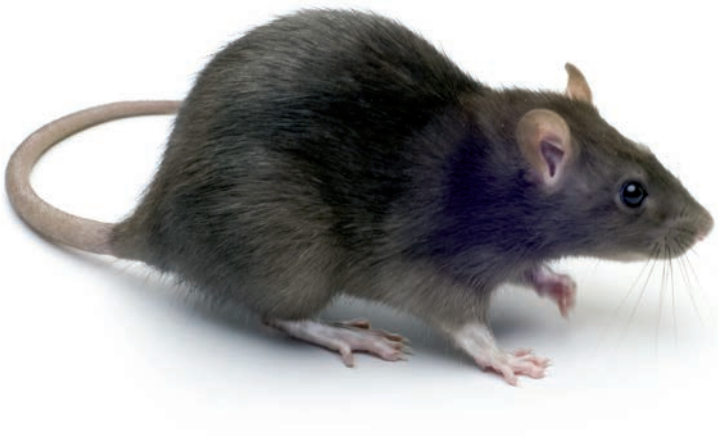

ENVIGO

Research Models and Services

Inbred Rats

BN (Brown Norway)

Origin

Developed in 1958 by Silvers and Billingham from a brown mutation maintained by King and Aptekman in a pen-bred colony (Billingham and Silvers 1959).

BN/RijHsd

In 1963, from Microbiological Associates Inc., Bethesda, USA to Radiobiological Institute-TNO, Rijswijk, The Netherlands. In 1994, to Harlan Nederland through acquisition. Harlan became Envigo in 2015.

BN/SsNOlaHsd

In 1980, from National Institutes of Health, Bethesda, USA to OLAC (now Envigo).

Research applications

Behavior, hydronephrosis, cancer research, myelocytic leukemia, aging, HgCl2-induced nephritis.

Characteristics

Animal model

The BN is an animal model for human acute myeloid leukemia (Colly and Hagenbeek, 1977). In this strain grows a transplantable myelocytic leukemia (BNML), which is a useful animal model for studying human acute myelocytic leukemia (Martens, *et al*, 1990).

Behavior

The BN strain is a docile rat. Poor performance in an active avoidance learning task, but good reference memory (Van Luijtelaar *et al*, 1988). Cannot be triggered into paradoxical sleep by dark pulse stimulation (Leung *et al*, 1992). Higher percentage of paradoxical sleep than LEW (Rosenberg *et al*, 1987). Low preference for ethanol and low capability to develop acute tolerance to ethanol hypnosis (York *et al*, 1994). Behavioral performance declined less rapidly with aging than in strain F344 (Spangler *et al*, 1994).

Drugs

Dimethylbenzanthracene induced a transplantable myeloid leukemia (Colly and Hagenbeek, 1977). Intermediate susceptibility to pentobarbital sodium with LD50 of 90 mg/kg (Shearer *et al*, 1973).

Genetics

Coat color genes	- *a, b, C, h^i* : non-agouti brown.
Histocompatibility	- *$RT1^n$*, *$RT2^a$* or *$RT2^b$*, *$RT3^b$*, *$RT8^b$*.
Biochemical markers	- *$Acon\text{-}1^a$*, *$Acp\text{-}2^a$*, *$Ahd\text{-}2^b$*, *$Akp\text{-}1^a$*, *Alb^a*, *$Amyl^b$*, *$Cryg\text{-}1^b$*, *$Es\text{-}1^a$*, *$Es\text{-}2^c$*, *$Es\text{-}3^d$*, *$Es\text{-}4^b$*, *$Es\text{-}6^b$*, *$Es\text{-}7^b$*, *$Es\text{-}8^a$*, *$Es\text{-}9^c$*, *$Es\text{-}10^b$*, *$Es\text{-}14^a$*, *$Es\text{-}15^c$*, *$Es\text{-}16^a$*, *$Es\text{-}18^b$*, *$Fh\text{-}1^a$*, *Gc^a*, *$Glo\text{-}1^a$*, *$Gox\text{-}1^b$*, *Hbb^a*, *$Igk\text{-}1^a$*, *$Lap\text{-}1^a$*, *$Mgd\text{-}1^b$*, *$Mup\text{-}1^a$*, *$Pg\text{-}1^a$*, *Pgd^b*, *$Svp\text{-}1^b$*. (Bender *et al*, 1994).

Substrains vary with respect to Pep-3 and RT2. The original BN strain has been maintained with forced heterozygosity for RT2. Hence, BN strains vary in this RT2 blood group antigen. (Paul and Carpenter, 1981).

- BN/RijHsd = *$Pep\text{-}3^a$* and *$RT2^a$*
- BN/SsNOlaHsd = *$Pep\text{-}3^b$* and *$RT2^b$*

Immunology

Resistant to induction of experimental allergic encephalomyelitis (Gasser *et al*, 1975; McFarlin *et al*, 1975). However, resistance can be modulated by endogenous corticosteroids (Peers *et al*, 1995). Resistant to induction of autologous immune complex glomerulonephritis (Stenglein *et al*, 1975).

Susceptible to the development of mercury-induced autoimmunity to renal basement membranes with the development of membraneous glomerulonephritis (Henry *et al*, 1988). Susceptible to the autoimmune effects of mercury showing a decrease of peripheral RT6.2(+) T lymphocytes compared with strain LEW (Kosuda *et al*, 1994), but no release of hydrogen peroxide in peritoneal polymorphonuclear leukocytes and macrophages, in contrast with LEW (Contrino *et al*, 1992). Susceptible to the development of autoimmunity to skin-injected $HgCl_2$, in contrast to LEW (Warfvinge and Larsson, 1994). Develop a T-helper 2 cell-mediated autoimmune syndrome following treatment with mercuric chloride, gold or D-penicillamine which may be associated with the response of mast cells (Oliveira *et al*, 1995). Moderately sensitive to the development of experimental glomerulonephritis following injection of nephritogenic antigen from bovine renal basement membrane (Naito *et al*, 1991). Develops severe experimental allergic encephalomyelitis when immunized with rat spinal cord and carbonyl iron adjuvant (Levine and Sowinski, 1975). Linington *et al*, (1986) induced experimental allergic neuritis using T-cells and bovine P2 (a peripheral nerve myelin protein). Resistant to the induction of Heymann nephritis (Badalamenti *et al*, 1987). High IgE response to Japanese cedar pollen antigen: may be a useful model for studying physiological and pathological changes in the nose after pollen challenge (Imaoka *et al*, 1993). Resident macrophages (ramified microglea) of the central nervous system are constitutively major histocompatibility complex class-II positive, in contrast with LEW (Sedgwick *et al*, 1993).

Following lethal irradiation and re-constitution with syngeneic bone marrow and given cyclosporin A for several weeks LEW rats will develop cyclosporin-induced autoimmunity after withdrawal of the cyclosporin. The condition resembles graft-versus host disease in terms of acute dermatitis and chronic scleroderma. However, BN rats do not develop this disease (Wodzig *et al*, 1993). Resistant to the induction of experimental autoimmune uveoretinitis and endotoxin-induced uveitis, which appears to be associated with the production of tumor necrosis factor (TNF) by retinal Muller glia and retinal-pigmented epithelium. LEW is susceptible. (Dekozak *et al*, 1994). Susceptible to the induction of proteinuria following treatment with the monoclonal antibody 5-6-1, like LEW and outbred Wistar, but unlike resistant outbred Sprague Dawley rats which were also resistant to glomerular damage (Gollner *et al*, 1995). Skin from neonatal males grafted onto syngeneic females induces tolerance to subsequent grafts of male skin. (Silvers and Conners, 1979). Low antibody response to phyto-hemagglutinin, concanavalin A and streptococcal group A carbohydrate (Koch 1976, Stankus and Leslie 1976, Williams *et al*, 1973). Good antibody response to a synthetic 20 amino acid peptide derived from the alpha helical region of the RT1-D^u beta chain (Murphy *et al*, 1994). Low activity of NK cells compared with other rat strains (Reynolds and Holden, 1982).

Infection

Resistant to the induction of encephalitis by coronavirus, with a much shorter delay in lymphocyte proliferation following infection than in the susceptible LEW strain (Imrich *et al*, 1994). Partly resistant to *Trypanosoma cruzi* (Rivera-Vanderpas *et al*, 1983).

Life-span and spontaneous disease

Endocardial disease 7% at an average age of 31 months. The lesion consisted of a proliferation of fibroblast-like cells within the endocardium (Boorman *et al*, 1973). Tumors of epithelium 28% in males, 2% in females. Ureter tumors 20% in females, 6% in males. Estimated median lifespan more than 24 months in males and more than 25 months in females (Boorman and Hollander, 1974). Median lifespan 30.0 months in males and 31.2 months in females (Mos and Hollander, 1987). Median lifespan 28 months in males and 30 months in females (Burek and Hollander, 1977). Median lifespan 30.9 months for female retired breeders (Kort *et al*, 1984). Most common neoplastic lesions in males were urinary bladder carcinoma 35%, pancreas islet adenoma 15%, pituitary adenoma 14%, lymphoreticular sarcoma 14%, adrenal cortex adenoma 12%, medullary thyroid carcinoma 9%, and adrenal pheochromocytoma 8%. Four other types of tumors were observed. In females: pituitary adenoma 26%, ureter carcinoma 22%, adrenal cortical adenoma 19%, cervix sarcoma 15%, mammary gland fibroadenoma 11% and islet adenoma 11%. Twelve other tumor types were observed (Burek and Hollander, 1977). Further details of an aging colony are given by Hollander (1976), Burek and Hollander (1977) and Burek (1978).

Vaginal and cervical tumors, mostly sarcomas but also seven squamous-cell carcinomas and four leiomyomas, were seen in 20% of animals that died naturally (Burek *et al*, 1976b). High incidence (31%) of hydronephrosis reported in 2-month-old BN/Rij (Cohen *et al*, 1970), but little seen by Gray *et al* (1982) before 30 months, after which the disease progressed slowly. The BN/Rij rat has a mild severity of chronic progressive nephritis (Gray *et al*, 1982). Granular cell tumors are found in untreated BN/Rij rats (Hollander *et al*, 1976). Spontaneous paresis and paralysis associated with degenerative spinal cord and spinal nerve root lesions occurred in aging rats (Burek *et al*, 1976a). Induction of atherosclerosis can be induced by immunization with ovalbumin (Nishisono *et al*, 1999)

Miscellaneous

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

Physiology and biochemistry

Low plasma ceruloplasmin levels (Stolc, 1984).

Reproduction

Low litter size (4.8 young/litter).

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