

C3H

C3H/HeNHsd

Developed in 1920 by Strong from a cross of Bagg albino female and DBA male. Strain CBA also originated from this cross. Strain CBA was selected for a low mammary tumor incidence and C3H for a high incidence. In 1930, to Andervont, National Cancer Institute, Bethesda, MD, USA and in 1941, to Heston and Law at the same institute.

Derived from a nucleus colony obtained from the National Institutes of Health, Bethesda, Maryland.

Harlan Laboratories Israel became an independent company in 2023

RESEARCH APPLICATIONS

Behavior, aggression, mammary tumors, metabolism, immunology, infectious diseases, parasitology, etc.

CHARACTERISTICS

Strain C3H was selected for a high mammary tumor incidence. Unfostered sub-lines have a very high incidence of mammary tumors caused by a virus (Bittner virus), which is transmitted, from mother to offspring through the milk.

Fostering of the young to a mammary tumor virus-free strain eliminates the virus and therefore all Germfree or SPF (Specified Pathogen Free) C3H mice will be free of this virus. Fostered C3H mice are widely used as a general-purpose strain.

Anatomy

Low total leukocyte count, low erythrocyte count, low hematocrit, and low hemoglobin (Russell et al, 1951).

Small thymus/body weight ratio (Belyaev et al, 1970), small thymus/body weight ratio (depending on age) (Albert et al, 1965). Large pituitary (Sinha et al, 1975). Adrenal gland X zone large, with high incidence of vacuolization (Delost and Chirvan-Nia, 1958). Low percentage of mice has accessory spleens (Hummel et al, 1966). Many Peyer's patches (Hummel et al, 1966). Plasma volume low at 5.97 ml/100 g and red cell volume low at 4.64 ml/100g body weight in He substrain (Kano and Mizuma, 1974). High bone density of femur (Beamer et al, 1996).

Behavior

C3H mice are easy to handle. Low intra-strain aggression (Southwick and Clark, 1966). Long latency to emerge from home-cage, low rearing, long latency to cross barrier in open-field, low hole-in-the-wall entries and low Y-maze exploration (McClearn et al, 1970). Low open-field activity (Bruell,

1964). Low open-field defecation (Bruell, 1969). High food drive (Thompson, 1953), but poor performance in food- seeking task (Henderson, 1970). Short time of immobility in a forced swimming test (Nikulina et al, 1991). Low shock-

avoidance learning (Bovet et al, 1966; Bovet et al, 1969). Good short-term but poor long-term memory in contrast with DBA/2 (Bovet et al, 1969). Good T-maze

learning (Stasik, 1970). Poor water-escape learning (Festing, 1973). Low radial-arm maze learning (Ammassari-Teule et al, 1993). High social grooming scores during aggressive encounters (Southwick and Clark, 1968). Carries the retinal degeneration gene and is capable of pattern discrimination up to 40 days, and brightness discrimination to at least 100 days (Nagy and Misanin, 1970).

Drugs

Susceptible to skin ulceration to DMBA (Thomas et al, 1973). Sensitive to the development of uterine tumors following treatment with DMBA at four weeks of age (Tsubura et al, 1993).

Susceptible to induction of subcutaneous tumors by 3-methylcholanthrene, depending on substrain (Kouri et al, 1973). Susceptible to tumor induction

by 3-methylcholanthrene in fostered and unfostered substrains (Whitmire et al, 1971; Whitmire and Salerno, 1972). Susceptible to induction of liver but resistant to pulmonary tumors

by neonatally administered DMBA (Flaks, 1968). High susceptibility to tumor induction by 3,4-benzopyrene (Liebelt et al, 1970). High



susceptibility to induction of mammary tumors

by urethane (Bentvelzen et al, 1970). High incidence of gastric tumors after administration of methylcholanthrene by gavage (Akamatsu and Barton, 1974). Susceptible to fibrosarcoma induction by methylcholanthrene (Strong, 1952).

Highly susceptible to the induction of hepatocellular tumors by various carcinogens, with the volume of hepatic

lesions being >100-fold greater than in more resistant strains.

Susceptibility is linked to at least six chromosomal regions (Dragani et al, 1995). Phenobarbitone

in the diet to give an intake of 85 mg/kg per day resulted in 70% of animals developing basophilic nodules by 91 weeks of age (contrast 4% in C57BL/6), but no increase in liver carcinomas (Evans et al, 1992). However, there was a two-fold greater level of DNA synthesis in C3H mice relative to C57BL/6 mice after partial hepatectomy, though partial hepatectomy is a tumor promoter in C57BL/6 but not in C3H mice (Bennett et al, 1995). Insensitive to histamine (Brown, 1965). Airways of C3H/HeJ hyporeactive to acetylcholine (Zhang et al, 1995). Resistant to teratogenic effect of acetazolamide (Green et al, 1973).

Pentobarbital i.p. induces hepatic epoxide hydase (Oesch et al, 1973). Sensitive

to X-irradiation (Roderick, 1963). Long survival on Warfarin (Lush and Arnold, 1975). Sensitive to hyperbaric oxygen (Hill et al, 1968). Sensitive uterine response

to estrogen's (Chai and Dickie, 1966). Short hexobarbital sleeping time (Vesell, 1968). Long survival in 90% oxygen and highly susceptible to pulmonary hyaline-membrane formation (Lieberman and Kellog, 1967). Resistant to the induction of pulmonary fibrosis by bleomycin (contrast C57BL/6) (Haston et al, 1996), and irradiation though the

sensitivity

of lung fibroblasts to irradiation in-vitro does not correlate with in-vivo sensitivity (Dileto and Travis, 1996). Sensitive to chloroform toxicity (Deringer et al, 1953). Susceptible to toxic effects of isoniazid (Taylor, 1976). High ED50 to behavioral effects of nicotine (Marks et al, 1989).

Low 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). No increase in renal lipid peroxidation following treatment with nickel (Misra et al, 1991). 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). High histamine release from peritoneal mast cells induced

by Ca²⁺ ionophore A23187 (contrast C57BL/6) (Toda et al, 1989). Cadmium highly hepatotoxic (Shaikh et al, 1993). Resistant to ozone-induced decreases of tracheal potential (Takahashi et al, 1995, Kleeberger et al, 1993). Susceptible to weight loss induced by cocaine, but this is attenuated by anisomycin (Shimosato et al, 1994). Estrogen does not induce

an increase in VLDL and LDL-cholesterol (like BALB/c, contrast C57BL/6 and C57L) (Srivastava, 1995).

Genetics

Coat colour genes

- A, B, C, D : agouti (wild type).

Histocompatibility

- H-2^k, 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^b, Hba^c, Hbb^a, Idh-1^a, Ldr-1^a, Mod-1^a, Mup-1^a, Pep-3^b, Pgm-1^b, Pgm-2^a, Trf^b.

This strain carries the Mus musculus musculus Y-chromosome, while others have the M. m. domesticus type (Nishioka, 1987).

Immunology

Sensitive to amyloid induction but low level of spontaneous amyloid formation (Ram et al, 1969). Low lymphocyte phytohemagglutinin response (Heiniger et al, 1975). Good immune response to small doses of bovine gamma globulin (Levine and Vaz, 1970). Poor immune response to Cholera A and B antigens (Cerny et al, 1971). Good splenic PFC immune response to pneumococcal polysaccharide (Amsbaugh et al, 1972). Immune response of SJL mice to type-III pneumococcal polysaccharide declines by 42 weeks, in contrast to BALB/c and C3H (Smith, 1976). Females fail to reject male skin grafts after 100 days (contrast nine strains) (Gasser and Silvers, 1971).

Poor immune response to ovomucoid and ovalbumin (Vaz et al, 1971). Poor primary immune response to bovine serum albumin (James and Milne, 1972). Good immune response to Salmonella anatum, S. senftenberg and S. strasbourg lipopolysaccharide (Di Pauli, 1972).

Responder to synthetic polypeptide Glu57, Lys38, Ala5 (Pinchuk and Maurer, 1965).

Good immune response to Vi antigen (Gaines et al, 1965). Precipitating and skin-sensitising antibodies have slow electrophoretic mobility (Fahey, 1965). High antibody affinity to HSA (Petty et al, 1972).

Erythrocytes have high agglutinability (Rubinstein et al, 1974). Low immune response to ferritin in He substrain (Young et al, 1976). Non-discriminator between 'H' and 'L' sheep erythrocytes (McCarthy and Dutton, 1975). High anti-DNP antibody concentration (Paul et al, 1970). Antibodies to lipoid A antigen do not cross-react with sheep red blood cells (contrast eight strains). Strain also resistant to toxic effect of Salmonella

lipopolysaccharide (Rank et al, 1969). Refractory to sensitising effects of HSF from Bordetella pertussis to histamine (contrast sixteen strains) (Bergman and Munoz, 1968). Good immune response to Pro-Gly-Pro-ovalbumin and (Pro- Gly- Pro)n (Fuchs et al, 1974). High susceptibility to IgE-mediated passive cutaneous anaphylaxis (De Souza et al, 1974). He substrain resistant to induction of anaphylactic shock by ovalbumin (Tanioka and Esaki, 1971). He and HeN

substrains are susceptible to experimental autoimmune orchitis induced by

two or three sc injections with viable syngeneic testicular germ cells without any adjuvants, but C3H/BiKi is resistant (Tokunaga et al, 1993). High immune response to ganglio-series gangliosides in C3H/HeN, but low response in C3H/

HeJ (Kawashima et al, 1992). Anti-BPO IgE monoclonal antibody did not produce potent systemic sensitisation sufficient

for provocation of lethal shock in most aged (six-ten months) mice (Harada et al, 1991). Carries a strain-specific allele at the alpha globin locus (Sato et al, 1996).

High natural killer cell response to the immunostimulant 7-allyl-8-oxoguanosine (Pope et al, 1994).

Infection

Resistant to infection by Salmonella typhimurium strain C5 (Plant and Glynn, 1974). Susceptible to Mycoplasma fermentans (Gabridge et al, 1972).

Experimental Mycoplasma pulmonis infection results in acute pneumonia with severe hemorrhage, edema and often death (Faulkner et al, 1995). Susceptible to mammary tumor virus, which is carried

in an active form in unfostered substrains (Murray and Little, 1967). Susceptible

to oncogenic effect of polyoma virus given at birth (Law, 1966). Susceptible to measles virus induced encephalitis, which correlates with a high cytotoxic T-lymphocyte response (like C57BL/6, contrast BALB/c) (Niewiesk et al, 1993).

Susceptible to Mycobacterium marinum (Shepard and Habas, 1967). Susceptible to infection by Mycobacterium marinum (Yamamoto et al, 1991). Susceptible to infection by Entamoeba histolytica (Neal and Harris, 1975). Resistant to mouse hepatitis virus (Bang and Warwick, 1960). 100% transmission of murine leukemia virus (Scripps) through three successive generations (Jenson et al, 1976). Highly susceptible to measles virus (Rager-

Zisman et al, 1976). Highly susceptible to tumor induction by polyoma virus (Freund et al, 1992). Following administration

of murine cytomegalovirus, C3H mice exhibited minimal carditis after neonatal or adult infection. However neonatal infection appears to accelerate age-related cardiopathy, which is severe in retired breeders of this strain. (contrast BALB/c and C57BL/10) (Price et al, 1991). Highly susceptible to Lyme borreliosis (Borrelia burgdorferi) when inoculated at three weeks of age and as adults.

Mice inoculated at age three weeks also developed polyarthritis, but severity was reduced when inoculated as adults.

Carditis was also common (Barthold et al, 1990), and mice were susceptible to the development of arthritis (contrast BALB/c) (Matyniak and Reiner, 1995). Resistant

to intra-vaginally inoculated Neisseria gonorrhoea (Johnson et al, 1989).

Resistant to infection with Ehrlichia risticii (Williams and Timoney, 1994). 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).

Life-span and spontaneous disease

Almost 100% of mammary tumors in females of unfostered substrains (Heston, 1963). Mammary adenocarcinomas

in unfostered substrains less than 1% in males, 95% in breeding and 88% in

virgin females. Lymphatic leukemia zero incidence (Hoag, 1963). Mammary tumors 40% at 18.8 months in C3HfC57BL, but 99% at 7.2 months in unfostered C3H (Heston and Vlahakis, 1971). Mammary tumors 37% at two years in fostered substrain (Bentvelzen et al, 1970). Median latent period to develop mammary tumors in unfostered substrains ranged from 276 to 566 days, depending on breeding status and environmental

stress (Riley, 1975). A high proportion of the mammary tumors are of the acinar type (Tengbergen, 1970). Incidence

of mammary tumors reduced by bromocriptine and interferon Stravaravdi et al, 1991). Hepatomas 72-91% in males at 14 months, 59% in virgin females,

30-38% in breeding females (Heston, 1963). Hepatomas have eosinophilic cytoplasmic inclusion bodies (Liebelt et al, 1971). Good model of genetic

predisposition to hepatocellular tumors, susceptibility being associated with six

chromosomal regions (Dragani et al, 1995). Point mutations in H-ras do not generally play a major or initiating role in spontaneous hepatocarcinogenesis in this strain (Enomoto et al, 1993).

Lung adenomas 2-10% in fostered A substrain, leukemia 6-

30% (Muhlbock and Tengbergen, 1971). Occasional Harderian gland tumors (Heston, 1963). Rare "lipomatous" hamartomas or choristomas have been noted (Adkison and Sundberg, 1991). Life-span in SPF fostered conditions intermediate in both sexes (590 days in males, 676 days in

females). Liver tumors 9-23%, lung tumors 2-10% and mammary tumors 21-36%.

Heart defects 13-26% and cystic ovaries 13-26% (Festing and Blackmore, 1971). The relationship of genotype, sex, body weight, and growth parameters to lifespan in inbred and hybrid mice is described

by Ingram et al (1982). The influence of MHC on aging is described by Smith and Walford (1977). Mean survival 98 ± 3.0 weeks. The influence of the H-2 and H-1 histocompatibility upon life-span and cancer incidence is described by Smith and Walford (1978). Tail lesions similar in appearance to bite wounds were found in grouped C3H/HeJ by Les (1972). Develop dystrophic cardiac calcification, which may be related to disturbed myocyte calcium metabolism (Brunnert, 1997). Can be made obese by a suitable diet (Fenton and Dowling, 1953).

Resistant to the development of aortic cartilaginous metaplasia (contrast C57BL/6) (Qiao et al, 1995). Resistant to diet-induced aortic fatty streak lesions which correlates with a high level of paroxinase mRNA (contrast C57BL/6) (Shih et al, 1996).

Miscellaneous Recommended host for the following transplantable tumors:

lymphosarcoma 6C3HED and mammary

adenocarcinomas C3HBA and H2712 (Kaliss, 1972).

Recommended host for sarcoma BP8 used as a model for screening potential anticancer

drugs

(EORTC Screening Group, 1972). High mortality after neonatal thymectomy (Law, 1966). High rate of spontaneous mutations and total deviants (Schlager and Dickie, 1967). Characteristics of the C3H strain have been described by Festing (1997) and Lyon et al, (1996).

Physiology and biochemistry

Low serum calcium in Fg substrain but He substrain has high level at 4

months (Barrett et al, 1975).

High serum

cholesterol (Bruell et al, 1962). High plasma cholesterol and triglycerides. High erythrocyte catalase (Hoffman and Rechcigl, 1971). Low serum haptoglobin level (Peacock et al, 1967). Low peripheral nerve conduction velocity (Hegmann, 1972). Low percentage of time spent sleeping with low percentage of slow-wave sleep and small diurnal variation (Valatx and Bugat, 1974). Low metabolic rate (Pennycuik, 1967). High liver tyrosine aminotransferase level in fasted mice (Blake, 1970). Low adrenal corticosteroid production (Nandi et al, 1967). High peptidyl proline hydroxylase activity in tumor tissue and mammary gland fat pad (Cutroneo et al, 1973). Slow cell turnover as judged by rate of clearance of DNA-bound radioactivity (Heiniger

et al, 1972). Harderian gland has a high porphyrin content (Margolis, 1971). Low hepatic ammonia-lyase activity in two substrains (Hanford et al, 1974).

Low spermatozoal beta-glucuronidase activity (Erickson, 1976). Low basal level of renal glutathione S-transferase but high basal level of renal glutathione reductase (Misra et al, 1991). Low hepatic nicotinamide N-methyltransferase

levels (Scheller et al, 1996). High level of alpha-fetoprotein in plasma at seven days (Adinolfi et al, 1990). Resistant to the development of atherosclerosis on a semi-synthetic high fat diet (Nishina et al, 1993). Loci on chromosomes 1, 3, 5 and 11 are associated with variation in high density lipoprotein levels with coordinate expression of cholesterol-

7-alpha hydroxylase in a cross involving atherosclerosis susceptible C57BL/6 mice (Machleder et al, 1997). Hepatic iodothyronine deiodinase activity was only 18% of that found in C57BL/6 mice (Schoenmakers et al, 1993).

Decreased levels of deiodinase mRNA and hyperthyroxinemia associated with a 21-base pair insert in the promoter region of the type 1 deiodinase gene (Maia et al, 1995). Resistant to severe hypercapnia with hypoxia assessed by elevated minute ventilation rate (Tankersley et al, 1994).

Has a slow and deep breathing pattern phenotype (contrast C57BL/6) (Tankersley et al, 1997). High intra-ocular pressure (John et al, 1997).

Reproduction

Breeding performance intermediate/ good. Good reproductive performance, litter size 6.4, sterility 10% (Nagasawa et al, 1973). Large litter size, high proportion of females produce four or more litters and high proportion of fertile matings (Fernandes et al, 1973). C3H/HeJ has shorter and less regular oestrus cycles than C57BL/6J (Nelson et al, 1992). Early opening of vagina and first cornification

(compared with C57BL/6 and DBA/2), but late onset of cyclicity (Nelson et al, 1990).

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