Origin:
Hereditary hypothalamic diabetes insipidus was first described in offspring from a Long-Evans stock of rats, later named Brattleboro strain (Valtin et al, 1962). In 1964 from Dr. Lewis Kinder, Harvard University, Boston to Blue Spruce Farms, Altamont, New York.

- **HsdBlu:BRAT-Avp^di**
  In 1988, to Harlan Sprague Dawley, Inc., through acquisition of Blue Spruce Farms.

Characteristics:
- **Animal Model**
The Brattleboro rat is an animal model for hereditary hypothalamic diabetes insipidus.
- **Anatomy**
  Homozygotes rats are smaller than heterozygotes or normal rats, possible of a deficiency in growth hormone (Sokol and Sise, 1973).
- **Behaviour**
  Memory impairment is found as evidence by an inferiority in acquiring and maintaining active and passive avoidance behaviour, including shuttle-box avoidance behaviour. Extinction of shuttle-box and pole jumping is facilitated (De Wied and Versteeg, 1979).
- **Genetics**
  Coat colour genes – *a, h*: black-hooded.
- **Miscellaneous**
  Histochemistry and ultrastructure of the renal papilla have been described by McAuliffe (1980). Growth and urine osmolality in young Brattleboro rats has been described by Dlouhá et al (1977). Characteristics of the *di* gene have been described by Hedrich (1990).
- **Physiology and Biochemistry**
  Brattleboro *di/di* rats are diabetic. Homozygotes are identified by their polydipsia, polyuria and low urine osmolality. Brattleboro rats have a high fluid turnover, which cannot be corrected by stimulating the hypothalamo-neurohypophyseal system, but by administering arginine vasopressin subcutaneously (Valtin, 1976). Rats homozygous for hypothalamic diabetes insipidus show marked hypertrophy in the hypothalamo-neurohypophyseal system. The supraoptic nucleus and the paraventricular nucleus contain enlarged cells with hypertrophic nuclei and nucleoli, and axons with very little or no neurosecretory material. Heterozygous rats possess hypothalamic and neurohypophyseal features intermediate between *di/di* and +/+ rats (Sokol and Valtin, 1965). Hence the mutation behaves like an incomplete dominant. Homozygous *di/di* rats lack not only biologically active vasopressin, but also its associated neurophysin II carrier (Sokol and Valtin, 1982). In heterozygous *di/+* rats, the production of vasopressin attains approximately half the normal amount (Sokol and Zimmerman, 1982).
As a consequence, renal resorption of water in the distal parts of the nephron is greatly impaired. The synthesis of oxytocin, the other neurohypophyseal hormone, however, seems to be unaffected by the di mutation (Russell et al., 1980), but the hormone is reduced in the pituitary, probably due to an enhanced release. It was shown that the defect is due to a single nucleotide deletion in exon B of the gene for vasopressin precursor (Schmale and Richter, 1984). The mutation gives rise to an open reading frame with subsequent abnormalities in translation and post-translation events (greatly altered vasopressin precursor: absent glycolysation site and drastically changed C-terminus).

The presence of immunoreactive arginine-vasopressin in adrenal glands of di/di rats suggests that this organ, unlike the hypothalamus, may be capable of post-translational modification of an abnormal precursor or that a second arginine-vasopressin gene is expressed in the adrenals of di/di rats (Nussey et al., 1984). Urine flow in di/di rats ranges from about 20 to 125 percent of body weight per day in contrast to less than 10 percent of body weight per day in +/+ rats (Saul et al., 1968). Water intake is correspondingly high (approximately 80% of body weight). Urine osmolarity ranges from about 100-200 mOsm/kg H2O in di/di rats, and from 1500-2500 mOsm/kg H2O in unaffected rats. The characteristics of water turnover in di/+ rats are intermediate between di/di and +/+ rats (Valtin, 1976). Serum sodium concentration is elevated (Peter and Moring, 1978). Alkalosis is present (Moring et al., 1974). Norepinephrine turnover rate in dorsal septal nucleus is higher and regional cathecholamine turnover in the brain is slower in the homozygote (De Wied and Versteeg, 1979).

**Reproduction**

In the original stock a high incidence of foetal deaths, stillbirths, and runting was observed to be associated with diabetes insipidus (Saul et al., 1968). Brattleboro females are good mothers and there is no need for foster rearing. Homozygous females are mated to homozygous males to produce homozygous (di/di) offspring. Average litter size is 7.5.

**References:**


