charles river

RESEARCH MODELS

C57BL/6 Mice

Nomenclature: C57BL/6NCrl

Research Applications

- Metabolic Disease
- Oncology
- Immunology
- Cardiology
- Addiction
- Toxicology
- Transgenic Model Creation

Strain Origin

Developed by C.C. Little in 1921 from a mating of Miss Abbie Lathrop's stock that also gave rise to strains C57BR and C57L. Strains 6 and 10 separated about 1937. To The Jackson Laboratory from Hall in 1948. To NIH in 1951 from The Jackson Laboratory at F32. To Charles River in 1974 from NIH.

Coat Color

Black

Availability

North America, Europe, China, and Japan

Charles River Health Profiles for C57BL/6N

VAF/Plus® (SPF)

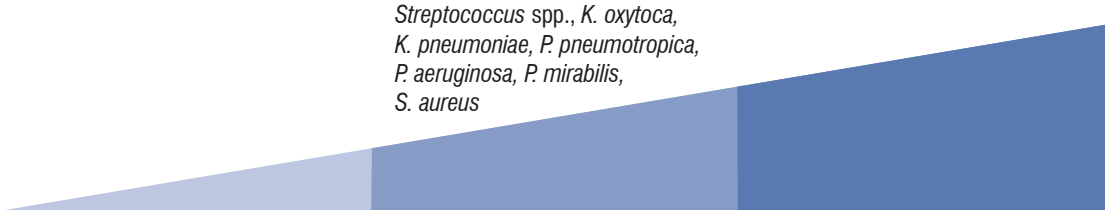
- Free of rodent pathogens

VAF/Elite® (SOPF)

- Free of all agents listed in the VAF / Plus® mouse profile, plus the opportunists Beta hemolytic *Streptococcus* spp., *K. oxytoca, K. pneumoniae, P. pneumotropica, P. aeruginosa, P. mirabilis, S. aureus*

Germ-Free (GF)

- Axenic
- Free of all microorganisms

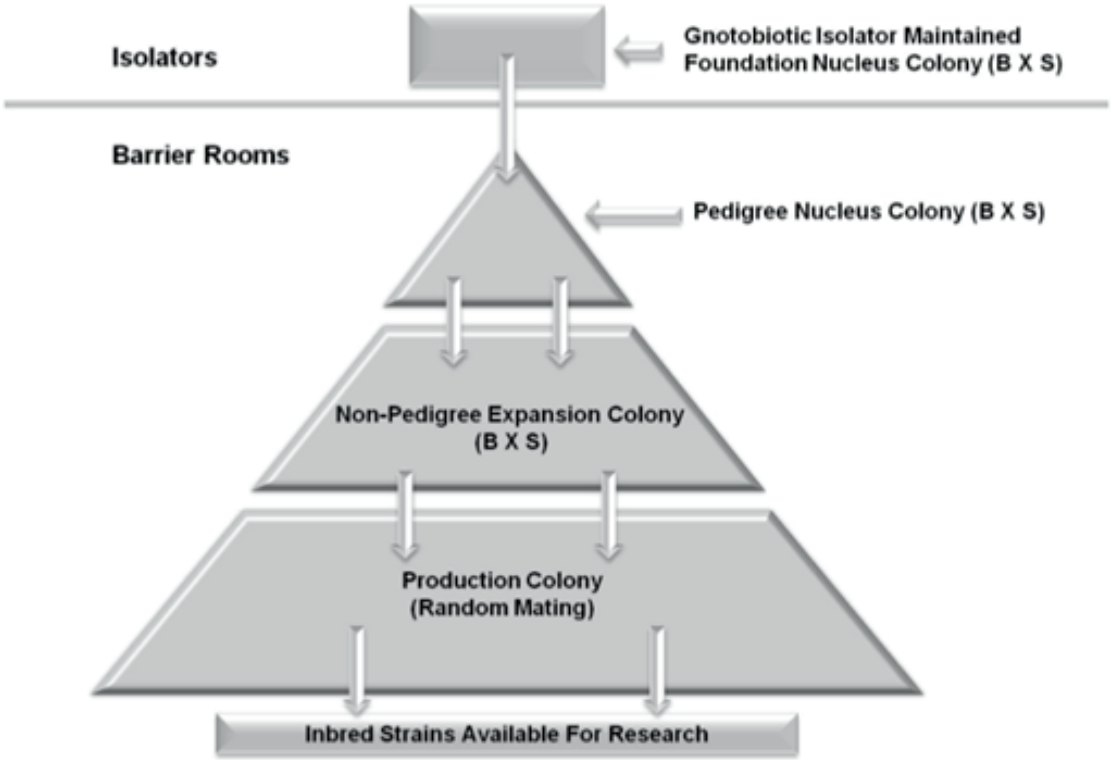


EVERY STEP OF THE WAY

Genetic Management of C57BL/6 Mouse Colony

Inbred strains are defined as animals produced by a minimum of 20 generations of brother-sister mating, traceable to a single founding pair. Individuals of an inbred strain are genetically uniform, also known as isogeneic. Inbred strains exhibit a high degree of uniformity in their inherited characteristics, or phenotypes, which include appearance, behavior, physiology, and responses to experimental treatments. Charles River uses our International Genetic Standardization (IGS) program coupled with a pyramid mating system designed to maintain authenticity and the highest possible levels of genetic uniformity. The pyramid mating system (see Figure 1) ensures that our C57BL/6 colonies are genetically identical within each strain (i.e., fundamentally free of genetic differences that could increase variation in experimental results). 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. The unidirectional flow of breed stock in this system helps to ensure that any genetic changes or mutations, which would be most likely to occur in the more populous expansion or production colonies than in the smaller nucleus colony, will "wash out" within a single generation. 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. For further information regarding Charles River's IGS program, please refer to the IGS Technical Sheet found at www.criver.com/info/rm.

Figure 1: Pyramid Mating System



Charles River C57BL/6NCrl Data

Clinical Chemistry

* North American colonies only/non-fasted values

+ Potassium levels reflect acidosis caused by CO_2 euthanasia

Age: 8-10 weeks

Screening Period:
January 2008 to November 2012

Diet: Purina 5L79 rodent chow

Euthanasia: CO_2

Temperature: 68-72°F

Bleed Route:
Cardiac puncture after euthanasia

Humidity: 40-60%

Analyzing Equipment:
Alfa Wassermann Ace Alera

C57BL/6NCrl*		ALB (g/dL)	ALK (U/L)	ALT (U/L)	AST (U/L)	TBIL (mg/dL)	BUN (mg/dL)	Ca (mg/dL)	CL (meq/L)	CHOL (mg/dL)
Male	Mean	3.2	195	68	131	0.3	14	11.0	117.0	114
95% Interval	Low	2.8	111	28	46	0.2	7	9.7	110.7	69
	High	3.8	275	129	392	0.6	28	12.5	129.8	169
	n	154	158	148	156	153	157	156	90	162
Female	Mean	3.4	228	57	133	0.3	14	11.1	118.4	104
95% Interval	Low	2.4	105	27	43	0.2	5	9.7	111.9	55
	High	4.3	370	195	397	0.6	26	12.3	134.0	164
	n	157	160	158	161	156	159	155	66	167

C57BL/6NCrl*		CRE (mg/dL)	GGT (U/L)	GLU (mg/dL)	P (mg/dL)	K+ (meq/L)	NA (meq/L)	TPR (g/dL)	TRIG (mg/dL)
Male	Mean	0.3	3	259	11.1	9.39	157.5	5.6	157
95% Interval	Low	0.2	0	172	7.9	7.59	145.2	4.8	67
	High	0.5	8	372	14.5	11.18	176.2	7.0	278
	n	141	53	158	159	90	90	156	161
Female	Mean	0.3	3	240	10.5	8.83	158.7	5.7	160
95% Interval	Low	0.2	0	177	7.3	7.27	147.5	4.8	75
	High	0.5	9	348	13.5	10.82	181.2	7.2	289
	n	141	49	159	161	66	66	159	167

Hematology

* North American colonies only/non-fasted values

Age: 8-10 weeks

Screening Period:
January 2008 to November 2012

Diet: Purina 5L79 rodent chow

Euthanasia: CO_2

Temperature: 68-72°F

Bleed Route:
Cardiac puncture after euthanasia

Humidity: 40-60%

Analyzing Equipment:
Drew Scientific HemaVet

C57BL/6NCrl*		WBC (K/µL)	RBC (M/µL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	RDW (%)
Male	Mean	8.90	9.48	14.2	46.6	49.2	14.8	30.2	17.9
95% Interval	Low	4.45	7.14	10.8	37.3	42.7	11.7	24.6	15.9
	High	13.96	12.20	19.2	62.0	56.0	16.3	34.9	20.3
	n	123	121	121	121	121	121	121	121
Female	Mean	8.44	9.24	13.8	45.4	49.2	15.0	30.7	17.9
95% Interval	Low	3.90	7.37	10.9	37.2	42.6	13.0	26.0	16.1
	High	13.94	11.50	18.1	58.0	55.6	16.8	35.9	21.1
	n	125	123	123	123	123	123	123	123

C57BL/6NCrl*		PLT (K/µL)	MPV (fL)	NEUT (K/µL)	LYMPH (K/µL)	MONO (K/µL)	EOS (K/µL)	BASO (K/µL)
Male	Mean	1347	5.0	1.44	6.87	0.41	0.14	0.03
95% Interval	Low	841	4.3	0.53	3.24	0.15	0.01	0.00
	High	2159	6.1	3.09	11.15	0.94	0.42	0.13
	n	115	115	123	123	123	123	123
Female	Mean	1167	4.9	1.19	6.71	0.36	0.15	0.03
95% Interval	Low	565	4.3	0.42	2.88	0.17	0.01	0.00
	High	1849	5.6	2.55	10.92	0.69	0.50	0.14
	n	117	117	125	125	125	125	125

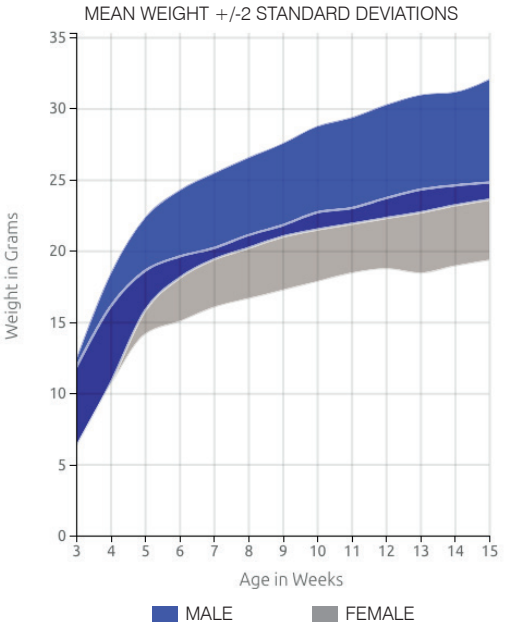
Strain Highlights

Important Features

- Global availability from Charles River through more than 20 breeding facilities
- Bred worldwide under the Charles River International Genetic Standardization (IGS) program
- VAF Plus®, VAF Elite®, and Germ-Free health status available
- Genetics managed under the IGS program

N Strain

- ES cells derived from C57BL/6N mice are used as the primary source for knocking out all mouse genes systematically by the International Knockout Mouse Consortium (Pettitt, S.J. et al. 2009)
- Enhanced ES cell growth and morphology vs. J substrain (Pettitt, S.J. et al. 2009)
- Lower incidence of vaginal septa vs. J substrain resulting in increased fertility among C57BL/6N mice (Gearhart, S. et al. 2004)
- Lower genetic variability among the N substrain vs. J substrain (Zurita, E. et al. 2010)
- Does not carry the Nnt deletion which is linked to glucose intolerance, reduced insulin secretion and redox abnormalities. (Freeman, H.C. et al. 2006)
- 29 SNPs differentiate the N substrain and the J substrain (<1% of the genotyped SNPs) (Pettitt, S.J. et al. 2009)
- More than 12,000 vectors and 9,000 conditional targeted alleles have been produced in highly germline-competent C57BL/6N embryonic stem cells (Skarnes, W. C. et al. 2011)
- Approximately 5,861 genes from C57BL/6N mice have been phenotyped and open source data is available on the IMPC portal (IMPC 2019)



Important Features

- Animals are tested at regular intervals for a wide variety of pathogens and opportunistic agents.
- A variety of testing techniques are utilized to ensure the highest quality of animals.
- Weekly colony health status reports available online.

Colony Health Monitoring and Surveillance

Frequency	Test	Methodology	Sample Type
Alternating Bi-weekly	Environmental & EAD Testing	PRIA™ PCR	Air exhaust grates, bedding, disposable equipment, various other sites
	Serology	MFIA	16 animals from each production room
Quarterly	Whole Animal Health Monitoring	Necropsy Direct Parasitology Microbiological Cultures Gross Pathology PCR Testing	12-16 animals from three different age groups per production room
Annually	Direct Animal Sampling	PRIA™ PCR	12-16 animals from three different age groups per production room

** PRIA® = PCR Infectious Agent Testing*

** EAD® = Exhaust Air Dust*

** MFIA® = Multiplexed Fluorometric ImmunoAssay®*

Animal Model Evaluation Program

Selecting the appropriate animal model for your studies is critical to the success of your research. The Animal Model Evaluation Program was developed to allow researchers in any phase of the research, drug discovery, and development continuum to assess the quality and compatibility of our models before making a commitment.

Common Applications

- Assess models in research protocols
- Conduct or fine-tune pilot studies
- Explore opportunities to switch models
- Refine or validate current studies
- Take your research in a different direction

No Cost: Select the model you would like to evaluate and we will provide them to you at no cost.

Risk Reduction: Determine whether a model fits your research protocols before making a significant time and financial investment.

Assess Quality: Assess the quality of our research animal models on your own terms.

Support: Gain access to Charles River's industry-leading customer support network.

How to Take Advantage of the Model Evaluation Program

If you would like to determine whether one of our animal models is the right fit for your research, please go to www.criver.com/evalform.

Research Applications and References

The C57BL/6 mouse is a multipurpose model that can be used in such fields as model creation, physiology, safety and efficacy, and genetics.

General Purpose

- Atochina, E.N. *et al*. Attenuated allergic airway hyperresponsiveness in C57BL/6 mice is associated with enhanced surfactant protein (SP)-D production following allergic sensitization. *Respiratory Research*, **4:15** (2003).
- Crabbe, J.C. *et al*. Genetics of mouse behavior: interactions with laboratory environment. *Science*, **284**, 1670-1672 (1999).
- Freeman, H.C. *et al.* Deletion of micotinamide nucleotide transhydrogenase: A new quantitative trait locus accounting for glucose intolerance in C57BL/6J mice. *Diabetes*, **55(7)**: 2153-2156 (2006).
- Hu. C.C. *et al*. Diet-induced changes in stearoyl-CoA sesaturase 1 expression in obesity-prone and -resistant mice. *Obesity Research*, **12(8)**: 1264-1270 (2004).
- Rogner, U. C., Avner, P. Congenic mice: cutting tools for complex immune disorders. *Nature Reviews-Immunology*, **3(3)**: 243-252 (2003).

Physiology

- Bryant, C.D. *et al*. Behavioral differences among C57BL/6 substrains: implications for transgenic and knockout studies. *J. Neurogenetics*, **22(4)**: 315-331 (2008).
- Gearhart, S. *et al*. Increased incidence of vaginal septum in C57BL/6J mice since 1976. *Comparative Medicine*, **54(4)**: 418-421 (2004).
- Toye, A.A. *et al*. A genetic and physiological study of impaired glucose homeostasis control in C57BL/6J mice. *Diabetologia*, **48(4)**: 675-686 (2005).

Model Creation/Genetics

- Hanson, G.W. *et al*. Large-scale gene trapping in C57BL/6N mouse embryonic stem cells. *Genome Research*, **18(10)**: 1679-1679 (2008).
- Pettitt, S.J. *et al*. Agouti C57BL/6N embryonic stem cells for mouse genetic resources. *Nature Methods*, **6(7)**: 493-495 (2009).
- Watkins-Chow, D.E., Pavan, W.J. Genomic copy number and expression variation within the C57BL/6J inbred mouse strain. *Genome Research*, **18(1)**: 60-66 (2008).
- Zurita, E. *et al*. Genetic polymorphisms among C57BL/6 mouse inbred strains. *Transgenic Research*. [Epub], (2010).
- Skarnes, W. C. *et al*. A conditional knockout resource for the genome-wide study of mouse gene function. *Nature*, **474(7351)**: 337–342. (2011).
- International Mouse Phenotyping Consortium. (Jun 2019). IMPC Release Notes (10.1). Retrieved from https://www.mousephenotype.org/data/release.