertson and Sima. 1980, Diabetes 29, 60-7

6) Greer et al. 2006, Am J Physiol Heart Circ Physiol 290, H146-53; How et al. 2006, Diabetes 55, 466-73

7) Werner et al. 1994, J Invest Dermatol 103, 469-73; Brem et al. 2007, Exp Gerontol 42, 523-31

8) Nishina et al. 1994, Metabolism 43(5), 549-53

DISEASE MODEL

Nomenclature B6.129P2-Apoe^{tm1Unc}/J

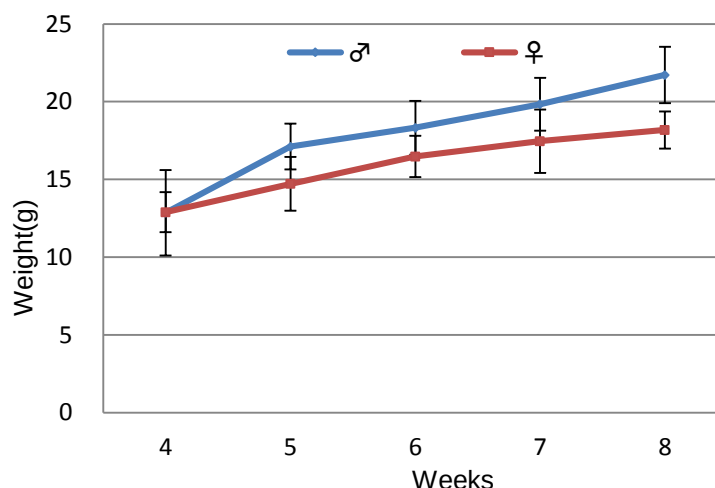
Common Name ApoEKO apoe null (JAX® Mice stock number:002052)

FEATURE

- Mice homozygous for the *Apoe*^{tm1Unc} mutation show a marked increase in total plasma cholesterol levels that are unaffected by age or sex.
- Fatty streaks in the proximal aorta are found at 3 months of age.
- The lesions increase with age and progress to lesions with less lipid but more elongated cells, typical of a more advanced stage of pre-atherosclerotic lesion.¹⁾
- Extensive phenotypic and SNP data available at the Mouse Phenome Database (<http://phenome.jax.org/db/q?rtn=strains/details&stocknum=002052>)
- Bred in Isolators

RESEACH APPLICATION

- Cardiovascular Research
- Dietary arteriosclerosis
- Hypercholesterolemia
- Hypertriglyceridemia
- Dietary obesity
- Memory impairment
- Alzheimer's disease



ORIGIN

This strain was introduced from The Jackson Laboratory to Charles River Japan and started to supply in 2015.

JAX® mice bred at Charles River Japan are genetically equivalent to those produced by The Jackson Laboratory.

This strain is carried on “Genetic Stability Program” The information of “Genetic Stability Program” is available at <https://www.jax.org/jax-mice-and-services/find-and-order-jax-mice/why-jax-mice/patented-genetic-stability-program>

COAT COLOR

Black



The Jackson Laboratory Genetic Stability Program is covered under U.S. Patent numbers 7592501 and 8110721; a license from JAX is required to practice under this patent.

MHC HAPLOTYPE

H2 : b



- 1) Ma et al. Clin Immunol. 2008 May;127(2):168-75
- 2) Wang et al. Am. J. Physiol. Heart Circ. Physiol. 278: H428-H434, 2000
- 3) MOGHADASIAN ET AL. The FASEB Journal Vol. 15 December 2001
- 4) Hazel Y. Stevens et al. Disease Models & Mechanisms 1, 175-181 (2008)
- 5) CRAIG J. HARTLEY et.al. Am J Physiol Heart Circ Physiol 279: H2326-H2334, 2000.
- 6) Zhenyu Qin et. al. The FASEB Journal express article 10. December 21, 2005
- 7) CRAIG J. HARTLEY et.al. Am J Physiol Heart Circ Physiol 279: H2326-H2334, 2000.
- 8) Hazel Y. Stevens st. al. Disease Models & Mechanisms 1, 175-181 (2008)
- 9) Yunkai Guo et. al. Hearing Research, Vol. , Issues 1-2, P54-67, 5
- 10) Christal G. Young et. al. Am J Physiol Heart Circ Physiol 288: H1683-H1689, 2005.

Pre-conditioning Mice

Trade Name **C57BL/6J-Aged** Common Name **B6J Aged**

RESEARCH APPLICATION

Aging Longevity Cardiovascular
Diabetes and Obesity Immunology Cancer

COAT COLOR

Black

MHC HAPLOTYPE

H2 : b

SPECIFICATION

- Using C57BL/6J Male • Up to 78 weeks of age
- Delivering animals may show several abnormal appearances due to aging (ex. Alopecia, Injuries of body surface, tail and ears, and Abnormal eyes)

Trade Name **C57BL/6J-DIO (C57BL/6J Diet induced obesity)**

Common Name **B6J DIO**

RESEARCH APPLICATION

Diabetes ^{1), 2) 3)}

Obesity ^{1), 2) 3)}

COAT COLOR

Black

MHC HAPLOTYPE

H2 : b

SPECIFICATION

- C57BL/6J Male
- Fed purified diet "D12492" (60kcal % fat) supplied by RESEARCH DIETS, Inc.
- Mice may appear glossy due to the diet.

1) Tao Jiang 2005 J. Biological Chemistry 208 (37) 32317-32325

2) Xing Xian 2008 Yu Am J Physiol Endocrinol Metab 294 W530-E539

3) Youn-Soo Cha 2004 J Med Food 422-429

Age in Weeks	Time of Feeding (Weeks)
6	2
7	3
8	4
9	5
10	6
11	7
12	8
13	9
14	10
15	11
16	12
17	13
18	14

Trade Name **C57BL/6J-NASH (C57BL/6J Diet induced Nonalcoholic steatohepatitis)**

Common Name **B6J NASH**

RESEARCH APPLICATION

NASH ^{1), 2) 3)}

COAT COLOR

Black

MHC HAPLOTYPE

H2 : b

SPECIFICATION

- C57BL/6J Male
- Fed purified diet "A06071302" (CDAHFD60) supplied by RESEARCH DIETS, Inc.
- Mice may appear glossy due to the diet.

1) Int. J. Exp. Pathol. (2013), 94(2):93-103

2) 日薬理誌(Folia Pharmacol. Jpn.)144, 69-74 (2014)

3) Suresh Giri et al., Keystone Symposia Conference, March 212-27, 2015 at Whistler, British Columbia, Canada

Age in Weeks	Time of Feeding (Weeks)
7	1
8	2
9	3
10	4
11	5
12	6
13	7
14	8
15	9
16	10
17	11
18	12

Evaluation data is available on our web site
<http://www.crj.co.jp>

JAX® MICE & SERVICE

PDX (Patient Derived Xenograft Model)

 Product Name **PDX Live™, JAX™-PDX**

 Common Name **PDX Live, JAX-PDX**

 Nomenclature: NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ (JAX® Mice stock number 5557), Common Name: NSG

- We are pleased to announce that the Jackson Laboratory (hereafter JAX®) and Charles River Laboratories Japan signed a contract for the supply of “PDX Live™ Tumor model” and “JAX™-PDX”.
- More than 450 unique PDX oncology tumors from both treatment naive and resistant patients have been engrafted into highly immunodeficient NSG™ mouse strain by JAX® and these models are now available under the contract. With this supply of JAX™-PDX mice, our valued customers can expect unprecedented new treatment effect on cancer patients.
- JAX® prepares the PDX Live™ mice transplanted with limited patient-derived tumors before receiving orders in order to ship them in a short period of time (within 6-12 weeks after receiving orders).
- At first, in this stock, you look for the availability of the model transplanted with the tumor which you wish to use.
- If it is not available, you look for that tumor in JAX™-PDX, and ask us to make the model bearing the tumor.

Common Name	PDX Live	JAX-PDX
Application	Drug Screening	
Restriction	Transplant, passage, proliferation, storage in your facilities or third party facilities, and provision, share, sale to third party are prohibited	
Use mouse strain	6~8weeks of age, Female, NSG	
Delivery time	6~12 weeks after firm ordered (Depend on each tumor)	3~5months after firm ordered (Depend on each tumor)
Order condition	Order received from 1 animal 5-6 animals / tumor constantly maintained	15 or more (After receiving orders frozen tumor will be melted and transplanted)
Animal quantity at delivery	Deliver animals up to 1.25 times the order quantity	

Note:

Since NSG mice are LMO (Living Modified Organism), customers should get the use permission of NSG from each institution before ordering.

hu-NSG (Humanized NSG mouse)

 Product Name **PDX Live™, JAX™-PDX**

 Common Name **PDX Live, JAX-PDX**

 Nomenclature: NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ (JAX® Mice stock number 5557), Common Name: NSG

- We are also pleased to announce that the Jackson Laboratory (hereafter JAX®) and Charles River Laboratories Japan signed a contract for the supply of “hu-NSG™ mice” which has human immune system in their body, being expected to be innovative research tool for Cancer, Infection, Allergy, Inflammation, Graft versus Host reaction and so on.
- JAX® has two kinds of hu-NSG™ mice, one is NSG mouse that is injected human cord blood cells (CD34+), another one is NSG mouse injected with human PBMC. Both of them have been already provided in the U.S. market.

Common Name	hu-CD34+	hu-PBMC
Human Cytokine Expression	N/A	
Benefit	A functional human immune system.	Enables short-term studies requiring human T cells
	T cell-dependent inflammatory responses.	Strong effector and memory T cell function
	No donor cell immune reactivity towards host.	T cell-driven GVHD
Life span	Long-term >12 months	Short-term <3months
Engraftment Stability	Stable through the lifespan of the mouse	Unstable because of the GVHD
Immune Development	B, T (MHC-restricted CD4 and CD8), Monocytes, Macrophages, Dendritic cells.	T cells (HLA-restricted CD4 and CD8), Natural Killer cells

Note:

Since NSG mice are LMO (Living Modified Organism), customers should get the use permission of NSG from each institution before ordering.

GENETICALLY ENGINEERED MODEL SERVICE



Do you have sufficient space or resources for colony management of genetically engineered mice and rats in your facility?

Charles River provides a full-service rodent colony management program based on your needs.

<Features of Service>

1. Isolator operation

Reduces the risk of contamination in both microbiologic and genetic.

- Work as a buffer facility since it is able to accept animals with various health status. Good for quarantine and rederivation to protect your facility.
- Offer fully-customized services based on your needs.



2. Model creation service by CRISPR-Cas9 technology

We have started Model creation services under collaborative alliance with Tsukuba University. CRISPR-Cas9 technology enables us to make models in a short period. After receiving purchase orders, models will be created at Tsukuba University. Charles River has a license to use the technology developed by Broad institutes (Cambridge, MA, USA). Under this license, we are granted the right to use CRISPR-Cas9 based genome editing technology, and Tsukuba University is defined as our sub-licensee in this license agreement. Models created in Tsukuba University through Charles River can be used for customers' own researches.

3. JAX mice and other rodents resources around the world

Mice resources distributed by The Jackson laboratory (TJL) is available in our breeding services. TJL has more than 7,000 strains ready for distribution. It consists of various human disease models, as well as research tools such as Cre mice or Reporter mice which promise to facilitate your researches. As the TJL's distributor in Japan, Charles River Laboratories Japan provides mice models and services exclusively.

In addition to JAX mice, we also offer import service for animal models produced in Charles River group across the world.

4. Internet Colony Management (ICM) system

We successfully digitized colony management by developing customized web/mobile application, and it is also useful as customer interface.

ICM™ is custom web/mobile application developed by Charles River for contract breeding services. Various data can be inputted into the system, with easy access for customers through the internet. We provides this application free-of-charge for service users.

<Other optional services>

We offer various other optional services as bellow. Please feel free to contact us.

Example

- | | |
|---|--|
| ■ GTS (Genetic testing services) | ■ MAX-BAX (SNPs analysis service for speed congenic) |
| ■ Frozen embryos for sale (Frozen embryos of domestically produced strains excepting JAX mice) | |
| ■ Quarantine and Rederivation | ■ Making Frozen stocks (embryo or sperm) and storage services |



HEALTH MONITORING SERVICES 1



Mouse and rat HM sets require live animals for testing, and PRIA sets use fecal pellets and oral swabs. Body swabs of mice or rats are required if the Ectoparasite PCR is added to the PRIA set.

Mouse Health Monitoring

Agents	Mouse HM Set				Mouse PRIA Set* ²			
	Method	Mini Set	Standard Set	ID HM Set* ¹	Method	Mini Set	Basic Set	ID Set
<i>Corynebacterium kutscheri</i>	Microbiology		■	■	PCR		■	■
<i>Salmonella</i> spp.		■	■	■		■	■	■
<i>Pasteurella pneumotropica</i>				■				■
<i>Pseudomonas aeruginosa</i>				■				■
<i>Staphylococcus aureus</i>				■				■
<i>Citrobacter rodentium</i>				■				■
MPUL	Serology	■	□	□		■	■	■
CPIL			■	■			■	■
MHV		■	■	■		■	■	■
SEND		■	■	■		■	■	■
ECRTO		■	■	■		■	■	■
LCMV		■	■	■		■	■	■
<i>Helicobacter hepaticus</i>	PCR			■				■
<i>Helicobacter bilis</i>				■				■
<i>Pneumocystis</i> spp.				■				
Ectoparasite	Parasitology (microscopic examination)		■	■		Parasitology Set (Additional charge will be applied) -Ectoparasite (<i>Myobia</i> , <i>Myocoptes</i> , <i>Radfordia</i>) -Pinworm (<i>Aspicularis</i> , <i>Syphacia</i>) -Endoparasite (<i>Giardia</i> , <i>Spironucleus</i>)		
Pinworm			■	■				
Endoparasite			■	■				

□: microbiological examination will be done, in addition to serology

Rat Health Monitoring

Agents	Rat HM Set				Rat PRIA Set* ²			
	Method	Mini Set	Standard Set	ID HM Set* ¹	Method	Mini Set	Basic Set	ID Set
<i>Corynebacterium kutscheri</i>	Microbiology		■	■	PCR		■	■
<i>Salmonella</i> spp.		■	■	■		■	■	■
<i>Bordetella bronchiseptica</i>			■	■			■	■
<i>Pasteurella pneumotropica</i>				■				■
<i>Pseudomonas aeruginosa</i>				■				■
<i>Staphylococcus aureus</i>				■				■
<i>Streptococcus pneumoniae</i>				■				■
MPUL	Serology	■	□	□		■	■	■
CPIL			■	■			■	■
SEND		■	■	■		■	■	■
SDAV		■	■	■		■	■	■
HANT		■	■	■		■	■	■
<i>Pneumocystis</i> spp.	PCR			■				
Ectoparasite	Parasitology (microscopic examination)		■	■		Parasitology Set (Additional charge will be applied) -Ectoparasite (<i>Myobia</i> , <i>Myocoptes</i> , <i>Radfordia</i>) -Pinworm (<i>Aspicularis</i> , <i>Syphacia</i>) -Endoparasite (<i>Giardia</i> , <i>Spironucleus</i>)		
Pinworm			■	■				
Endoparasite			■	■				

□: microbiological examination will be done, in addition to serology

PCR Agents*³

The following PCR panels can be added to PRIA standard or HM sets. Also a request of single agent PCR is accepted*⁴.

Corynebacterium bovis, CARB, CPIL, *Helicobacter bilis*, *Helicobacter hepaticus*, MPUL, *Pasteurella pneumotropica*, *Pneumocystis* spp.*⁵, *Streptobacillus moniliformis*, MHV, MNV, EDIM, TMEV, *Entamoeba* spp., *Giardia* spp., *Cryptosporidium* spp., *Spironucleus muris*, *Tritrichomonas* spp., *Aspicularis tetraptera*, *Syphacia muris*, *Syphacia obvelata*

*1: If the serology panels of the ID HM sets for mice or rats, the results of *Helicobacter* spp., *Streptobacillus moniliformis*, β-hemolytic *Streptococcus*, *Streptococcus pneumoniae* (for mouse HM set only) will be reported to meet the FELASA's annual recommended health monitoring panels.

*2: Other than fecal pellets and oral swabs, Exhaust Air Dusts (EAD) are also accepted for PRIA standard set.

*3: An agent, which is included in the PRIA sets, can be requested as single agent PCR.

*4: The prices of the PCR are different when agents are added to PRIA set and when single agent PCR is ordered.

*5: The lung samples will be required for the *Pneumocystis* spp. PCR.

HEALTH MONITORING SERVICES 2



Serology

Serology tests require serum or plasma samples of mice or rats.

Mouse	Tracking plus	MPV, MVM, MHV, MNV, TMEV, EDIM, SEND, REO, PVM, MPUL, CPIL
	Assessment plus	MPV, MVM, MHV, MNV, TMEV, EDIM, SEND, REO, PVM, MPUL, CPIL, ECTRO, LCMV, MAV, K, POLY, MCMV, MTLV, CARB, ECUN, HANT
	FelasaA	MPV, MVM, MHV, MNV, TMEV, EDIM, SEND, REO, PVM, MPUL, CPIL, ECTRO, LCMV, MAV
Rat	Tracking plus	SEND, REO, PVM, MPUL, RPV, H-1, KRV, RMV, SDAV, RTV, CPIL, PCAR
	Assessment plus	SEND, REO, PVM, MPUL, RPV, H-1, KRV, RMV, SDAV, RTV, CPIL, PCAR, MAV, CARB, HANT, ECUN, LCMV
	FelasaA	SEND, REO, PVM, MPUL, RPV, H-1, KRV, RMV, SDAV, RTV, CPIL, PCAR, MAV, CARB, HANT

Zebrafish Health Monitoring (PCR)

Agents	Basic Set	Mycobacteria Set	Survey Set	Survey Plus Set
ISKNV			■	■
IPNV				■
<i>Mycobacterium abscessus</i>		■	■	■
<i>Mycobacterium chelonae</i>		■	■	■
<i>Mycobacterium fortuitum</i>		■	■	■
<i>Mycobacterium haemophilum</i>		■	■	■
<i>Mycobacterium marinum</i>	■	■	■	■
<i>Mycobacterium peregrinum</i>		■	■	■
<i>Edwardsiella ichtaluri</i>	■		■	■
<i>Flavobacterium columnare</i>			■	■
<i>Aeromonas hydrophilia</i>			■	■
<i>Saprolegnia brachydans</i>				■
<i>Pseudoloma neurophilia</i>	■		■	■
<i>Pleistophora hyphessobryconis</i>	■		■	■
<i>Piscinoordinium pilulare</i>			■	■
<i>Ichthyophthirius multifiliis</i>			■	■
<i>Pseudocapillaria tomentosa</i>	■		■	■

ISKNV=Infectious spleen and kidney necrosis virus, IPNV=Infectious Pancreatic Necrosis Virus

Abbreviated word

MPV	Mouse Parvovirus	K	Mouse Pneumonitis Virus
MVM	Minute Virus of Mice	POLY	Polyoma Virus
MHV	Mouse hepatitis Virus	MCMV	Mouse Cytomegalovirus
MNV	Murine Norovirus	MTLV	Mouse Thymic Virus
TMEV	Theiler's Murine Encephalomyelitis Virus	CARB	Cilia-associated Respiratory Bacillus
EDIM	Epizootic Diarrhea Infant Mice Virus	ECUN	<i>Encephalitozoon cuniculi</i>
SEND	Sendi Virus	HANT	Hantavirus
REO	Reovirus	RPV	Rat Parvovirus
PVM	Pneumonia Virus of Mice	H-1	Toolan's H-1 Virus
MPUL	<i>Mycoplasma pulmonis</i>	KRV	Kilham Rat Virus
CPIL	<i>Clostridium piliformis</i>	RMV	Rat Minute Virus
ECTRO	Ectromelia Virus	SDAV	Sialodacryoadentitis Virus
LCMV	Lymphatic Choriomeningitis Virus	RTV	Rat Theilovirus
MAV	Mouse Adenovirus (type 1 & 2)	PCAR	<i>Pneumocystis carinii</i>

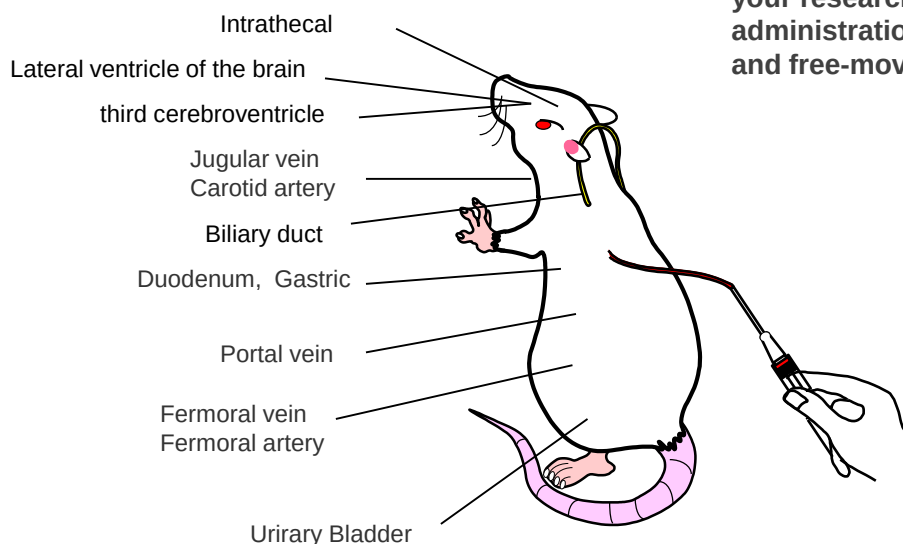
Non-Clinical Research Use Only: Do NOT use the Health Monitoring results for medication or diagnose clinical symptoms.

SURGICAL SERVICE / BIOMEDICAL MATERIALS

Charles River Japan offer various surgical service on rats and mice.
Further, we offer various biomedical materials including serum, plasma, exenterate organs.

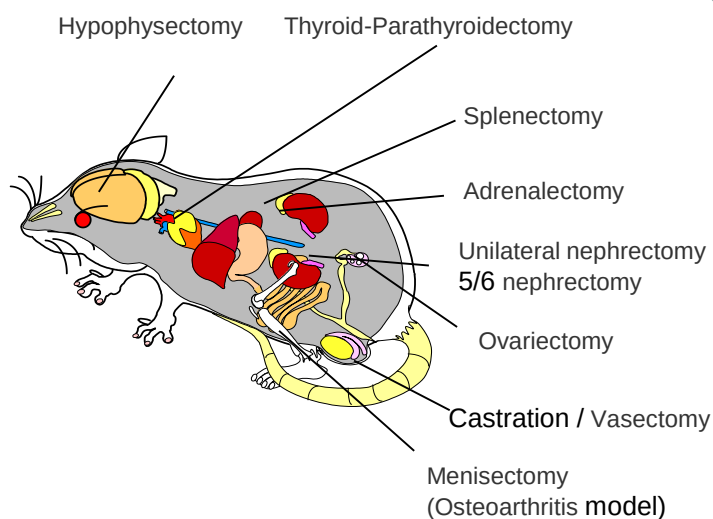
Cather Procedures

We are pleased to arrange catheterized animals to meet your research purpose like administration, blood sampling and free-moving study.



Soft Tissue Procedures

Please contact us if you require another operative procedure .
We are pleased to have collaborative research with customers.



Customer Support Center (Call Center)
 INNOTECH Bldg 11F
 3-17-6 Shin-Yokohama, Kohoku-ku, Yokohama-shi, Kanagawa
 222-0033
 Phone : 045-474-9350
 FAX : 045-474-9351
 Email : web_order@crl.com

General Terms & Conditions of Sale (“Terms and Conditions”)

Charles River Laboratories, Inc. and its affiliates (“**Charles River**”) will provide the products (“**Products**”) and services (“**Services**”) described in the Charles River invoice, quotation, protocol, or statement of work as applicable (“**SOW**”) and Charles River’s customer (“**Customer**”) will purchase the Products and Services pursuant to the specifications contained in the SOW and in accordance with these Terms and Conditions. These Terms and Conditions will also apply to all future purchases of Products and Services by Customer.

1.Binding Character

All sales and/or purchases of Products and Services are (a) governed by these Terms and Conditions and (b) made expressly conditioned upon Customer’s acceptance of these Terms and Conditions.

Customer’s acceptance of delivery of Products or Services will be deemed agreement to the Terms and Conditions. No other document attempting to negate or otherwise modify the terms hereof, including any purchase order or request for proposal or any deviating or supplementing standard terms and conditions of Customer, will be binding upon Charles River unless expressly agreed to by Charles River in writing. Instead these Terms and Conditions, including any special terms and conditions set forth separately as supplemented by any applicable provisions of Applicable Law (defined below), shall exclusively govern the sale of Products and Services by Charles River. This also applies if Charles River delivers Products or provides Services despite being aware of conflicting or additional standard terms and conditions of Customer.

2.Provision of the Products and Conduct of the Services

Charles River will adhere to all laws, rules and regulations applicable to the provision of the Products and the conduct of the Services at the place of performance (“**Applicable Law**”). If an amendment to the SOW requires additional or different work on the part of Charles River, Charles River may agree to conduct such work and will be paid an amount mutually agreed to by the parties. Deviations from the SOW may be made in an emergency without Customer’s approval, provided that Charles River uses commercially reasonable efforts to obtain Customer’s verbal approval, which will be subsequently confirmed by Customer in writing. The parties acknowledge that during the course of performing the Services in accordance with the SOW, additional costs may be incurred by Charles River as a result of procedural changes, which do not amount to, or require a change in, the SOW, but which are deemed necessary by Charles River to successfully perform the Services, and which could not be foreseen at the time of the preparation of the SOW. If such procedural change occurs, Charles River will advise Customer prior to implementation and solicit Customer’s agreement as to the necessity and additional cost thereof. If Charles River is unable to contact Customer in advance, Customer agrees that in order to maintain the integrity of the Services, Charles River may proceed accordingly, and be entitled to recover such additional costs from Customer upon presentation of an explanation of such procedural changes and the necessity thereof.

3.Restrictions on Use and Breeding

Customer understands that Charles River engages in a comprehensive health monitoring, bioexclusion and quality control program. Customer agrees the results of this program only provide retrospective information relating to the timing and effectiveness of sampling and that Charles River’s program is not a substitute for customer’s own health monitoring and bioexclusion practices. Charles River does not warrant the Products will be free of infectious agents or other defects at time of delivery. Charles River will provide assistance for monitoring and testing to Customer upon written request subject to the availability of such assistance and Customer paying the standard fees for such assistance.

Products will be used by Customer in a safe manner and in accordance with all Applicable Laws. Customer agrees and will ensure that all animals purchased from Charles River, descendants of those animals derived by inbreeding or crossbreeding, including unmodified derivatives of those animals or their descendants (“**Models**”) will not be: (i) used for any purpose other than the internal research of Customer in compliance with Applicable Law, (ii) bred (for sale or otherwise) or provided to any third party for any use, or (iii) provided to any agent or other third party to provide breeding or other services, unless Charles River provides Customer with prior written authorization. For safety reasons, Customer will not, without the prior written consent of Charles River, return Products or shipping containers to Charles River.

The purchase of any Products conveys to Customer the non-transferable, non-sublicensable, non-exclusive right to internally use the Product and the components of the Products only in research conducted by Customer and specifically in accordance with the SOW. Customer cannot sell or otherwise transfer or make available to a third party the Products or their components or the Services for Commercial Purposes. “**Commercial Purposes**” means any activity for cash or other consideration including, but not limited to: (1) use of the Products or their components or materials made using the Products or their components in manufacturing, or to provide a service, information or data, or for clinical, therapeutic, diagnostic or prophylactic purposes or (2) resale of the Products or their components or materials made using the Product or its components, except by licensed distributors of Charles River, whether or not resold for use in research. The foregoing limitations are required by Charles River given the nature and sensitivity of the Products and Services provided by Charles River. To the extent that Charles River owns or controls (with the right to sublicense) patent rights or other intellectual property rights applicable to the Products or their intended use, those rights are licensed to Customer on a limited, revocable, non-exclusive, non-transferable and non-sublicensable basis only for the internal uses expressly permitted above and solely for the Products purchased. If Customer fails to comply with the foregoing limitations, in addition to any other remedies available to Charles River, the right of use granted under the preceding sentence will automatically terminate.

4.Compensation

Unless otherwise agreed to by the parties, prices will be as per the price list (if applicable, price of Models is based on highest weight range) on the day of delivery, and they do not include applicable taxes, packaging, insurance or shipment expenses. The price list may be reviewed by Charles River annually. Customer will pay Charles River as set forth in the SOW. All invoices are due and payable thirty (30) days from the date of the invoice without any deductions and Customer agrees to pay all invoices submitted. Customer will not withhold payment, assert a right of retention or set off any counterclaims unless Customer’s counterclaims have been finally adjudicated by a competent court or have been acknowledged by Charles River in writing. All amounts not paid by Customer when due will accrue interest from the applicable due date until paid, at a rate of the lower of 14.6% per annum and the highest rate permitted under Applicable Law. Charles River may also elect to cease or suspend the supply of the Products, any work on the Services or withhold required reports or other deliverables if Customer does not make payments when due and payable.

All applicable termination, delay or cancellation fees will be set forth in the SOW.

If in the judgment of Charles River, Customer’s financial condition is precarious or there has been a materially adverse change in Customer’s financial condition, Charles River will have the right to demand payment or other assurances which it deems adequate before providing any Products and Services.

General Terms & Conditions of Sale (“Terms and Conditions”)

5. Test Article

Customer will provide Charles River with sufficient amounts of compounds, materials, animals, substances, devices and protocols meeting relevant specifications, including health and genetic data (“**Test Articles**”) with which to perform the Services. Customer will provide Charles River with complete and accurate data to apprise Charles River of the identity, strength, purity, stability, composition or other characteristics, proper storage and safe handling requirements of the Test Articles, including a Material Safety Data Sheet or equivalent documentation. Customer will certify to Charles River that the methods of synthesis, fabrication, or derivation of the Test Article have been documented. All costs associated with shipping the Test Articles to Charles River will be the responsibility of Customer, and Charles River will not be responsible for any loss, damage or destruction of the Test Articles while in transit. All Test Articles and Products used in connection with the Services will remain the property of Customer.

6. Reports

Charles River will keep complete and accurate records of the status and progress of the Services if, and as required by, the SOW. Charles River will furnish a report or data containing information as specified in the SOW. All reports will be prepared in the standard format of Charles River.

Neither Charles River nor Customer will publish any report or data prepared for Customer by Charles River without the prior written consent of the other party, which will not be unreasonably withheld.

If Charles River provides electronic access to the data, records, reports and other documentation and Customer elects to use such electronic access, the use of such electronic access will be governed by Charles River's standard access terms and conditions which are available on request.

7. Inspections

Upon reasonable advance written notice and during regular business hours, Charles River will permit Customer to visit the Charles River facilities where the Services are performed to monitor Charles River's performance of the Services, in compliance with Charles River's biosecurity measures, taking into account Charles River's business requirements and ensuring an uninterrupted course of business at Charles River's premises.

Charles River will notify Customer as soon as practical in the event of any regulatory inspection of Charles River's facilities that directly impact the Services provided to Customer.

8. Ownership

Any inventions, techniques and intellectual property, technology, commercial and industrial secrets, regardless of whether patented or registered, for providing the Products or performing the Services are, and will remain, Charles River's exclusive property including, but not limited to, present and future documentation, scientific and technical data, test procedures and other information that is owned or licensed by Charles River and is not developed hereunder. Charles River will have the right to use concurrent control data as part of its general historical database. Any data, discoveries or inventions developed or generated, which directly relate to any information or materials provided by Customer hereunder including, without limitation, new data, uses, processes or compositions, will be the exclusive property of Customer. Charles River agrees to assist Customer in securing any patents, copyrights or other proprietary rights in such data, discoveries or inventions, and to perform all acts that may be reasonably required to vest in Customer all right, title and interest in such data, discoveries or inventions, and Charles River will be compensated at its standard rates for such assistance. All costs and expenses associated with establishing Customer's rights therein will be Customer's responsibility.

9. Archiving

All reports and supporting documentation resulting from the Services are Customer's property (“**Materials**”). Except as

otherwise set forth in the SOW, and if requested in writing by Customer, Charles River will retain the Materials for a period of one year following the date of any final report, or for such shorter period as may be required by Applicable Law. At the end of such period, Charles River will contact Customer to determine disposition of the Materials as follows: (a) extended storage of the Materials; (b) return of the Materials to Customer at Customer's expense or (c) disposal of Materials at Customer's expense. If Customer requests Charles River to continue to store the Materials and Charles River agrees, the cost for storage of the Materials will continue to be invoiced to Customer at Charles River's then current rates. If Customer fails to give such instructions, Charles River will notify Customer, and if instructions are not forthcoming within thirty (30) days of said notification, Charles River will have the option of continuing to store the Materials or returning the Materials to Customer at Customer's expense. Customer will be liable for storage charges until the Materials are returned to Customer. While the Materials are in transit to Customer, all risk of loss or exposure to the Materials will be borne by Customer.

If the Materials require special storage requirements, additional charges for storage will be assessed and invoiced to Customer. Invoices will be issued annually in advance and are due and payable upon receipt.

10. Warranties

Customer warrants that it owns all rights, title and interest in the Test Articles furnished to Charles River and the intellectual property related thereto, and that Charles River's use of the Test Articles does not infringe any third party rights.

Charles River warrants that the Products and Services will conform to the specifications contained in the SOW and Applicable Law. Charles River does not warrant or represent that the results of the Services will be acceptable to any regulatory or governmental agency to which they are presented nor that the results of the Services will enable Customer to further develop, market or otherwise exploit the Test Articles or any other product or service.

THE WARRANTY BY CHARLES RIVER SET FORTH HEREIN IS IN LIEU OF ANY AND ALL OTHER REPRESENTATIONS OR WARRANTIES, EXPRESS, IMPLIED OR STATUTORY INCLUDING, WITHOUT LIMITATION, ANY IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, SUITABILITY OF THE PRODUCTS AND SERVICES FOR CUSTOMER'S PURPOSES, IMPACT OF THE PRODUCTS AND SERVICES ON CUSTOMER'S OPERATIONS, OR NON-INFRINGEMENT OF A PATENT, TRADEMARK OR OTHER INTELLECTUAL PROPERTY RIGHT.

Any claim for breach of this warranty must be made in writing to Charles River within ten (10) business days after the Products are delivered or the completion of Services, after which time the Products or Services will be deemed finally accepted.

Risk of loss and title to the Products will pass to Customer once the Products leave Charles River's facility or are delivered to a common carrier, as applicable.

11. Limitation of Liability

Charles River will not be liable for penalties or liquidated damages or for special, indirect, consequential punitive, exemplary or incidental damages of any type or kind (including, without limitation, lost profits) regardless of whether any such losses or damages are characterized as arising from breach of contract, breach of warranty, tort, negligence, strict liability or otherwise, even if Charles River is advised of the possibility of such losses or damages, or if such losses or damages are foreseeable.

Charles River's liability, regardless of the form of action, will be limited to actual and foreseeable damages and will not exceed the total price paid for the Products or Services pursuant to which such liability arises. Charles River will not be liable for any damages arising from, or in connection with, any decision by Customer or any third party to further research, develop or market the Test Articles or any derivative or product or service related

General Terms & Conditions of Sale (“Terms and Conditions”)

thereto, or the use made of the Products, Services or Test Articles derivative or service related thereto.

Subject to the limitations set forth in this Section, if Charles River commits a breach of the warranty set forth above, Charles River's sole liability, and Customer's sole remedy will be for Charles River to replace the Products or issue a credit therefore, or conform the work or portion of the Services affected by the breach to the relevant specification.

12. Indemnities

Customer will defend, indemnify, save and hold harmless Charles River and its parent, subsidiaries and affiliates and their respective directors, officers, employees and agents from and against any claims, demands, suits, actions, causes of action, losses, damages, fines and liabilities, including reasonable professional fees (“**Claim**”) arising out of or in connection with or attributable to (a) the research, development, manufacture, distribution, use, sales or other disposition by Customer, or any distributor, collaborator, Customer, sublicense, representative or agent of Customer, of the Test Articles and/or any other substances upon which the Services were performed or any use made of the Products, or (b) any infringement of any third party's patent or other intellectual property rights or unauthorized use or misappropriation of its know-how or trade secrets, or (c) Customer's gross negligence or willful misconduct, or breach of this agreement or (d) personal injury related to contact with the Products during visits to Charles River's facilities or after delivery of the Products to Customer, and will pay any costs and damages which, by final judgement, after exhaustion of all reasonable appeals, may be assessed against them, provided that Customer is given written notice of the Claims within five (5) days of the date of notice to Charles River and is given information, reasonable assistance and sole authority to defend and/or settle the Claim.

13. Insurance

Each party will have insurance sufficient to cover its interest or potential liabilities hereunder including, but not limited to, worker's compensation, if applicable, and comprehensive general liability.

14. Confidentiality

In the course of providing the Products or performing the Services, Charles River and Customer may exchange proprietary and confidential information. The parties will identify, in writing, such information as confidential and/or proprietary. If a party intends to disclose confidential information to the other party orally, the disclosing party will (i) alert the other party of the confidential nature of the disclosure prior to the disclosure and (ii) provide written notice to the other party of the confidential nature and contents of such disclosure within ten (10) days of the original disclosure. Each party will use its commercially reasonable efforts to maintain such information in confidence and will employ reasonable and appropriate procedures to prevent its unauthorized publication or disclosure unless required by Applicable Law to disclose such information. Neither party will use the other party's proprietary and/or confidential information for any purpose other than in performance of this Agreement. The obligations of confidentiality set forth in this Section will survive termination or expiration of this Agreement for a period of five (5) years.

The confidentiality provisions in this Section will not apply to any part of such information, which (i) is known to the receiving party at the time it was obtained from the disclosing party; (ii) is acquired by receiving party from a third party, and such third party did not obtain such information directly or indirectly from the disclosing party under obligation not to disclose; (iii) is or becomes published or otherwise in the public domain other than by violation of this Agreement by the receiving party; (iv) is independently developed by the receiving party without reference to or reliance upon the information provided by the disclosing party; or (v) is required to be disclosed by the receiving party to comply with applicable laws or governmental regulations (for this (v), only with respect to such confidential information as so required to be disclosed); provided that the receiving party provides prompt written notice of such disclosure to the disclosing party and cooperates with the

disclosing party's reasonable and lawful actions to avoid and/or minimize the extent of such disclosure.

15. Termination

Unless otherwise specified in the SOW, Customer will have the right to terminate the SOW at any time without cause upon thirty (30) days prior written notice to Charles River. In the event of such termination, Charles River will be paid for all Products provided or Services rendered through the effective date of termination, together with any additional expenses incurred in connection with the shutdown of the Services including, without limitation, any irrevocably committed costs and any cancellation or termination fee set forth in the SOW.

Either party may terminate these Terms and Conditions or SOW, as applicable, at any time upon thirty (30) days prior written notice to the other party, for material breach of the Terms and Conditions by the other party if such breach is not remedied to the non-breaching party's reasonable satisfaction within the thirty (30) day notice period.

Upon termination, neither party will have any further obligations, except that (i) the liabilities accrued through the date of termination and (ii) the obligations which by their terms survive termination, including the applicable confidentiality, record keeping, regulatory compliance, intellectual property and indemnification provisions of these Terms and Conditions, will survive termination.

16. Force Majeure

Except with respect to the payment of any amount due hereunder, neither party will be considered in default of the performance of any obligation hereunder to the extent that the performance of such obligation is prevented or delayed by fire, flood, earthquake, hurricane, explosion, disease, contamination, strike, acts of terrorism, war, insurrection, embargo, government requirement, civil or military authority, animal activism, act of God, or any other event, occurrence or condition which is not caused, in whole or in part, by that party, and which is beyond the reasonable control of that party.

17. Governing Law and Dispute Resolution

These Terms and Conditions and any dispute arising from or in connection with the sale of the Products and/or Services are governed by, and will be construed in accordance with, the laws of Delaware, excluding the United Nations Convention on the International Sale of Goods and without regard to any choice of law principle that would dictate the application of the law of another jurisdiction.

The parties will attempt to resolve through negotiations any controversy, claim, or dispute arising out of or in connection with these Terms and Conditions or its validity. If the negotiations are not successful, the controversy, claim, or dispute will be submitted to third-party mediation upon terms reasonably acceptable to the parties. If such claim, controversy or dispute is not resolved through mediation, upon written demand of either party, the claim, controversy or dispute will be submitted to arbitration. Such arbitration will take place in Boston, Massachusetts, will be conducted in English, and will proceed in accordance with the United Nations Commission on International Trade Law Arbitration Rules in force from time to time. A record and transcript of the proceedings will be maintained. Any award will be made in writing and in reasonable detail, setting forth the findings of fact and conclusion of law supporting the award. The determination of a majority of the panel of arbitrators will be the decision of the arbitrators, which will be binding regardless of whether one of the parties fails or refuses to participate in the arbitration. The arbitrators will decide on the recovery of the costs of the arbitration, except expert and attorneys' fees.

18. Miscellaneous

All notices from one party to the other will be in writing. Notices will be sent by internet transmission, overnight courier, or certified mail, return receipt requested. All notices will be effective upon receipt. The business relationship of Charles River to Customer is that of

General Terms & Conditions of Sale (“Terms and Conditions”)

an independent contractor and not of a partnership, joint venture, employer, agent or any other kind of relationship.

These Terms and Conditions, and the rights and obligations hereunder, may not be assigned or transferred by either party without the prior written consent of the other party.

These Terms and Conditions, together with the SOW, set forth the entire agreement and understanding between the parties, superseding any and all previous statements, negotiations, documents, agreements and understandings, whether oral or written, as to the subject matter hereof.

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