ENVIGO

Research Models and Services

Inbred Mice

DBA/2

Origin

Developed in 1909 by Little from mice used in color experiments and this strain is the oldest of all inbred strains of mice. In 1929-30, crosses were made between sub-lines, and several new lines established; two of these were called 12 (now DBA/1) and 212 (now DBA/2).

DBA/2NHsd

In 1951, from Mider to the National Institutes of Health (NIH), Bethesda, Maryland, USA. Harlan obtained a breeding nucleus from NIH. Harlan became Envigo in 2015

DBA/2OlaHsd

Obtained by Laboratory Animals Centre, Carshalton from the Jackson Laboratory, Bar Harbor in 1959. In 1972, to OLAC (now Envigo).

DBA/2JRccHsd

The DBA/2JRccHsd mice originate from Jackson Laboratory, Bar Harbor, Maine and were moved in 1974 to RCC Ltd. (formerly Ibm and BRL) in Füllinsdorf, Switzerland. To Harlan Laboratories through acquisition in 2004. Harlan became Envigo in 2015.

Research applications

Coat color, behavior, audiogenic seizures, epilepsy, calcification, metabolism, fetal resorption, immunology, infectious diseases, etc.

Characteristics

Anatomy

Large testes weight (Shire and Bartke, 1972). Low brain weight (Storer, 1967; Roderick *et al*, 1973; Wahlsten *et al*, 1975). High total leukocyte count, high erythrocyte count, low hematocrit, low mean corpuscular volume and low hemoglobin (Russell *et al*, 1951). Small forebrain, neocortex and hippocampus volume (Wimer *et al*, 1969). Cerebellum has an intraculminate fissure between vermian lobule IV and vermian lobule V (the ventral and dorsal lobules of the culmen) (contrast SJL, C57BL/10 and BALB/c) (Cooper *et al*, 1991). Large heart/body weight (Mokler and Iturrian, 1973). High proportion of acidophilic and low proportion of chromophobe cells in adenohypophysis of DBA/Sy substrain (Keramidas and Symeonidis, 1973). Hematopoietic stem cell pool 11-fold higher than in C57BL/6. This is largely due to loci on chromosome 1 (Muller-Sieburg and Riblet, 1996). High level of spontaneous sister chromatid exchange (Nishi *et al*, 1993).

Behavior

Low alcohol preference (Fuller, 1964; Rodgers, 1966; McClearn, 1965). High severity of ethanol withdrawal symptoms compared with C57BL/6, possibly associated with differences in neuroactive steroid sensitivity (Finn *et al*, 1997). High shock-avoidance learning (Bovet *et al*, 1966); Bovet *et al*, 1969). Low avoidance conditionability (Royce, 1972). Long time of immobility in a forced swimming test (Nikulina *et al*, 1991) Low shuttle-box avoidance, high wheel activity (Messeri *et al*, 1972). Good long-term memory compared with C3H/He (Bovet *et al*, 1969). Slow extinction of learned conditioned avoidance response (Schlesinger and Wimer, 1967). Susceptible to audiogenic seizures (Fuller and Sjursen, 1967). Long latency to attack crickets (Butler, 1973). High rearing, low defecation in Y-maze (McClearn *et al*, 1970).

Low locomotor activity when grouped but not when single (Davis *et al*, 1967). Low social dominance of males in competition for females (DeFries and McClearn, 1970). Low balsa-wood gnawing activity (Fawdington and Festing, 1980). Low preference for sweet tasting substances (saccharin, sucrose, dulcin and acesulfame, averaged) (Lush 1988).

DBA/2 mice failed to react to a spatial change of objects in an open field, and therefore resemble

rats with dorsal lesions of the hippocampus. They may represent a model of hippocampal dysfunction (Ammassari-Teule *et al*, 1995). Feed restriction for nine days causes a high incidence of stereotypic cage cover climbing (contrast C57BL/6) (Cabib and Bonaventira, 1997).

Drugs

Resistant to skin ulceration by DMBA (Thomas *et al*, 1973). Resistant to induction of subcutaneous tumors by 3-methylcholanthrene (Kouri *et al*, 1973; Whitmire *et al*, 1971). Resistant to induction of adenocarcinomas of the colon by 1,2-dimethylhydrazine (Evans *et al*, 1974). Resistant to teratogenic effect of 1-ethyl-1-nitrosourea (Diwan, 1974). Phenobarbital i.p. does not induce hepatic epoxide hydrase (Oesch *et al*, 1973). Resistant to lethal effects of ozone (Goldstein *et al*, 1973). Susceptible to induction of cleft palate by cortisone (Kalter, 1965). Good ovulatory response to 3 I.U. of PMS but zero response to 7 I.U. (Zarrow *et al*, 1971). Low incidence of convulsions induced by flurothyl (Davis and King, 1967). Long hexobarbital sleeping time and low liver hexobarbital oxidase level (Vesell, 1968). Sensitive to chloroform toxicity (Hill *et al*, 1975; Deringer *et al*, 1953). Sensitive to seizures induced by nicotine (Marks *et al*, 1989). Sensitivity may be related to brain alpha-bungarotoxin binding, which is significantly higher in ST/b than in sensitive DBA/2 mice (Marks *et al*, 1996). High self-selection of nicotine which is inversely correlated with sensitivity to nicotine-induced seizures (Robinson *et al*, 1996). High bronchial reactivity to methacholine and serotonin (Konno *et al*, 1993). Resistant to daunomycin-induced nephrosis (Kimura *et al*, 1993). High neural sensitivity to pentylenetetrazol convulsions (Kosobud *et al*, 1992). Sensitive to neurotoxic effects of monocrotophos (Rao *et al*, 1991). Low histamine release from peritoneal mast cells induced by compound 48/80, a calcium dependent histamine releaser (Toda *et al*, 1989). High histamine release from peritoneal mast cells induced by Ca2+ ionophore A23187 (contrast C57BL/6) (Toda *et al*, 1989). Carries gene (*Tpmt*) for high levels of thiopurine methyltransferase activity, catalysing the S-methylation of 6-mercaptopurine and other heterocyclic and aromaticthiol compounds (unlike C57BL/6 and AKR) (Otterness and Weinshilboum, 1987a; 1987b). Resistant (contrast five strains) to the induction of micronuclei by polycyclic aromatic hydrocarbons, presumably due to uninducible Ah locus (Sato *et al*, 1987). Iron overload does not cause inhibition of hepatic uroporphyrinogen decarboxylase and uroporphyria in contrast with C57BL/10ScSn. This was not correlated with the Ah locus in a study involving 12 mouse strains (Smith and Francis, 1993). Resistant to hepatotoxic effects of cadmium (Shaikh *et al*, 1993). Low voluntary consumption of morphine in two-bottle choice situation (Belknap *et al*, 1993).

Less susceptible to the development of micronuclei than BALB/c following treatment with clastogenic base analogues and nucleosides (Sato *et al*, 1993). Unique poor responsiveness to the antinociceptive effects of nitrous oxide, a polygenic trait (Quock *et al*, 1996). Nine-fold lower ED50 for haloperidol-induced catalepsy than C57BL/6, but this is not associated with numbers of cholinergic neurons (Dains *et al*, 1996). Airways hyperreactive to acetylcholine (Zhang *et al*, 1995). Resistant to rate-depressant effects of ethanol on schedule-controlled behavior (Elmer and George, 1995). A diet containing 15% dairy fat, 1% cholesterol and 0.5% cholic acid did not cause a high incidence of cholesterol gallstones (like AKR, SM contrast C57L, SWR, A) (Faulkner *et al*, 1995).

Genetics

Coat color genes	- *a, b, C, d* : non-agouti, dilute brown.
Histocompatibility	- *H-2*^{d}, *Thy-1*^{b}.
Biochemical markers	- *Apoa-1*^{b}, *Car-2*^{b}, *Es-1*^{b}, *Es-2*^{b}, *Es-3*^{c}, *Gpd-1*^{b}, *Gpi-1*^{a}, *Hba*^{g}, *Hbb*^{d}, *Idh-1*^{b}, *Ldr-1*^{a}, *Mod-1*^{a}, *Mup-1*^{a}, *Pep-3*^{b}, *Pgm-1*^{b}, *Pgm-2*^{a}, *Trf*^{b}.

Although the DBA/1 and DBA/2 are substrains of the DBA there are differences between these strains, probably due to a substantial residual heterozygosity following the crosses between the substrains. DBA/1 and DBA/2 differ at least at the following loci: *Car-2, Ce-2, Hc, H-2, If-1, Lsh, Tla*, and *Qa-3*. With such large differences, they should probably be regarded as different strains rather than substrains of the same strain. This strain carries the *Mus musculus musculus* Y-chromosome, while others have the *M. m. domesticus* type (Nishioka, 1987).

Immunology

Resistant to experimental allergic encephalomyelitis (Levine and Sowinski, 1973). Low lymphocyte phytohemagglutinin response (Heiniger *et al*, 1975). Serum antinuclear factor 26% incidence (Barnes and Tuffrey, 1967). Poor immune response to type III pneumococcal polysaccharide (Braley and Freeman, 1971). Good immune response to synthetic double-stranded RNA (Steinberg *et al*, 1971). Poor immune response to cholera A and B antigens (Cerny *et al*, 197l). Poor immune response to both ovomucoid and ovalbumin (Vaz *et al*, 1971).

Precipitating and skin-sensitising antibodies have fast electrophoretic mobility (Fahey, 1965). Non-discriminator between `H' and `L' sheep erythrocytes (McCarthy and Dutton, 1975). Low anti-DNP antibody concentration (Paul *et al*, 1970). Poor immune response to Pro-Gly-Pro-ovalbumin and (Pro-Gly-Pro)n, but good immune response to (Pro^{66}, Gly^{34}) n (Fuchs *et al*, 1974). High susceptibility to IgG_1-mediated but low susceptibility to IgE-mediated passive cutaneous anaphylaxis (De Souza *et al*, 1974). Develops a lethal form of syngeneic graft-vs-host disease when treated with cyclosporine (unlike five other strains) (Prud'homme *et al*, 1991). Erythrocytes have a high agglutinability (Rubinstein *et al*, 1974). Poor immune response to *Salmonella strasbourg* lipopolysaccharide, depending on substrain) (Di Pauli, 1972). Low PHA-stimulated lymphocyte blastogenic response (Hellman and Fowler, 1972). Low immune response to ferritin (Young *et al*, 1976). Resistant to induction of anaphylactic shock by ovalbumin (Tanioka and Esaki, 1971). Resistant to experimental autoimmune orchitis induced by two

or three sc injections with viable syngeneic testicular germ cells without any adjuvants (Tokunaga *et al*, 1993). Anti-BPO IgE monoclonal antibody failed to produce potent systemic sensitization sufficient for provocation of lethal shock in most aged (six-ten months) mice (Harada *et al*, 1991). High expression of neutral glycosphingolipid GgOse(4)Cer in concanavalin A stimulated T lymphoblasts (Muthing, 1997).

Infection

Resistant to infection by *Salmonella typhimurium* strain C5 (Plant and Glynn, 1974). Susceptible to liver fluke *Opisthorchis felineus* (Zelentsov, 1974). Susceptible to natural intestinal helminth infection (Eaton, 1972). Develops a chronic non-healing lesion on infection with *Leishmania tropica*, the parasite causing cutaneous leishmaniasis (Howard *et al*, 1980). Susceptible to the induction of dental caries due to infection with *Streptococcus mutans* (Kurihara *et al*, 1991). Susceptible to the development of chronic Chagas' cardiomyopathy in post-acute *Trypanosoma cruzi* infection (Rowland *et al*, 1992). Infection with larval *Echinococcus multilocularis* by transportal injection of hyatid homogenate results in well developed protoscoleces (Nakaya *et al*, 1997). Highly susceptible to infection with *Pseudomonas aeruginosa* with rapid accumulation of bacterial burden and high mortality, in contrast with resistant BALB/c mice (Morissette *et al*, 1995). Susceptibility is associated with a delay in inflammatory response and the initiation of bacterial clearance (Morisette *et al*, 1996). Susceptible to disseminated *Cryptococcus neoformans* (Irokanulo *et al*, 1995). Highly susceptible to infection with *Candida albicans* (Ashman *et al*, 1996). Resistant, with low amylase response to the fungus *Paracoccidioides brasiliensis* (Xidieh *et al*, 1994). Highly susceptible, with high mortality following infection with *Mycoplasma pulmonis* (Cartner *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). Low susceptibility to BALB/Tennant leukemia virus (Tennant, 1965). Hyperglycemia can be induced by encephalomyocarditis virus, which also causes diabetes mellitus (Boucher and Notkins, 1973; Boucher *et al*, 1975).

High susceptibility to develop leukemia on infection with Friend virus (Dietz and Rick, 1972). Mouse mammary tumor proviral loci have been identified by Lee and Eicher (1990).

Life-span and spontaneous disease

Primary lung tumors 1% in males, 2% in females. Lymphatic leukemia zero in males, 2% in females and 3% in virgin females. Mammary adenocarcinomas in unfostered substrains 1% in males, 72% in breeding females and 48% in virgin females (Hoag, 1963). A high proportion of mammary tumors are of the acinar type (Tengbergen, 1970). Overall tumor incidence 15% in males, 49% in females, including lymphomas 10% in males and 12% in females; mammary tumors zero in males and 31% in virgin females (Smith *et al*, 1973). Leukemia 3% (Myers *et al*, 1970). Long life-span in SPF fostered conditions (629 days in males, 719 days in females) with 6-35% liver and 1-23% lung tumors (Festing and Blackmore, 1971). Long life-span in conventional conditions (707 days in males, 714 days in females) (Storer, 1966). Life-span 722 days in males and 683 days in females (Goodrick, 1975). High incidence of expression of RNA tumor virus group-specific antigen (Diwan *et al*, 1973). Type B reticulum cell neoplasms 18% at about 20 weeks (Dunn and Deringer, 1968). Spontaneous calcified heart lesions progress with age. 90% of individuals affected by one year (Rings and Wagner, 1971). Incidence of calcareous heart lesions high among some related strains (Di Paola *et al*, 1964). Dystrophic cardiac calcification may be related to disturbed myocyte calcium metabolism (Brunnert, 1997). Chronic hypertropic gastritis, duodenal polyps and calcareous pericarditis frequently observed. Other lesions include malignant lymphoma and degenerative processes in the myocardium, skeletal muscle, subcutaneous adipose tissue, cornea and blood vessels. Lesions partly depend on diet (Hare and Stewart, 1956). Carry three separate recessive genes similar to those found separately in C57BL/6J, BALB/cBy and WB/ReJ, causing age-related hearing loss (Willott *et al*, 1995).

Miscellaneous

Recommended host for the following transplantable tumors: fibrosarcoma SaD2, lymphatic leukemia P1534 and mammary adenocarcinoma CaD2 (Kaliss, 1972). Hybrids involving DBA/2 are recommended host for transplantable leukemia L1210, melanoma S91 and MOPC myeloma used as models in screening potential anticancer drugs (EORTC Screening Group, 1972). The *Fv2*^{r} allele appears to be lethal on the DBA/2 genetic background (Blank and Lilly, 1976). High mortality after neonatal thymectomy (Law, 1966).

The relationship of genotype, sex, body weight, and growth parameters to lifespan in inbred and hybrid mice is described by Ingram *et al* (1982). Characteristics of the DBA/2 strain have been described by Festing (1997) and Lyon *et al*, (1996).

Physiology and biochemistry

High metabolic rate (Storer, 1967). High metabolic rate at 26°C (Pennycuik, 1967). High cell turnover as estimated by rapid clearance of DNA-bound radioactivity (Heiniger *et al*, 1972). High proportion of paradoxical (REM) sleep (Pagel *et al*, 1973).

High concentration of epinephrine and norepinephrine in adrenals (Ciranello *et al*, 1972). Low Na/K ratio in erythrocytes but high ratio in plasma (Waymouth, 1973). Arterial blood has a high pH (Bernstein, 1966). Low concentration of prostaglandin F in epididymus (Badr, 1975). High plasma cholinesterase (Angel *et al*, 1967). Low liver tyrosine amino transferase activity in fasted mice (Blake, 1970). High calcium uptake by the heart (Mokler and Iturrian, 1973). High sensitivity to thyrotropin (Levy *et al*, 1965). High coumarin hydroxylating ability (Lush and Arnold, 1975). High coumarin hydroxylase activity in both sexes (Van Iersel *et al*, 1994). Low N'-methylnicotinamide oxidase activity in both sexes (Huff and Chaykin, 1967). High serum haptoglobin level (Peacock *et al*, 1967). Low hepatic benz (alpha) pyrene hydroxylase activity (Kodama and Bock, 1970).

High hepatic delta-aminolaevulinate dehydratase activity (Doyle and Schimke, 1969). Low aldehyde and alcohol dehydrogenase activity compared with C57BL/6 (Sheppard *et al*, 1968). High hepatic delta-aminolaevulinic acid synthetase activity after DISC treatment (Gross and Hutton, 1971). High hepatic urokinase activity (Hanford *et al*, 1974). High basal level of growth hormone at 78 days and low basal level of serum prolactin (Sinha *et al*, 1975). High brain L-glutamic acid decarboxylase, choline acetyltransferase and acetylcholinesterase activity (Tunnicliff *et al*, 1973). Low brain sulphatide and plasmalogen and high brain sterol (Sampugna *et al*, 1975). Low brain cholinesterase (Pryor *et al*, 1966). Resistant to the development of atherosclerosis on a semi-synthetic high fat diet (Nishina *et al*, 1993). Hyporesponsive to diets containing high levels of fat and cholesterol (Kirk *et al*, 1995). Mild hypercapnia with hypoxia significantly elevated minute ventilation rate (Tankersley *et al*, 1994).

Reproduction

The DBA/2 strain has a poor breeding performance and the young mice are very small at time of weaning. Colony output 0.85 young/female/week. Low litter size at weaning of 4.7 (Festing, 1976). Poor breeding performance. Litter size 4.2, sterility 31% (Nagasawa *et al*, 1973). Intermediate breeding performance (Hansen *et al*, 1973). Corpora lutea may persist over many cycles, becoming hyalinized and calcified (Chai and Dickie, 1966). Has shorter and less regular estrus cycles than C57BL/6J (Nelson *et al*, 1992). Susceptible to fetal resorption resulting from restraint-induced stress when mated to C3H/HeJ males, in contrast with CBA/J and A/J. This was reduced by alloimmunization with C3H cells (Clark *et al*, 1993).

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