C57BL/6

**Origin**
Developed in 1921 by Little from brother - sister pair (female 57 x male 52) of Miss Abby Lathrop's stock. The same cross gave rise to strains C57L and C57BR. Female 58 mated with the same male gave rise to strain C58. Strains 6 and 10 separated prior to 1937. In 1946, to the Jackson Laboratory, Bar Harbor.

**C57BL/6JOlalHsd**
In 1974, from the Jackson Laboratory to Laboratory Animals Centre, Carshalton. To OLAC (now Envigo) in 1983. In 1997 to Harlan Nederland (now Envigo).

**C57BL/6NHsd**
In 1974, from the Jackson Laboratory to the National Institutes of Health, Bethesda, Maryland. Harlan Sprague Dawley, Inc., derived the strain from this breeding nucleus. Harlan became Envigo in 2015.

**C57BL/6JRccHsd**
In 1973, from the Jackson Laboratory to the Biological Research Laboratories-RCC Ltd. Füllinsdorf, Switzerland. In 2005, Harlan obtained a breeding nucleus after acquisition of RCC Ltd. Harlan became Envigo in 2015.

**Research applications**
Behavior, learning, atherosclerosis, metabolism, alcohol preference anatomy, irradiation, carcinogenesis, immunology, infections.

**Characteristics**
The C57BL is easily the most widely used of all inbred strain. Used as a genetic background for many mutants e.g. obese, diabetes and beige. This is a long-lived strain with few tumors, some spontaneous congenital abnormalities.

**Anatomy**

**Behavior**
High alcohol (ethanol) preference (Fuller, 1964; Rodgers, 1966). The mean maximally preferred concentrations of ethanol were 17.7% for C57BL/6 and 6.8% for ICR mice. The consumption of ethanol represents a preferred source of calories for the C57BL/6 mouse (McMillen et al, 1998). Achieve blood alcohol levels of 60 mg% when access to alcohol is restricted to 60 min per day (Le et al, 1994). Alcohol preference may be associated with strain differences in mesolimbic enkephalin gene expression (Ng et al, 1996). A quasi-congenic QTL introgression strain carrying a low alcohol consumption gene from BALB/c has lower voluntary alcohol consumption than C57BL/6, with 96% of loci in common (Vadasz et al, 1996).

Drugs
Susceptible to skin ulceration by DMBA (Thomas et al, 1973). Susceptible to induction of subcutaneous tumors by 3-methylcholanthrene (Kouri et al, 1973; Whitmire et al, 1971). High incidence of lymphomas after methylcholanthrene administration by gavage (Akamatsu and Barton, 1974). Susceptible to toxic effects of DMBA (Schmid et al, 1966). Pre-treatment with beta-naphthoflavone 48 hr, before administration of N-nitrosoethylurea (ENU), once weekly for four weeks caused a significant doubling in the number of lung tumor bearers (contrast 4 strains) (Anderson et al, 1990). Phenobarbitone in the diet to give an intake of 85 mg/kg per day resulted in 4% of animals developing basophilic nodules by 91 weeks of age (contrast 70% in C3H/He), but no increase in liver carcinomas (Evans et al, 1992). However, there was a two-fold lower level of DNA synthesis in C57BL/6 mice relative to C3H mice after partial hepatectomy, though partial hepatectomy is a tumor promoter in C57BL/6 but not in C3H mice (Bennett et al, 1995). Sensitive to teratogenic effects of acetazolamide (Green et al, 1973). Resistant to teratogenic effect (cleft palate) by cortisone acetate (Kalter 1981). Hepatic epoxide hydrase activity induced by pentobarbital i.p. (Oesch et al, 1973). Resistant to teratogenic effects of cortisone acetate (Dostal and Jelinek, 1973). Resistant to lethal effects of ozone (Goldstein et al, 1973), but susceptible to ozone-induced decreases of tracheal potential (Takahashi et al, 1995) and to airway inflammation (contrast C3H/He) (Kleieberger et al, 1993). Susceptible to ozone-induced lung inflammation, which is exacerbated by vitamin A deficiency (Paquette et al, 1996). High incidence of convulsions induced by flurothyl (Davis and King, 1967). Susceptible to hyperbaric oxygen (Hill et al, 1968). Resistant to chloroform toxicity (Hill et al, 1975; Deringer et al, 1953). Resistant to toxic effects of isoniazid (Taylor 1976). Sensitive, as judged by eosinophil response, to cortisone acetate (Wragg and Speirs, 1952). High (89%) ovulatory response to three I.U. of PMS in immature mice, but only a 56% response to 7 I.U. No facilitation by exposure to males at these doses (Zarrow et al, 1971). High locomotor activity after treatment with p,-amphetamine (Babbin et al., 1974). Nicotine increases learning ability (Bovet et al, 1966). Resistant to colon carcinogenesis by 1,2-dimethylhydrazine (Evans et al, 1977). Low ED50 to behavioral effects of nicotine (Marks et al, 1989). High self-selection of nicotine which is inversely correlated with sensitivity to nicotine-induced seizures (Robinson et al, 1996). Low bronchial reactivity to methacholine and serotonin (Konno et al, 1993). Resistant to daunomycin-induced nephrosis (Kimura et al, 1993).

Low neural sensitivity to pentyleenetetrazol convulsions (Kosobud et al, 1992). Susceptible to biliary tract injury following oral dosing with 500 micrograms of the fungal toxin sporidesmin (Bhathal et al, 1990). Low histamine release from peritoneal mast cells induced by compound 48/80, a calcium dependent histamine releaser (Toda et al, 1989). Low histamine release from peritoneal mast cells induced by Ca2+ ionophore A23187, (contrast BALB/c, C3H/He, DBA/2 etc.) (Toda et al, 1989). Carries gene (Tpmt) for low levels of thiopurine methyltransferase activity, catalyzing the S-methylation of 6-mercaptopurine and other heterocyclic and aromaticthiol compounds (like AKR, unlike DBA/2) (Otterness and Weinshilboum 1987a;b). More sensitive to acute toxic effects of aflatoxin B-1 than strains CBA/J or BALB/c (Almeida et al, 1996). Airways hyporeactive to acetylcholine (Zhang et al, 1995). High voluntary consumption of morphine in two-bottle choice situation (Belknap et al, 1993). Estrogen induces an increase in VLDL and LDL-cholesterol (like C57L, contrast BALB/c and C3H) (Srivastava, 1995). Nine-fold higher ED50 for haloperidol-induced catalepsy than DBA/2, but this is not associated with numbers of cholinergic neurons (Dains et al, 1996). Accumulates three to five-fold lower levels of mercury in liver and blood than DBA/2 or A.SW after four weeks exposure to mercuric chloride, but higher levels in spleen following 8-12 weeks of exposure (Griem et al, 1997).

Genetics
Coat color genes - a, B, C, D : black. Histocompatibility - H-1^a, H-2^b, H-3^c. Biochemical markers - Apoa-1^a, Car-2^b, Es-1^c, Es-2^c, Es-3^c, Gpd-1^a, Gpr-1^a, Hba^a, Hbb^b, Idh-1^a, Ldr-1^a, Mod-1^a, Mup-1^a, Pep-3^c, Pgm-1^a, Pgm-2^b, Trp^c.
Four major substrains, A, GrFa, 6 and 10 appear to be quite similar, and any differences are consistent with what might be expected from the accumulation of new mutations and a small amount of residual heterozygosity, though McCleve et al. (1994) have found that B6 and B10 differ at multiple loci on chromosome 4 including the microsatellite markers D4Mit69, D4Mit71 and D4Mit72. Additional microsatellites, which distinguish between B6 and B10 are given by Slingsby et al. (1996). Substrains 6 and 10 differ at the H-9, IgH-2 and Lv loci. All Envigo C57BL/6 sublines still carry the Nnt (nicotinamide nucleotide transhydrogenase) gene, which is missing in the original C57BL/6/J from Jackson Laboratories.

C57BL/6/JOlaHsd mice lack α-synuclein due to a small deletion of the locus (Schecht and Schoepfer, 2001). α-Synuclein belongs to a family of structurally related proteins expressed highly in the brain. However, α-synuclein is not essential for spatial learning tasks (Chen et al., 2002). This deletion isn’t present in the C57BL/6/JRccHsd subline!

Description of the difference between FVB/N and C57BL/6J for 272 microsatellites (Neuhaus et al., 1997). A probe designated B6-38 to the pseudoautosomal region of the X and Y chromosome has a characteristic Pst I pattern of fragment sizes which is present only in the C57BL family of strains (Kalcheva et al., 1995). C57BL/6 mice carry the Mus musculus musculus Y-chromosome, while others have the M. m. domesticus type (Nishioha, 1987).

The C57BL/6/NHsd subline carries a retinal degeneration 8 mutation - rd8 (Caspi et al, 2012)

Immunology


Poor immune response to Pro-Gly-Pro-ovalbumin and (Pro46, Gly49)n but good immune response to Pro-Gly-Pro(n) (Fuchs et al., 1974). High PHA- stimulated lymphocyte blastogenic response (Hellman and Fowler, 1972). Erythrocytes have low agglutinability (Rubinstein et al., 1974). High immune response to territin in B6-Tia (Young et al., 1976). Low responder to dextran (Blomberg et al., 1972). Low responder to E. coli β-D-galactosidase, with “memory” developing in absence of antibody formation (De Macario and Macario 1980). Precipitating and skin sensitising antibodies have slow electrophoretic mobility (Fahey, 1965). Resistant to anaphylactic shock (Treadwell, 1969). Susceptible to induction of autoimmune prostatitis (contrast BALB/c) (Keetch et al., 1994). High expression of neutral glycosphingolipid GgOse(4) Cer in concanavalin A stimulated T lymphoblasts (Muthig, 1997). Anti-BPO IgE monoclonal antibody produced potent systemic sensitization sufficient for provocation of lethal shock in most aged (6 to 10 months) mice (Harada et al., 1991). Susceptible to immunosuppression of contact hypersensitivity by ultraviolet B light (Noonan and Hoffman, 1994). The potential influence of circadian changes and laboratory routine on some immune parameters has been described by Kolaczkowska et al. (2000).

Infection

Develops a slowly progressing parasitosis (”low responder”) after infection with the Cornell strain of Toxoplasma gondii (Macario et al., 1980). Did not support sustained growth of six strains of Leishmania mexicana mexicana (contrast BALB/c) (Monroy-Ostria et al., 1994). Resistant to Leishmania major (contrast BALB/c) (Laskay et al., 1995; Scott et al., 1996). Susceptible to L. major mexicana, and vaccination against the parasite using liposomes with parasite membrane antigens was effective (cf CBA/ Ca but contrast C57BL/10) (Lezama-Dávila, 1997). Susceptible to Salmonella typhimurium strain C5 (Robson and Vas, 1972). 100-fold more resistant to Listeria monocytogenes than A/J when measured by median lethal dose (Sadarangani et al., 1980). This seems to be associated with increased levels of gamma interferon and granulocyte-macrophage colony stimulating factor compared with susceptible A/J mice (Iizawa et al., 1993). Resistant to Mycoplasma fermentens (Gabridge et al., 1972). Resistant to Mycoplasma pulmonis infection (Cartner et al., 1996). Resistant to infection by Mycobacterium marinum (Yamamoto et al., 1991). Resistant to infection by liver fluke Opisthorchis felineus (Zelentsov, 1974). Resistant to infection with the helmint worm Angiostrongylus costaricennsis (Ishii and Sano 1989). Relatively susceptible to infection with Helicobacter felis (contrast C57BL/6) (Mohammadi et al., 1996). Susceptible to infection by Helicobacter felis with moderate to severe chronic active gastritis in the body of the stomach, which increased over time (Sakagami et al., 1996). H. felis induces hypertropic gastropathy (Fox et al., 1996). Highly resistant to the mammary tumor virus which is thought not to be carried by the strain (Murray and Little, 1967). Resistant to Herpes simplex virus (Lopez, 1975). Resistant to herpes simplex virus-1 (contrast BALB/c) (Brenner et al, 1994). Susceptible to mouse hepatitis virus type 3 infection (Le Prevost et al, 1975).

Develops antibodies to mouse hepatitis virus which can be reliably detected by the complement fixation test, in contrast to five other strains (Kagiyama et al, 1991). Low mortality in a natural epizootic of ectromelia (Briody, 1966). High expression of RNA tumor virus group-specific antigen in some substrains but low in others (Whitmire and Salerno, 1972). Resistant to development of leukemia on infection by Friend virus (Dietz and Rich, 1972). Resistant to...
Borrelia}

\[\text{gamma response (contrast BALB/c) (Autenrieth}\]

\[M. paratuberculosis (contrast C3H/HeJ) (Tanaka}\]

\[\text{and can be used to test anti-mycobacterial agents}\]

\[\text{agent rifabutin (Furney}\]

\[\text{a 120-day period with the antimycobacterial}\]

\[\text{the infections can be sterilized by treatment over}\]

\[\text{of C57BL/6-bg. The course of such infections}\]

\[\text{selectively deplete CD4+ T cells are susceptible}\]

\[\text{intravenously infused with monoclonal antibody to}\]

\[\text{et al}\]

\[\text{burgdorferi}\]

\[\text{to carditis on infection with Lyme borreliosis ( contrast}\]

\[\text{type 2 including the type strain, two isolates from}\]

\[\text{meningitis in pigs and two isolates from tonsils of}\]

\[\text{clINically healthy pigs (Kataoka et al, 1991).}\]

\[\text{to carditis on infection with Lyme borreliosis (Borreliia}\]

\[\text{burgdorferi) (contrast C3H, SWR, BALB/c) (Barthold}\]

\[\text{et al, 1990). Thymectomized C57BL/6 mice that were}\]

\[\text{infusion with hyatid homogenate results}\]

\[\text{infection with larval Echinococcus multilocularis by}\]

\[\text{transportal injection of hyatid homogenate results}\]

\[\text{in a multivesiculation form of hyatid development}\]

\[\text{Nakaya et al, 1997). Susceptible to mouse}\]

\[\text{adenovirus type 1 which causes a fatal hemorrhagic}\]

\[\text{encephalomyelitis (contrast BALB/c) (Guida}\]

\[\text{virus B1, in contrast with C57BL/10 and B10 congenic}\]

\[\text{Resistant to chronic weakness and inflammation}\]

\[\text{within eight-ten days, in contrast with the more}\]

\[\text{infection could only be established}\]

\[\text{with all mice developing erythrocytic infection}\]

\[\text{1994). Highly susceptible to}\]

\[\text{the fungus}\]

\[\text{1994). Susceptible, with high amylase response to}\]

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\[\text{S. neurona}\]

\[\text{1992). Resistant to}\]

\[\text{Trypanosoma congolense}\]

\[\text{Trypanosoma cruri infection (Rowland et al 1992).}\]

\[\text{Resistant to infection with Trypanosoma congolense with}\]

\[\text{an initial peak of parasitemia on day six, followed by}\]

\[\text{rapid apparent clearance in an average of three}\]

\[\text{days (contrast BALB/c) (Ogunremi and Tabel, 1995).}\]

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\[\text{adenovirus type 1 which causes a fatal hemorrhagic}\]

\[\text{encephalomyelitis (contrast BALB/c) (Guida}\]

\[\text{virus B1, in contrast with C57BL/10 and B10 congenic}\]

\[\text{Resistant to chronic weakness and inflammation}\]

\[\text{within eight-ten days, in contrast with the more}\]

\[\text{infection could only be established}\]

\[\text{with all mice developing erythrocytic infection}\]

\[\text{the same level of infection could only be established}\]

\[\text{in BALB/c with 10,000 sporozoites (Scheller et al,}\]

\[\text{1994). Infection with P. berghei results in low blood}\]

\[\text{parasitemia and death with neurological symptoms}\]

\[\text{within eight-ten days, in contrast with the more}\]

\[\text{resistant BALB/c (Moumaris et al, 1995).}\]

\[\text{Resistant to chronic weakness and inflammation}\]

\[\text{following infection with Tucan strain of coxsackie}\]

\[\text{virus B1, in contrast with C57BL/10 and B10 congenic}\]

\[\text{strains (Tam and Messner, 1996).}\]
C57BL/6 mice carry a single recessive gene different from that found in BALB/cBy and WB/ReJ, causing age-related hearing loss (Willott et al, 1995). Hearing loss is caused by degeneration of the organ of Corti, originating in the basal, high frequency region and then proceeding apically over time. This results in a severe sensorineural hearing loss by 14 months of age (Walton et al, 1995). More susceptible to noise-induced hearing loss than CBA/J (Erway et al, 1996).

Median life-span 22.4 months in C57BL/6 males and 23.6 months in C57BL/6 females (Storer, 1966). Median life-span 24.7 and 29.6 months in C57BL/6 males and 23.6 and 29.8 months in C57BL/6 females (Les, 1969). Median life-span 27.6 months in C57BL/6 males and 27.3 months in C57BL/6 females (Goodrick, 1975). Median life-span 29.3 months in C57BL/6 males and 26.5 months in C57BL/6 females (Kunstyr and Leuenberger, 1975). Median life-span 20.0 months (Curtis, 1971). Gross tumor incidence 70%, maximum life-span about 40 months in SPF conditions (Mewissen, 1971).

Dermatitis with intense pruritis leading to self-mutilation and death, and sometimes associated with the mite Myobia musculi appears to be more severe in this strain than others (Csiza and McMartin, 1976). Impaired axonal regeneration involving multiple genetic loci (Lu et al, 1994).

Miscellaneous

Physiology and biochemistry

Low basal levels of kidney catalase, superoxide dismutase and renal glutathione reductase (Misra et al, 1991). Iron overload causes inhibition of hepatic uroporphyrinogen decarboxylase and uroporphyrin in C57BL/10ScSn but not DBA/2 mice. This was not correlated with the Ah locus in a study involving 12 mouse strains (Smith and Francis, 1993). Low levels of apoA-IV messenger RNA in liver compared with 129/J (Reue et al, 1993). Low susceptibility to audiogenic seizures (Deckard et al, 1976). Long tau DD, the endogenous (free-running) period of the circadian pacemaker measured in constant environmental darkness (Schwartz and Zimmerman 1990). Has defective secretory group II phospholipase A2 gene (cf strains 129/Sv and B10. RIII) (Kennedy et al, 1995). Susceptible to severe hypercapnia with hypoxia assessed by elevated minute ventilation rate (Tankersley et al, 1994). Has a rapid and shallow breathing pattern phenotype (contrast C3H) (Tankersley et al, 1997). Susceptible to cerebral ischemia following bilateral carotid occlusion with 90% of mice showing typical neurological signs such as torsion of the neck and rolling fits with selective neuronal death in the hippocampus and caudoputamen after 20 minutes of ischemia (Yang et al, 1997).

Reproduction
References


