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ENVIGO

Research Models  
and Services

Inbred Rats

## ACI (August Copenhagen Irish)

### Origin

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).

### ACI/SegHsd

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 LD<sub>50</sub> (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 <sup>i</sup> : black agouti with white belly and feet.
Histocompatibility	- RT1 <sup>av1</sup> .
Biochemical markers	- Acon-1 <sup>b</sup> , Acp-2 <sup>a</sup> , Ahd-2 <sup>c</sup> , Akp-1 <sup>b</sup> , Alb <sup>a</sup> , Amyl-1 <sup>b</sup> , Cryg-1 <sup>b</sup> , Es-1 <sup>b</sup> , Es-2 <sup>a</sup> , Es-3 <sup>a</sup> , Es-4 <sup>b</sup> , Es-6 <sup>b</sup> , Es-7 <sup>b</sup> , Es-8 <sup>b</sup> , Es-9 <sup>a</sup> , Es-10 <sup>a</sup> , Es-14 <sup>a</sup> , Es-15 <sup>a</sup> , Es-16 <sup>a</sup> , Es-18 <sup>a</sup> , Fh-1 <sup>b</sup> , Gc <sup>a</sup> , Glo-1 <sup>b</sup> , Gox-1 <sup>a</sup> , Hbb <sup>b</sup> , Igk-1 <sup>b</sup> , Lap-1 <sup>b</sup> , Mgd-1 <sup>a</sup> , Mup-1 <sup>b</sup> , Pep-3 <sup>a</sup> , Pgd <sup>b</sup> . (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 LDH<sub>A</sub> and LDH<sub>B</sub>; 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<sup>a</sup> (Noss and Stauch, 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).

## References

- Armerding D, Katz DH, Benacerraf B (1974a) Immune response genes in inbred rats. I. Analysis of responder status to synthetic polypeptides and low doses of bovine serum albumin. *Immunogenet.* 1, 329-339.
- Armerding D, Katz DH, Benacerraf B (1974b) Immune response genes in inbred rats. II. Segregation studies of the GT and GA genes and their linkage to the major histocompatibility complex. *Immunogenet.* 1, 340-351.
- Bender K, Balogh P, Bertrand MF, den Bieman M, von Deimling O, Eghtessadi S, Gutman GA, Hedrich HJ, Hunt SV, Kluge R, Matsumoto K, Moralejo DH, Nagel M, Portal A, Prokop C-M, Seibert RT, van Zutphen LFM (1994) Genetic characterization of inbred strains of the rat (*Rattus norvegicus*). *J. Exp. Anim. Sci.* 36, 151-165.
- Biesecker G, Koffler D (1988) Resistance to experimental autoimmune myasthenia gravis in genetically inbred rats. *J. Immunol.* 140, 3406-3410.
- Boulter J, Sell S (1984) Polymorphism of rat albumin genes. *Tumor Biol.* 5, 365-370.
- Buttemeyer R, Rao U, Jones NF (1995) Peripheral-nerve allograft transplantation with FK506 – functional, histological, and immunological results before and after discontinuation of immunosuppression. *Annals of Plastic Surgery* 35, 396-401.
- Cameron TP, Lattuada CP, Kornreich MR, Tarone RE (1982) Longevity and reproductive comparisons for male ACI and Sprague-Dawley rat aging colonies. *Lab. Anim. Sci.* 32, 496-499.
- Cramer DV, Gill III TJ (1975) Genetics of urogenital abnormalities in ACI inbred rats. *Teratology* 12, 27-32.
- Cremer MA, Griffiths MM, Terato K, Kang AH (1995) Type XI and II collagen-induced arthritis in rats: characterization of inbred strains of rats for arthritis-susceptibility and immune-responsiveness to type XI and II collagen. *Autoimmunity* 20, 53-61.
- Dunning WF, Curtis MR, Segaloff A (1947) Strain differences in response to diethylstilbestrol and the induction of mammary gland and bladder cancer in the rat. *Cancer Res.* 7, 511-521.
- Esber HJ, Menniger FF Jr, Bogdon AE (1974) Variation in serum hormone concentrations in different rat strains. *Proc. Soc. Exp. Biol. Med.* 146, 1050-1053.
- Festing MFW (1979) Inbred strains, in *The Laboratory Rat Vol. I. Biology and Diseases* (Baker HJ, Lindsey JR and Weisbroth SH, eds), pp. 55-72. Academic Press, New York.
- Fujita K, Fujita HM, Ohtawara Y, Suzuki K, Tajima A, Aso Y (1979) Hydronephrosis in ACI/N rats. *Lab. Anim.* 13, 325-327.
- Glowa JR, Hansen CT (1994) Differences in response to an acoustic startle stimulus among forty-six strains. *Behav. Genet.* 24, 79-84.
- Goldner-Sauve AJ, Fuks A, Guttman RD (1985) Structural studies of the class-II histocompatibility antigens in the ACI rat. *Can. J. Biochem. Cell Biol.* 63, 1241-1249.
- Greenhouse DD, Festing MFW, Hasan S, Cohen AL (1990) Catalogue of inbred strains of rats. In: *Genetic monitoring of inbred strains of rats* (Hedrich HJ, ed). Stuttgart, New York: Gustav Fischer Verlag, pp 410-480.
- Griffiths MM, DeWitt CW (1984) Genetic control of collagen-induced arthritis in rats: the immune response to type II collagen among susceptible and resistant strains and evidence for multiple gene control. *J. Immunol.* 132, 2830-2836.
- Hansen CT, Judge FJ, Whitney RA (1973) Catalogue of NIH Rodents. DREW Publication N° 74-606. Department of Health, Education, and Welfare, Washington, DC, USA.
- Hansen CT, Potkay S, Watson WT, Whitney RA (1981) NIH Rodents, 1980 Catalogue. NIH Publication N° 81-606. Department of Health and Human Services, Washington, DC, USA.
- Harrington GM (1971) Strain differences among rats initiating exploration of differing environments. *Psychon. Sci.* 23, 348-349.
- Hirono I, Ogino H, Fujimoto M, Yamada K, Yoshida Y, Ikagawa M, Okumura M (1987) Induction of tumors in ACI rats given a diet containing ptaquiloside, a bracken carcinogen. *J. Natl. Cancer Inst.* 79, 1143-1149.
- Holtzman S, Stone JP, Shellabarger CJ (1979) Influence of diethylstilbestrol treatment on prolactin cells of female ACI and Sprague-Dawley rats. *Cancer Res.* 39, 779-784.
- Holtzman S, Stone JP, Shellabarger CJ (1981) Synergism of estrogens and X-rays in mammary carcinogenesis in female ACI rats. *J. Natl. Cancer Res.* 67, 455-459.
- Hosaka S, Nagayama H, Hirono I (1984) Suppressive effect of caffeine on the development of hepatic-tumors induced by 2-acetylaminofluorene in ACI rats. *Gann* 75, 1058-1061.
- Inoue M, Peeters BWMM, van Luijtelaar ELJM, Vossen JMH, Coenen AML (1990) Spontaneous occurrence of spike-wave discharges in five inbred strains of rats. *Physiol. Behav.* 48, 199-201.
- Isaacs JT (1984) The aging ACI/Seg versus Copenhagen male rat as a model system for the study of prostatic carcinogenesis. *Cancer Res.* 44, 5785-5796.
- Kasai N, Kamimura A, Miyoshi I, Ariga T (1993) Ganglioside distribution in the liver of inbred strains of rats and the cancerous liver of LEC rats. *Journal of Biochemistry* 113, 251-257.
- Ketchum RJ, Moore WV, Hegre OD (1992) Increased islet allograft survival after extended culture by a mechanism other than depletion of donor apcs - lack of correlation between the elimination of donor MHC class-II-positive accessory cells and increased transplantability. *Transplant.* 54, 347-351.
- Kondo Y, Homma Y, Aso Y, Kakizoe T (1994) Promotional effect of 2-generation exposure to a high-fat diet on prostate carcinogenesis in ACI/Seg rats. *Cancer Res.* 54, 6129-6132.
- Kunstryl I, Naumann S, Werner J (1982) Urolithiasis in female inbred SPF rats. Possible predisposition of DA and ACI strains. *Z. Versuchstierk.* 24, 214-218.
- Kunz HW, Gill TJ III (1974) Genetic studies in inbred rats. I. Two new histocompatibility alleles. *J. Immunogenet.* 1, 413-420.
- Levy AE, Alexander JW (1995) Administration of intragraft interleukin-4 prolongs cardiac allograft survival in rats treated with donor-specific transfusion/cyclosporin. *Transplant.* 60, 405-406.
- Luderer AA, Maurer PH, Woodland RT (1976) Genetic control of the immune response in rats to the known sequential polypeptide (Tyr-Glu-Ala-Gly)n. I. Antibody responses. *J. Immunol.* 117, 1079-1084.
- Maekawa A, Odashima S (1975) Spontaneous tumors in ACI/N rats. *J. Natl. Cancer Inst.* 55, 1437-1441.
- Marshall FF, Garcia-Bunuel R, Beisel DS (1978) Hydronephrosis, renal agenesis, and associated genitourinary anomalies in ACI rats. *Urology* 11, 58-61.
- Marshall FF, Beisel DS (1978) The association of uterine and renal anomalies. *Obstet. Gynecol.* 51, 559-562.
- Miranda M, Bartoli G, Ragnelli AM, Cittadini A, Palozza P, Aimola P, Zarivi O, Bonfigli A (1992) Copper deficiency in the rat – morphofunctional aspects. *Journal of Submicroscopic Cytology and Pathology* 24, 273-279.
- Naito I, Kagawa M, Sado Y, Okigaki T (1991) Strain specific responses of inbred rats on the severity of experimental autoimmune glomerulonephritis – presence of a broad-spectrum of the susceptibility. *Int. J. Immunopath. Pharmacol.* 4, 145-154.
- Noss G., Staunch G (1984) Oncogenic activity of the BK type of human papovavirus in inbred rat strains. *Arch Virol* 81, 41-51.
- Ohgaki H, Kawachi T, Matsukura N, Morino K, Miyamoto M, Sugimura T (1983) Genetic control of susceptibility of rats to gastric carcinoma. *Cancer Res.* 43, 3663-3667.
- Ohshima M, Ward JM, Wenk ML (1985) Preventive and enhancing effects of retinoids on the development of naturally-occurring tumors of skin, prostate-gland, and endocrine pancreas in aged male ACI/SegHapBR rats. *J. Natl. Cancer Inst.* 74, 517-524.
- Page JG, Vesell ES (1969) Hepatic drug metabolism in ten strains of Norway rat before and after pretreatment with phenobarbital. *Proc. Soc. Exp. Biol. Med.* 131, 256-261.
- Rothschild TC, Boylan ES, Calhoun RE, Vonderharr BK (1987) Transplacental effects of diethylstilbestrol on mammary development and tumorigenesis in female ACI rats. *Cancer Res.* 47, 4508-4516.
- Russell Lindsay J (1970) Historical foundations. In: *The laboratory rat*. (Baker HJ, Russell Lindsay J, Weisbroth SH, eds). New York: Academic Press, pp 1-36.
- Scolnik MD, Servadio C, Abramovici A (1994) Comparative-study of experimentally induced benign and atypical hyperplasia in the ventral prostate of different rat strains. *J. Androl.* 15, 287-297.
- Shain SA, McCullough B, Segaloff A (1975) Spontaneous adenocarcinomas of the ventral prostate of aged AxC rats. *J. Natl. Cancer Res.* 55, 177-180.
- Shearer D, Creel D, Wilson CE (1973) Strain differences in the response of rats to repeated injections of pentobarbital sodium. *Lab. Anim. Sci.* 23, 662-664.
- Shibutani M, Maekawa A, Okeda R, Mitsumori K, Imazawa T, Yoshida J, Onodera H, Hayashi Y (1993) An experimental-model for anaplastic astrocytomas and glioblastomas using adult F344 rats and N-methyl-N-nitrosourea. *Acta Pathologica Japonica* 43, 464-474.
- Shoji R (1977) Spontaneous occurrence of congenital malformation and mortality in prenatal inbred rats. *Proc. Japan Acad.* 53, 54-67.
- Siebert U, Wollnik F (1991) Wheel-running activity rhythms in 2 inbred strains of laboratory rats under different photoperiods. *Physiol. Behav.* 50, 1137-1143.
- Solleveld HA, Boorman GA (1986) Spontaneous renal lesions in five rat strains. *Toxi. Pathol.* 14, 168-174.
- Straeten E (1987) An animal model for adenosine-induced bronchoconstriction. *Am. Rev. Respir. Dis.* 136, 374-378.
- Sugimura T, Inoue R, Ohgaki H, Ushijima T, Canzian F, Nagao M (1995) Genetic polymorphisms and susceptibility to cancer development. *Pharmacogenetics* 5, S161-S165.
- Tanaka H, Hirose M, Hagiwara A, Imaida K, Shirai T, Ito N. (1995) Rat strain differences in catechol carcinogenicity to the stomach. *Food and Chemical Toxicology* 33, 93-98.
- Tanase H, Yamori Y, Hansen CT, Lovenberg W (1982) Heart size in inbred strains of rats. Part 1. Genetic determination of the development of cardiovascular enlargement in rats. *Hypertension* 4, 864-872.
- Tchervenkov JI, Cofer BR, Davies C, Alexander JW (1995) Indefinite allograft survival induced by the combination of multiple donor-specific transfusions, cyclosporine, and an anti-T cell monoclonal-antibody in a protocol relevant to cadaveric organ-transplantation - the importance of prolonged posttransplant cyclosporine coverage. *Transplant.* 59, 821-824.
- Teramoto K, Bowers JL, Khetry U, Palombo JD, Clouse ME (1993) A rat fatty liver-transplant model. *Transplant.* 55, 737-741.
- Vanmoorselaar RJA, Ichikawa T, Schaafsma HE, Jap PHK, Isaacs JT, Vanstratum P, Ramaekers FCS, Debruyne FMJ, Schalken JA (1993) The rat bladder-tumor model system RBT resembles phenotypically and cytogenetically human superficial transitional-cell carcinoma. *Urological Research* 21, 413-421.
- Vieregge VT, Hackbarth H, Bercher P (1987) Die Pentobarbitalschlafzeit zur pharmakogenetischen Differenzierung von Ratteninzzuchtstammen. *Z. Versuchstierk.* 29, 209-217.
- Ward JM, Reznik G, Stinson GF, Lattuada CP, Longfellow DG, Cameron TP (1980) Histogenesis and morphology of natural occurring prostatic carcinoma in the ACI/SegHap BR rat. *Lab. Invest.* 43, 517-522.
- Westendorf J, Pfau W, Schulte A (1998) Carcinogenicity and DNA adduct formation observed in ACI rats after long-term treatment with madder root, *Rubia tinctorum* L. *Carcinogenesis* 19, 2163-2168.
- Wollnik F (1991) Strain differences in the pattern and intensity of wheel running activity in laboratory rats. *Experientia* 47, 593-598.
- Wollnik F, Bihler S (1996) Strain differences in the distribution of arginine-vasopressin- and neuropeptide Y-immunoreactive neurons in the suprachiasmatic nucleus of laboratory rats. *Brain Res.* 724, 191-199.
- Würzburg U, Schütt-Gerowitt H, Rajewski K (1993) Characterization of an immune response gene in rats. *Eur. J. Immunol.* 3, 762-766.
- Yang R, Lin Q, Rescorla FJ, Grosfeld JL (1995) Experimental liver-cancer – improved response after hepatic-artery ligation and infusion of tumor-necrosis-factor-alpha and interferon-gamma. *Surgery* 118, 768-774.
- Yoshiki T (1995) Chronic progressive myeloneuropathic in WKAR rats induced by HTLV-1 infection as an animal model for HAM/TSP in humans. *Intervirology* 38, 229-237.
- Yosida TH et al (1985) Polymorphism of the external on the uterus of the inbred strain of the rat *Rattus norvegicus* and its genetics. *Proc. Jap. Acad.* 61, 125-127.



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