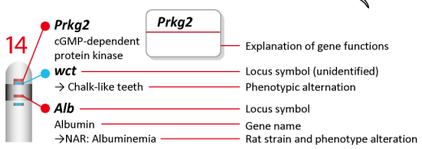
NBRP-Rat Rat Mutant Map

Rat genome

The laboratory rat (Rattus norvegicus) genome comprises 20 autosomes and two sex chromosomes, X and Y. A 'draft' sequence of the BN/SsNHsd strain was first reported in 2004 and has been updated several times since then. The rat genome is 2.75 Gb and is smaller than the human genome at 2.9 Gb. However it is larger than the mouse genome at 2.6 Gb. The number of genes that has been predicted to exist in the rat genome ranges from 24,000 to 47,000. Almost all human genes that are known to be associated with diseases have orthologs in the rat genome.

How to use this map

The map below illustrates functional polymorphisms of the rat strains that are deposited at the NBRP-Rat. Mutations for which 56 causative genes have been identified are indicated by the red lines and those for seven unidentified genes are indicated by the blue lines.



100506

Tyr (C)

- Tyrosinase catalyzed the first two steps of tyrosine-to-melanin conversion.
- The absense of gene function results in the albino phenotype, defined as white coat color and red eyes, or the Himalayan phenotype, defined as pigmentation along the edge of the nose and on the hips and ears.

Ptprk

- *Ptprk* is associated with T-cell development.
- LEC rats possess a mutation in this gene and exhibits defective T-cell mutation.

Oca (P)

- Murine homolog of oculocutaneous albinism II.
- Rats that are homozygous for this mutation exhibit light coat color and light pink eyes.

Kcnq1

1
- ***Ptprk*** Receptor type protein tyrosine phosphatase
- ***Oca2 (P)*** Oculocutaneous albinism 2
- ***Tyr (C)*** Tyrosinase
- ***Rab38*** RAS-associated protein →TM, FH: Light coat color, ruby eye, bleeding
- ***Kcnq1*** Potassium channel →WTC-dfk: Extended QT interval, deafness
- ***Lipa*** Lipase A →ALD: Abnormal lipid metabolism
- ***Lgi1*** Leucine-rich, glioma inactivated 1 →Epilepsy
- ***Prlhr*** Prolactin releasing hormone receptor →OLETF: Obesity

Arsb

- Enzyme associated with mucopolysaccharidosis VI, lysosomal storage disorder.
- MPR rats possess a mutation in this gene and exhibit retarded growth, facial abnormalities, low ARSB activity, and excrete dermatan sulfate in their urine.

Gja8

- Gap junction protein that is found in the lens of the eye.
- Defects in this gene cause cataracts.

Unc5c

- A family of netrin-1 receptors which is believed to mediate the chemorepulsive effect of netrin-specific axons.
- F344.CVD-*cvd* and HOB rats possess mutations in this gene and exhibit defects in the cerebellar vermis.

2
- ***Arsb*** Arylsulfatase B
- ***Gja8*** Gap-junction protein
- ***Unc5c*** A family of netrin-1 receptors

Scn1a

- A causative gene for human SMEI and GEFS+.
- F344-*Scn1a*^{m1Kyo} rats, from ENU-mutant archive, show convulsion after heat stimulation.

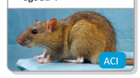
Atrn

- Attractin membrane protein is involved in the interaction between the agouti molecule and the MCR1 receptor.
- Rats that are homozygous for Atrn exhibit a brownish-black "mahogany" coat color.

3
- ***Scn1a*** Sodium channel
- ***Mertk*** Tyrosyl oxidase →RCS: Retinal dystrophy
- ***Avp*** Vasopressin →DDI: Diabetes insipidus
- ***Atrn*** Attractin
- ***Asip (A)*** Agouti signaling protein

Asip (A)

- The agouti gene encodes a paracrine signaling molecule that causes hair follicle melanocytes to synthesize the yellow pigment pheomelanin, instead of the black pigment eumelanin.
- Since the agouti molecule is cyclically secreted in the hair follicles of rodents, their coat color is yellowish-black "agouti".



Cd36

- Among SHR strains, the *Cd36* mutation is present in some strains but not in others.
- *Cd36* deficiency causes insulin resistance, defictive fatty acid metabolism, and hypertriglyceridemia.

Gimap5

- *Gimap5* exhibits sequence similarity to a novel and largely uncharacterized protein family, which is distinguished by a well conserved GTP binding motif and is involved in immune system function.
- BB rats possess a frameshift deletion in this gene and exhibit lymphopenia, which is requisite for type I diabetes.

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- ***Reln*** Reelin →KZC: Cytoarchitecture abnormality in the brain.
- ***Cd36*** Scavenger receptor (CD36)
- ***Gimap5*** GTPase, IMAP family member 5
- ***Kcna1*** Potassium channel →KER: Epilepsy

Tyrp1 (B)

Lepr

- An adipocyte-specific hormone that regulates adipose tissue mass through hypothalamic effects on satiety and energy expenditure.
- KZF rats possess a mutation in this gene and become obese.

5
- ***Tyrp1 (B)*** Tyrosinase-related protein 1 →Brown coat color
- ***Lepr*** Leptin receptor

Abcg5

- Regulates the absorption of dietary cholesterol.
- SHR, SHRSP and WKY rats possess a mutation in this gene and exhibit phytosterolemia.

6
- ***Abcg5*** ATP-binding cassette

Tg

- Glycoprotein precursor of thyroid hormones.
- WIC-*rdw* rats possess a missense mutation in this gene and exhibit hereditary dwarfism, which is the result of thyroid gland dysfunction.

Krt71

- *Krt71* is associated with frizzy hair.
- KFRS5A rats possess a mutation in this gene and exhibit frizzy hair and whiskers.

7
- ***Tg*** Thyroglobulin
- ***khr*** → Hairless
- ***Krt71*** Keratin 71

Myo5a (D)

- *Myo5a* performs multiple functions such as polarized transportation of the centrosome, and transportation of pigment granules.
- Defects in this gene result in human Griscelli disease and mouse "dilute".
- DOP rats possess intragenic rearrangements in Myo5a and exhibit light coat color and ataxia.

8
- ***Myo5a (D)*** Myosin 5a
- ***vf*** → Vacuolation in the CNS

Actr3

- *Actr3* has been suggested to participate in the organization of filament/membrane adhesion.
- BUF/Mna rats possess a missense mutation in this gene and develop proteinuria due to focal and segmental glomerulosclerosis.

Lmx1a

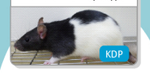
- *Lmx1* is expressed throughout the roof plates along the neuraxis during CNS development and is required for roof plate development.
- qc rats possess a defect in this gene and display short tales, neurologic disorders and cerebellar hypoplasia.

12
- ***furue*** →Tremors

13
- ***Actr3*** ARP3 actin-related protein
- ***Lmx1a*** LIM homeobox transcription factor
- ***Fcgr2a*** Fc fragment of IgG →Glomerulonephritis

Cblb

- *Cblb* is the E3 ubiquitin ligase gene and plays an important role in regulating T cell signaling, particularly through the CD28 pathway.
- KDP rats possess a mutation in Cblb and develop type I diabetes with the RT1^{u} haplotype.



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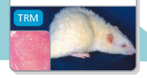
- ***Cblb*** Cas-Br-M (murine) ecotropic retroviral transforming sequence b
- ***Kng2*** Kininogen 2 →BN/Ka: Plasma kininogen deficiency

Aspa

- Aspartoacylase is an enzyme that hydrolyzes N-acetyl-L-aspartic acid (NAA) to acetate and acetate.
- Mutation of the human *ASPA* gene is associated with Canavan's disease.
- TRM rats lack this gene and exhibit absents like seizures and spongy degeneration of the CNS.



Flcn

- *Flcn* is a possible tumor suppressor gene that is associated with hereditary renal carcinoma.
- Nihon rats possesses a mutation in this gene and serve as a model of Birt-Hogg-Dubé syndrome.
- Homozygous rats are embryonic lethal and heterozygous rats develop renal carcinoma.

Foxn1

10
- ***Flcn*** Folliculin
- ***Srebf1*** Sterol regulatory element binding transcription factor 1 →SHR: Hepatic steatosis
- ***Foxn1*** Forkhead box N1 →nude rat: athymic, hairless
- ***Aspa*** Aspartoacylase
- ***Gh1*** Growth hormone →SDR: Pituitary dwarfism

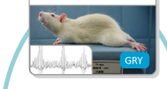
9
- ***Ugt1*** Uridine diphosphate glycosyltransferase 1

Ugt1

- Mutations in human *UGT1* are responsible for type I and type II Crigler-Najjar syndromes.
- Gunn's rat possesses a mutation in this gene and develops hyperbilirubinemia.

Cacna1a

- *Cacna1a* encodes the alpha subunit of the P/Q-type Ca^{2+} channel.
- GRY rats possess a missense mutation in this gene and exhibit ataxia and absence-like seizures.



19
- ***Cacna1a*** Calcium channel
- ***Cyba*** Cytochrome b-245, alpha polypeptide

Cyba

- *CYBA* is an indispensable component of the NADPH oxidase complex, which catalyzes the production of superoxide.
- MES rats possess a deletion in this gene and exhibit hypereosinophilia and wryneck.

20
- ***RT1*** Major histocompatibility complex
- ***Cdkn1a*** Cyclin-dependent kinase inhibitor →Susceptibility to prostate cancer
- ***Lss*** Lanosterol synthase →SCR: Cataracts
- ***Pcdh15*** Protocadherin 15

RT1

- A genomic region that includes the genes which encode rat major histocompatibility complex (MHC) antigen molecules.
- The rat *RT1* region spans approximately 4,000,000 base pairs and includes at least 220 genes.

Pcdh15

- *Pchd15* plays an important role in the morphogenesis and cohesion of stereocilia bundles and in the maintenance of retinal photoreceptor cells.
- The KCI rat possesses a mutation in *Pcdh15*, which causes human Ucher syndrome type IF, and exhibits circling behavior and deafness.

Il2rg

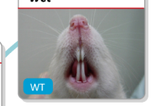
- *Il2rg* is associated with the X-linked form of severe combined immunodeficiency (X-SCID).
- X-SCID rats exhibit hypoplastic thymus and diminished IgG, IgA, T cells, B cells and NK cells.

X
- ***Il2rg*** Interleukin 2 receptor, gamma
- ***Plp1*** Proteolipid protein

Plp1

- Proteolipid protein is the major component of myelin.
- Reduced expression or overexpression of *PLP1* causes Pelizaeus-Merzbacher disease in humans.
- MD rats, which are deficient in *Plp1*, die a few weeks after birth owing to myelin deficiency.

wct



hooded

Cckar

- *Cckar* encodes a receptor for CCK, which is a peptide hormone of the gastrointestinal system.
- OLETF rats possess a deletion in this gene and exhibit hyperglycemia and mild obesity.

Prkg2

- *Prkg2* encodes a molecule which triggers the change from chondrocyte proliferation to hypertrophic chondrocyte differentiation during endochondral ossification.
- KMI rats exhibit a deficiency in this gene and their rate of body growth is retarded by about 60 to 70% compared to normal control rats.

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- ***Prkg2*** cGMP-dependent protein kinase
- ***wct*** → Chalk-like teeth
- ***Alb*** Albumin →NAR: Albuminemia
- ***hooded*** →Hooded
- ***Cckar*** Cholecystokinin A receptor
- ***Smek2*** SMEK homolog 2, suppressor of mek1 →EXHC/Ta: Diet-induced hypercholesterolemia

Gulo

- *Gulo* encodes the enzyme that synthesizes vitamin C.
- Primates and the guinea pig have lost the ability to produce this enzyme and therefore require dietary vitamin C.
- ODS rats exhibit defects in this gene and cannot survive without dietary vitamin C.

Ednrb

- The AR rat, a model of human Hirschsprung's disease, possesses a deletion in this gene and dies from intestinal obstruction at between 1 to 5 weeks of age.

15
- ***Fdft1*** Farnesyl diphosphate farnesyl transferase →SCR: Modifier of cataract
- ***Gulo*** Gulonolactone oxidase
- ***Ednrb*** Endothelin receptor

Atp7b

- *Atp7b* encodes a polypeptide that acts as a membrane copper-transport protein.
- Mutations in the human *ATP7B* are associated with Wilson's disease.
- LEC rats exhibit hepatitis which occasionally develops into liver cancer.

Jund

- *Jund*, an AP-1 transcription factor, is a major determinant of macrophage activity and is associated with susceptibility to glomerulonephritis.
- WKY/NCrl rats overexpress Jund and are susceptible to glomerulonephritis.

16
- ***Jund*** Jun D proto-oncogene
- ***Atp7b*** ATPase, Cu++ transporting, beta polypeptide

Lyst (Bg)

- *Lyst* is thought to play a role in the fusion and/or fission of specific organelle precursors.
- Beige rat, the rat model of Chediak-Higashi syndrome, displays decreased pigmentation of the hair and eye, and leukocytes with giant granules.

17
- ***dmy*** →Demyelination
- ***Lyst (Bg)*** Lysosomal trafficking regulator
- ***swh*** →Sparse and wavy hair

swh

Apc

- *Apc* plays a significant role in tumor development.
- KAD rats, from the ENU-mutant archive, exhibit high sensitivity for AOM/DSS-induced colon carcinogenesis.

18
- ***Apc*** Adenomatous polyposis coli