ACI (August Copenhagen Irish)

ACI/SegHsd

Developed in 1926 by Curtis and Dunning, Columbia University Institute for Cancer Research, after accidental mating between an August male with an Irish coat and a COP (Copenhagen 2331) female (Russell-Lindsay, 1979). To Heston in 1945, then to National Institute of Health, Bethesda, USA, in 1951 at F41 (Hansen *et al*, 1981).

Derived from a nucleus colony obtained from Dr. A. Segaloff's colony at the Ochsner Medical Center, Jefferson, Louisiana, USA.

RESEARCH APPLICATIONS

Hepatitis, P-450, locomotor activity, alcohol, spontaneous tumors of endocrine glands, congenital malformations, stomach tumors.

CHARACTERISTICS

Animal model

The ACI rat is an animal model for congenital genitourinary anomalies (Marshall and Beisel, 1978). A diet deficient in choline and methionine has been used to develop a rat model of fatty liver transplantation (Teramoto *et al*, 1993). Will grow Morris hepatomas 3924A, which can be used as a model for the treatment of liver cancer (Yang *et al*, 1995).

Anatomy

Uterus of type "uterus bipertitus" (Yosida *et al*, 1985).

Behavior

The ACI rat is docile. Long latency to emerge into familiar and novel environment (Harrington 1971). Strong 24-hr rhythm in wheel running activity when compared with LEW (Siebert and Wollnik, 1991). Intermediate response to an acoustic stimulus (Glowa and Hansen, 1994). Differences exist in the coupling of the multiple circadian oscillators that generate the overall pattern of wheel running activity (Wollnik, 1991). The mean area of arginine-vasopressin-immunoreactive (AVP-ir) fibres was significantly larger in strain LEW than in strains ACI and BH (Wollnik and Bihler, 1996).

Drugs

Ptaquiloside, a carcinogen in bracken fern, induces adenomas, adenocarcinomas, and malignant fibrous histiocytomas of the ileum and transitional cell carcinomas, keratinizing squamous cell carcinomas, and sarcomas of the urinary bladder in females (Hirono *et al*, 1987). Caffeine suppresses 2-acetylaminofluorine-induced hepatic tumors (Hosaka *et al*, 1984). Susceptible to the development of glioblastomas of a mixed oligoastrocytic type following treatment with N-methyl-N-nitrosourea in the drinking water (Shibutani *et al*, 1993). Like F344, refractory to the development of prostatic hyperplasia induced by citral compared with outbred Wistar and Sprague-Dawley rats (Scolnik *et al*, 1994). Highly sensitive to the development of N-methyl-N'-nitrosoguanidine (MNNG) induced gastric cancer though levels of adduct were same as in the resistant BUF strain (Sugimura *et al*, 1995).

Susceptible to the induction of tumors of the large intestine and forestomach by 1-hydroxyanthraquinone, though incidence can be reduced by the nonsteroidal anti-inflammatory drug indomethacin (Tanaka *et al*, 1995). ACI females are very sensitive to the induction of mammary tumors by estrogens (Holtzman *et al*, 1979; Holtzman *et al*, 1981). Lucidin, present in the madder root (*Rubia tinctorum*) is carcinogenic in ACI rats (Westendorf *et al*, 1998).

High hepatic metabolism of aniline in females (Page and Vesell, 1969). Absorbs diethylstilboestrol at intermediate rate, leading to a high incidence of mammary tumors (Dunning *et al*, 1947; Rothschild *et al*, 1987). High LD50 (120 mg/kg) for pentobarbital sodium (Shearer *et al*, 1973). Long pentobarbitone sleeping time (Vieregge *et al*, 1987). Susceptible to the induction of gastric tumors by N-methyl-N-nitro-N-nitrosoguanidine (Ohgaki *et al*, 1983).

Genetics

Coat color genes

- *A, B, h^{i}* : black agouti with white belly and feet.

Histocompatibility

- *RT1^{av1}*.

Biochemical markers

- *Acon-1^{b}, Acp-2^{a}, Ahd-2^{c}, Akp-1^{b}, Alb^{a}, Amyl-1^{b}, Cryg-1^{b}, Es-1^{b}, Es-2^{a}, Es-3^{a}, Es-4^{b}, Es-6^{b}, Es-7^{b}, Es-8^{b}, Es-9^{a}, Es-10^{a}, Es-14^{a}, Es-15^{a}, Es-16^{a}, Es-18^{a}, Fh-1^{b}, Gc^{a}, Glo-1^{b}, Gox-1^{a}, Hbb^{b}, Igk-1^{b}, Lap-1^{b}, Mgd-1^{a}, Mup-1^{b}, Pep-3^{a}, Pgd^{b}.* (Bender *et al*, 1994).

Immunology

Widely used in transplantation immunology, particular using transplantation of ACI to LEW heart and other tissues (Buttemeyer *et al*, 1995; Levy and Alexander, 1995; Tchervenkov *et al*, 1995). Resistant to the development of experimental autoimmune glomerulonephritis (Naito *et al*, 1991). Resistant to the development of experimental autoimmune myasthenia gravis (Biesecker and Koffler, 1988). Resistant to the induction of arthritis by type II collagen (Griffiths and DeWitt, 1984). Sensitive to the induction of arthritis by type II collagen, but resistant the induction of arthritis by type XI (Cremer *et al*, 1995). Neonatal pancreatic islets derived by non-enzymic (in vitro) isolation procedures cannot be transplanted across MHC barriers without any immune suppression like most other strains but in contrast with F344 (Ketchum *et al*, 1992). The major histocompatibility complex has been studied (Armerding *et al*, 1974a; 1974b; Goldner-Sauve *et al*, 1985; Kunz and Gill, 1974; Luderer *et al*, 1976). Low antibody response to porcine LDHA and LDH_B; high antibody response to BSA and to the NIP hapten coupled to BSA (Würzburg *et al*, 1973). Alphafetoprotein and albumin genes studied by Boulter and Sell (1984).

Infection

More resistant to the tumorigenic effect of human polyomavirus BK (BKV) because of RT1^{a} (Noss and Staunch, 1984). Does not develop chronic progressive myeloneuropathy induced by HTLV-1, in contrast with WKAH (Yoshiki, 1995)

Life-span and spontaneous disease

Mean survival time 26.1 months for males, 24.9 months for females. (Maekawa and Odashima, 1975). Mean survival time 31.5 months for males (Cameron *et al*, 1982). Urogenital abnormalities in 22-28% of males and 18-20% of females.

The most common neoplastic lesions in males were: testis 46%, adrenal medulla 16%, pituitary 5%, skin and ear duct 6%. In females: pituitary 21%, uterus 13%, mammary gland 11% and adrenal medulla 6% (Maekawa and Odashima, 1975). Spontaneous adenocarcinomas of ventral prostate (Shain *et al*, 1975; Ward *et al*, 1980; Isaacs, 1984). This is substantially increased by a high fat diet (Kondo *et al*, 1994). High survival to 2 years of age at 74% in males and 70% in females. However, a high incidence of relatively mild chronic renal disease and a high incidence of hydronephrosis and the congenital renal agenesis may make the strain unsuitable for long-term toxicological studies (Solleveld and Boorman, 1986). Four spontaneous kidney and five bladder tumors found among a cohort of 300 rats maintained for 30 months (Vanmoorselaar *et al*, 1993).

Aplasia of one kidney almost always associated with aplasia of ipsilateral genital tract. (Marshall and Beisel, 1978; Marshall *et al*, 1978). Transmission of these defects is polygenic (Cramer and Gill, 1975). Hydronephrosis (4-6%) in both sexes may be due to a mesonephric duct deformity (Fujita *et al*, 1979).

Effects of retinoids on tumors of the skin, prostate and endocrine pancreas studied by Ohshima *et al* (1985). Urolithiasis seen at an average age of 144 days (Kunstyr *et al*, 1982).

Miscellaneous

Will grow Morris hepatomas 3924A, which can be used as a model for the treatment of liver cancer (Yang *et al*, 1995). Characteristics of the ACI strain have been described by Festing (1979) and Greenhouse *et al* (1990).

Physiology and biochemistry

Low serum thyroxine (Esber *et al*, 1974). Low systolic blood pressure (Hansen *et al*, 1973). Low blood pressure, reaching 124 mmHg at ten weeks of age (Tanase *et al*, 1982). Almost free of spike-wave discharges associate with absence epilepsy seen in strain WAG/Rij, while BN/Rij was intermediate (Inoue *et al*, 1990). Copper deficiency results in pigmented patterns similar to that of mottled mouse, a model for Menkes' kinky hair syndrome (Miranda *et al*, 1992). Liver gangliosides are of the a-type (cf LEA,LEW and BUF) (Kasai *et al*, 1993)

Reproduction

Poor reproductive performance and low litter size (Hansen *et al*, 1973). High (11%) early prenatal mortality and high (10%) incidence of congenital malformations (Shoji 1977). High in-utero embryo mortality, which depends on maternal genotype (Cramer and Gill 1975).

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