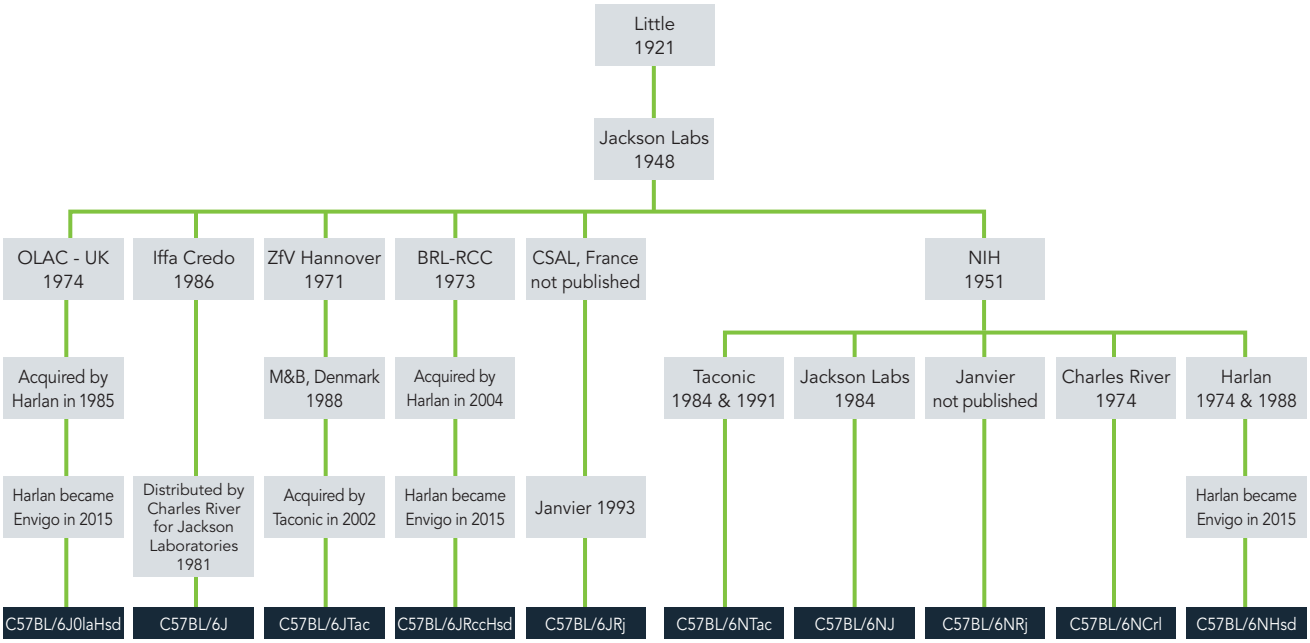
ENVIGO

Research Models and Services

Inbred Mice

C57BL/6
Substrain Information



Research Use

+ Background for induced and genetically modified models
+ Diet-Induced Obesity
+ Toxicology
+ Cardiovascular
+ Superovulation
+ Immunology
+ Aging
+ Drug Addiction
+ Alcoholism
+ General Purpose

General Characteristics

	C57BL/6NHsd	C57BL/6JOlaHsd	C57BL/6JRccHsd
Origins	Originally developed by Little in 1921; to the Jackson Laboratory, Bar Harbor, Maine, 1946		
	to National Institutes of Health (NIH), Bethesda, Maryland in 1951; to Harlan Laboratories in 1988. Harlan became Envigo in 2015.	to Laboratory Animal Centre United Kingdom, in 1974; to Harlan Laboratories in 1985. Harlan became Envigo in 2015.	to the Jackson Laboratory, Bar Harbor, Maine, 1946; to Rcc, Fullinsdorf, Switzerland, in 1973; to Harlan Laboratories in 2004. Harlan became Envigo in 2015.
Litter Average 6.0	6.0		
Common Characteristics	Low tumor incidence, high preference for alcohol, micropthalmia, hydrocephalic, age-related hearing loss, alopecia		
Coat Color	a/a; black		
Haplotype	*H1^{c}, H-2^{b}, H-3^{a}*		
Common Genetic Characteristics	*Thy1.2, Cdh23^{Ahi}, Ahr^{b}, Apoa-1^{a}, Car-2^{a}, Es-1^{a}, Es-2^{b}, Es-3^{a}, Gpd-1^{a}, Gpi-1^{b}, Hbbs, Idh-1^{a}, Ldr-1^{a}, Mod-1^{b}, Pep-3^{a}, Pgm-1^{a}, Trf^{b}, Ptprc^{a}*		
Additional Notes	Although there is some anecdotal information on different research uses and subline differences in performance for specific model, there is relatively little published information in this area. Much of this information is complicated by improper identification of sources and strain/subline nomenclature in many peer-reviewed publications. We have no evidence that most of these sublines are not interchangeable, unless published or internal data has demonstrated an important difference in response that affects the interpretation of experimental results.		

Substrain Gene Mutations

STRAIN	SUPPLIER	DELETION			
		Nnt	*Scna*	*Mnrn1*	*Rd8*
C57BL/6JOlaHsd	Envigo	No	Yes	Yes	No
C57BL/6JRccHsd	Envigo	No	No	No	No
C57BL/6NHsd	Envigo	No	No	No	Yes
C57BL/6J	Jackson Laboratory	Yes	No	No	No
C57BL/6ByJ	Jackson Laboratory	No	No	No	No
C57BL/6J	Charles River	Yes	No	No	No
C57BL/6JCrl	Charles River	Yes	No	No	No
C57BL/6NCrl	Charles River	No	No	No	Yes
C57BL/6JBomTac	Taconic	No	No	No	No
C57BL/6NTac	Taconic	No	No	No	Yes
C57BL/6JRj	Janvier	Not published	Not published	Not published	Not published
C57BL/6NRj	Janvier	Not published	Not published	Not published	Not published

Impact of Genetics on Research

Nnt = nicotinamide nucleotide transhydrogenase; this gene encodes an integral protein of the inner mitochondrial membrane. The enzyme couples hydride transfer between NAD(H) and NADP(+) to proton translocation across the inner mitochondrial membrane.

Scna = alpha synuclein; one in a family of structurally related proteins that are prominently expressed in the brain, particularly in areas associated with learning and adaption. The exact function of alpha synuclein is not yet known.

Mnrn1 = multimerin 1; multimerin 1 is a stored platelet and endothelial cell adhesive protein that shows significant conservation. In vitro, multimerin 1 supports platelet adhesion and it also binds to collagen and enhances von Willebrand factor-dependent platelet adhesion to collagen.

Rd8 = retinal degeneration 8; the rd-8 mutation is due to a single base pair mutation in the CRB1 gene. This gene when mutated in humans is linked to macular degeneration and other age-related vision loss. Mice with this mutation are nearly blind by the time they are 8 weeks of age.

Nicotinamide nucleotide transhydrogenase

The absence of the NNT protein has been associated with impaired glucose homeostasis control and reduced insulin secretion and is also required for normal mitochondrial function including metabolism and protection from oxidative stress (Huang et al, 2006).

Alpha synuclein

Although C57BL/6JOlaHsd mice have a loss-of-function deletion in the *Scna* gene, they display no up regulation of beta-synuclein or gamma-synuclein and the expression of synphilin-1 is unaffected. Spatial learning also seems to be unaffected (Specht, 2001).

Multimerin 1

C57BL/6JOlaHsd mice display impaired platelet adhesion and impaired thrombus formation that can be rescued by a functioning copy of multimerin-1 (Reheman et al, 2010).

Rd8

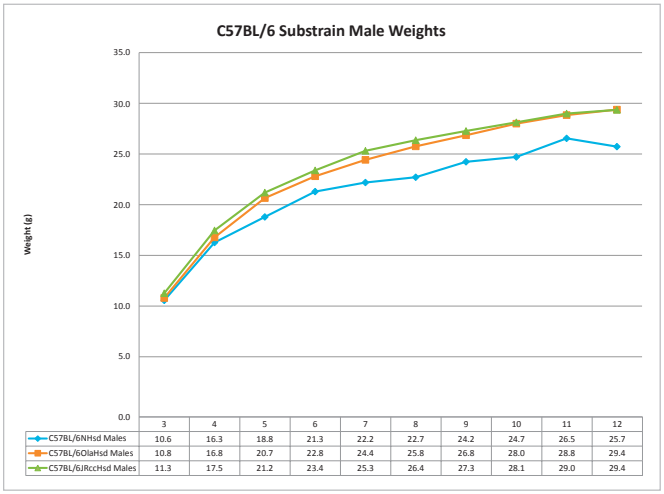
The *rd8* mutation is a single nucleotide deletion in the *Crb1* gene, which results in a form of retinal degeneration appearing with distinct clinical appearance including multiple light-colored spots in the fundus of the eye that correspond histologically to retinal folds, pseudorosettes, and focal retinal dysplasia and degeneration (Chang et al, 2002).

Genetic Concordance Among C57BL/6 Substrains

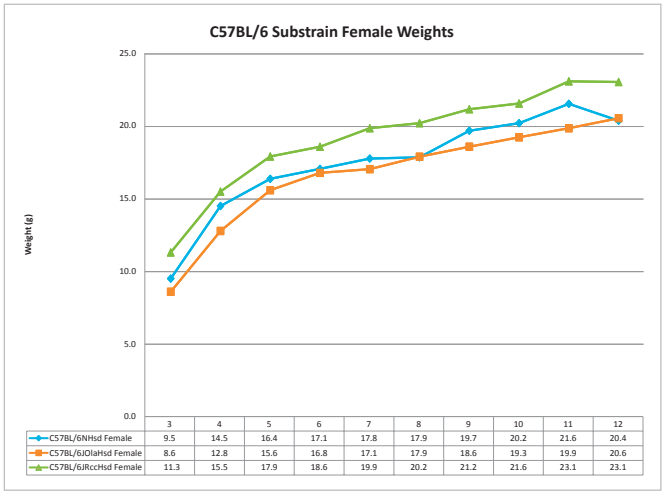
	C57BL/6J	C57BL/6JRccHsd	C57BL/6JOlaHsd	C57BL/6NHsd	C57BL/6NTac	C57BL/6NCrl
C57BL/6J	--	98.5%	98.5%	97.8%	97.8%	97.8%
C57BL/6JRccHsd	98.5%	--	100%	99.3%	99.3%	99.3%
C57BL/6JOlaHsd	98.5%	100%	--	99.3%	99.3%	99.3%
C57BL/6NHsd	97.8%	99.3%	99.3%	--	100%	100%
C57BL/6NTac	97.8%	99.3%	99.3%	100%	--	100%
C57BL/6NCrl	97.8%	99.3%	99.3%	100%	100%	--

Genetic drift is the change in frequency in which a gene appears in a population, through mutation, regardless of the adaptive value of the mutation. In an inbred population, natural random mutation occurs rather infrequently. Genetic drift is a normal process for any breeding population and thus cannot be prevented. It can only be slowed through various breeding and cryopreservation techniques. Most random mutations in a populations are single nucleotide polymorphisms and do not affect phenotype due the redundancy of the genetic code. Envigo utilizes a single source for all inbred populations of the same strain, a common parent rule to prevent subline divergence, and we are in the process of developing a global breeding and cryopreservation program for all C57BL/6 substrains worldwide. The single nucleotide polymorphism (SNP) panel for the above concordance table contained 560 SNP's. For more information regarding SNP testing of our C57BL/6 substrains or our global breeding and cryopreservation program, please contact Envigo's Veterinary Science, Research and Support Team at **RMSTechnicalServices.na@envigo.com**.

Genetic Concordance Among C57BL/6 Substrains



	3	4	5	6	7	8	9	10	11	12
C57BL/6NHsd Males	10.6	16.3	18.8	21.3	22.2	22.7	24.2	24.7	26.5	25.7
C57BL/6OlaHsd Males	10.8	16.8	20.7	22.8	24.4	25.8	26.8	28.0	28.8	29.4
C57BL/6JRccHsd Males	11.3	17.5	21.2	23.4	25.3	26.4	27.3	28.1	29.0	29.4



	3	4	5	6	7	8	9	10	11	12
C57BL/6NHsd Female	9.5	14.5	16.4	17.1	17.8	17.9	19.7	20.2	21.6	20.4
C57BL/6JOlaHsd Female	8.6	12.8	15.6	16.8	17.1	17.9	18.6	19.3	19.9	20.6
C57BL/6JRccHsd Female	11.3	15.5	17.9	18.6	19.9	20.2	21.2	21.6	23.1	23.1

Selected References

Alpha-synuclein

Kurz, A., Wöhr, M., Walter, M., Bonin, M. & Auburger, G. (2009). Alpha-synuclein deficiency affects brain Foxp1 expression and ultrasonic vocalization. *Neuroscience*, 166, 785-795.

Siegmund, A., Langnaese, K. & Wotjak, C. T. (2005). Differences in extinction of conditioned fear in C57BL/6 substrains are unrelated to expression of alpha-synuclein. *Behavioural Brain Research*, 157, 291-298.

Behavior

Bryant, C., Zhang, N. N., Sokoloff, G., Fanselow, M. S., & Ennes, H. S. et. al. (2009). Behavioral differences among C57BL/6 substrains: implications for transgenic and knockout studies. *Journal of Neurogenetics*, 22, 315-331.

Department of Health and Human Services. (1982). NIH Rodents: 1980. Catalogue (NIH Publication No. 83-606). Capital Systems Group, Inc.

Lyon, M. F., Rastan, S., & Brown, S. D. (Eds.). (1996). Genetic Variants and Strains of the Laboratory Mouse (3rd Ed.) (Vol. 2). New York: Oxford University Press.

Mayorga, J. & Lucki, I. (2001). Limitations on the use of the C57BL/6 mouse in the tail suspension test. *Psychopharmacology*, 155, 110-112.

McMillen, B.A. & Williams, H. L. (1998). Role of taste and calories in the selection of ethanol by C57BL/6NHsd and Hsd:ICR mice. Alcohol, 15, (3), 193–198.

Stiedl, O., Radulovic, J., Lohmann, R., Birkenfeld, & K. Palve et. al. (1999). Strain and substrain differences in context- and tone-dependent fear conditioning of inbred mice. *Behavioural Brain Research*, 104, 1-12.

Central Nervous System

Asuni A., Hilton K., Siskova Z., Lunnon K., Reynolds R., & V. Perry et al (2010). Alpha-synuclein deficiency in the C57BL/6JOlaHsd strain does not modify disease progression in the ME7-model of prion disease. *Neuroscience*, 165(3):662-74.

Chen, P., Sprecht, C., Morris, R. & R. Schoepfer. Spatial learning is unimpaired in mice containing a deletion of the alpha-synuclein locus. *European Journal of Neuroscience*, 16 Jul (1), 154-8.

Muller, C., Groticke, I. Hoffman, K., Schughart, K. & W. Loscher (2009). Differences in sensitivity to the convulsant pilocarpine in substrains and sublines of C57BL/6 mice. *Genes, Brain and Behavior*, 8, 481-492.

Specht, C. & R. Schoepfer (2001). Deletion of the alpha-synuclein locus in a subpopulation of C57BL/6J inbred mice. *BMC Neuroscience*, 2:11.

Cardiovascular

Reheman, A. Tasneem, S., Ni, H., & C. Hayward (2010). Mice with deleted multimerin 1 and α-synuclein genes have impaired platelet adhesion and impaired thrombus formation that is corrected by *multimerin 1. Thrombosis Research*, 125: 177–183. Diet Induced Obesity

Hu, C. C., Qing, K., & Chen, Y. (2004). Diet-induced changes in Stearoyl-CoA Desaturase 1 expression in obesity-prone and –resistant mice. *Obesity Research*, 12, 1264-1270.

Kolonin, M. G., Saha, P. K., Chan, L., Pasqualini, R., & Arap, W. (2004). Reversal of obesity by targeted ablation of adipose tissue. *Nature Medicine*,10, 625-632.

Lewis, J. G., Graham, D. G., Valentine, W. M., Morris, R. W., Morgan, D. L., & Sills, R. C. (1999). Exposure of C57BL/6 mice to carbon disulfide induces early lesions of atherosclerosis and enhances arterial fatty deposits induced by a high fat diet. *Toxicological Sciences*, 49, 124-132.

Genetics

Chang B, Hawes NL, Hurd RE, Davisson MT, Nusinowitz S, Heckenlively JR. Retinal degeneration mutants in the mouse. *Vision Res* 2002;42:517-525.

Huang, T. T. et. al. (2006). Genetic modifiers of the phenotype of mice deficient in mitochondrial superoxide dismutase. Hum Mol Genet. 2006 Apr 1;15(7):1187-94.

Mattapallil, Mary J. et al. The rd8 mutation of the Crb1 gene is present in vendor lines of C57BL/6N mice and embryonic stem cells, and confounds ocular induced mutant phenotypes. *IOVS 2012.*

Mekada, K., Abe K., Murakami A., Nakamura S., & N. Nakata et al (2009). Genetic differences among C57BL/6 substrains. *Experimental Animal*, 58(2):141-9.

Mulligan, M., Ponomarev, I., Boehm, S., Owen, J., & P. Levin et al (2008). Alcohol trait and transcriptional genomic analysis of C57BL/6 substrains. *Genes, Brain and Behavior*, 6, 677-89.

Petkov, P., Cassell, M., Sargent, E., Donnelly, C., & P. Robinson et al (2004). Development of a SNP genotyping panel for genetic monitoring of the laboratory mouse. *Genomics*, 83(5):902-11.

Tsang S., Zhonghe S., Luke B., Stewart, C., & Nicole Lum et al (2005). A comprehensive SNP-based genetic analysis of inbred mouse strains. *Mammalian Genome*, 16, 476–480.

Contact us

North America 800.793.7287 EU and Asia envigo.com/contactus info@envigo.com

Envigo RMS Division, 8520 Allison Pointe Blvd., Suite 400, Indianapolis, IN 46250, United States