ENVIGO

Research Models and Services

Inbred Rats

DA (Dark Agouti)

Origin

Inbred by Odell, Oak Ridge National Laboratory, Tennessee, from heterogeneous stocks with unknown antecedents. To Wilson at Wistar Institute, who named it DA because it expressed the 'd' blood group allele, and it is a (agouti) in colour (Wilson, 1965). Palm and Black (1971) suggested that it might be related to COP, even though they differ in coat colour. To Agricultural Research Centre, Cambridge.

DA/OlaHsd

From Agricultural Research Centre to OLAC (now Envigo) in 1979.

Research applications

Urinary bladder tumors, autoimmune diseases, multiple sclerosis, collagen-induced arthritis.

Characteristics

Animal model

Defective bile acid transport found in females, might serve as an animal model for debrisoquine hydroxylation in man. (Reichen *et al*, 1986).

Anatomy

Study of the ossification of long bones of BDIX, BDE, BN, DA, LEW, AVN, and WISTAR (Štark *et al*, 1996). The thymus weight of virgin female DA rats is higher than that of AO rats (Leeming *et al*, 1984). DA rats have significantly larger intra- and infrapyramidal mossy fibre terminal fields (IIP-MF) than BDE (Prior *et al*, 1997).

Behavior

An extremely docile strain. Very rare episodes of absence (Willoughby and Mackenzie, 1992). DA is superior to BDE in on the radial-maze. DA rats revealed little freezing and had a high rearing activity, whereas BDE rats showed frequent freezing and reared rarely. (Prior *et al*, 1997). Acquisition and full performance in skilled forelimb use as measured by the 'staircase test'. Average acquisition, good final performance (Nikkhah *et al*, 1998). DA is more sensitive than SD to the induction of stereotyped behavior by dextrorotatory opoids (Ishmael *et al*, 1998).

Drugs

Susceptible to the development of 4-nitroquinoline 1-oxide induced squamous cell carcinomas of the tongue, with high proliferative response of the tongue epithelium (Kitano *et al*, 1992).

Genetics

Coat colour genes	- *A, B, C, H, P* : agouti.
Histocompatibility	- $RT1^{av1}$, $RT2^{b}$, $RT3^{a}$, $RT7^{a}$.
Biochemical markers	- $Acon\text{-}1^{b}$, $Acp\text{-}2^{a}$, $Akp\text{-}1^{b}$, Alb^{a}, $Amyl^{a}$, $Cryg\text{-}1^{a}$, $Es\text{-}1^{b}$, $Es\text{-}2^{a}$, $Es\text{-}3^{a}$, $Es\text{-}4^{b}$, $Es\text{-}6^{a}$, $Es\text{-}7^{b}$, $Es\text{-}8^{b}$, $Es\text{-}9^{a}$, $Es\text{-}10^{a}$, $Es\text{-}14^{a}$, $Es\text{-}15^{a}$, $Es\text{-}16^{a}$, $Es\text{-}18^{a}$, $Fh\text{-}1^{b}$, Gc^{a}, $Glo\text{-}1^{a}$, $Gox\text{-}1^{a}$, Hbb^{b}, $Igk\text{-}1^{b}$, $Lap\text{-}1^{b}$, $Mgd\text{-}1^{a}$, $Mup\text{-}1^{b}$, $Pep\text{-}3^{b}$, $Pg\text{-}1^{a}$, Pgd^{b}. (Bender *et al*, 1994).

Immunology

Widely used by immunologists and this strain is the inbred partner strain for a number of congenic strains. Susceptible to the induction of a number of autoimmune diseases. Susceptible to the induction of autoimmune thyroiditis (Rose, 1975). Develop severe collagen-induced arthritis following immunisation with bovine, chick or rat type II collagens. This is exacerbated by infection with rat cytomegalovirus. (Griffiths *et al*, 1994). Develops arthritis after injection of Freund's incomplete adjuvant alone (oil-induced arthritis, OIA). This is a self-limiting acute disease whereas collagen-induced arthritis follows a chronic course (Holmdahl and Kvick, 1992). DA is sensitive whereas LEW are relatively resistant (Holmdahl *et al*, 1992). A strong local expression of TNF-alpha, induced by arthritogenic stimuli may be important for the induction of arthritis (Mussener *et al*, 1995). After immunization with rat type II collagen (RCII) in incomplete Freund's adjuvant, DA rats showed a marked humoral RCII response and a Th1 cytokine profile, with expression of interferon-gamma and interleukin (IL)-2 mRNA (Mussener *et al*, 1997). Sensitive to the induction of arthritis by bovine type II and type XI collagen-induced arthritis (Cremer *et al*, 1995). Susceptible to the development of experimental allergic encephalomyelitis upon treatment with a myelin basic protein-specific T cell line derived from an F1 hybrid between resistant AO and susceptible DA strain rats (Mostaricastrojkovic *et al*, 1992). Although DA and LEW are both highly susceptible to the development of EAE, there are marked differences in the array of myelin epitopes capable of inducing the disease as well as MHC restriction of these epitopes between the two strains (Stepaniak *et al*, 1995). Rodent models of EAE have been described by Goverman and Brabb, 1996). Resistant to the development of experimental glomerulonephritis following injection of nephritogenic antigen from bovine renal basement membrane (Naito *et al*, 1991). Met-enkephalin increased H2O2 production by macrophages (Radulovic *et al*, 1995). The major histocompatibility complex has been described by Günther *et al*, 1972; Holmdahl and Kvick, 1992; Štark *et al*, 1968). Cyclic variations in the weight of lymphoid organs and in the lymphoid proliferation during the oestrus cycle (Habbal *et al*, 1988). Two epitopes of the myelin basic protein, residues 63-76 and 66-81, are encephalitogenic for DA (Smeltz *et al*, 1998).

Infection

Infection with *Hymenolepis diminuta* cysticercoids results in significant mastocytosis six weeks post infection and low persistence of worms (Ishih, 1992). Resistant to the induction of *Trypanosoma cruzi* (Rivera-Vanderpas *et al*, 1983). Sensitive to induction of arthritis by *Mycoplasma arthriditis* (Binder *et al*, 1990). No clinical signs after infection with sialodacryoadenitis virus (SDAV) in contrast with WAG/Rij rats (Bhatt and Jacoby, 1985). Average capacity for expulsion of *Trichinella spiralis*, ten days after infestation (Bell, 1992).

Life-span and spontaneous disease

Urinary bladder tumors 54% in males and 14% in females, with a peak incidence at 25-30 months of age (Deerberg *et al*, 1985). High incidence of hormone-dependent endometrial adenocarcinoma. A transplantable cell line (RUCA-I) derived from such a tumour in DA rats can produce these tumors in ectopic sites. The rate of proliferation is reduced by tamoxifen, and this cell line appears to be a suitable model for the study of molecular aspects of oestrogen and tamoxifen-dependent gene expression. (Schutze *et al*, 1992). Urolithiasis found in female rats at an average age of 118 days (Kunstyr *et al*, 1982). Genetic and pathologic influences on longevity of WIST, SPRD, DA and BDII have been described by Deerberg (1991).

Miscellaneous

Characteristics of the DA strain have been described by Festing (1979) and Greenhouse *et al* (1990).

Physiology and biochemistry

Possible model for deficiency of debrisoquine hydroxylation due to a lack of Cyp2D1 activity, which is equivalent to human Cyp2D6 (Al-Dabbagh *et al*, 1981), with the defect being due to a structurally altered db1 protein (Gonzalez *et al*, 1987). At least one other isoform of P450 of the Cyp2C or Cyp3A families may also be missing. Although DA rats may be used as a preliminary screen to identify Cyp2D6 substrates, interspecies differences in metabolism means that this strain could not be used to provide quantitative information regarding the contribution of Cyp2D6 to an oxidation in humans (Barham *et al*, 1994). Defective bile acid transport found in females, which may be related to deficient debrisoquine hydroxylation (Reichen *et al*, 1986). Hackbarth *et al* (1981) have described the glomerular filtration rate and renal plasma flow in DA and other strains. Hematological parameters and their relation to diet have been described by Hackbarth *et al* (1983). In studies of food intake and body weight gain, DA rats ingested mainly proteins and fats, in contrast with outbred Wistar rats, which are about equal quantities of fat, protein and carbohydrate (Larueachagiotis *et al*, 1994). Study of incorporation of lipids into the plasma lipid fractions of DA, GH, P and HW (Gibson *et al*, 1992). Low cholesterol response after hypercholesterolaemic diets (Bottger *et al*, 1995).

Reproduction

Short gestation period: 22.13 ± .71 days (Peters, 1986). Moderate production performance.

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RMS-1116-EU-02-PS-14