

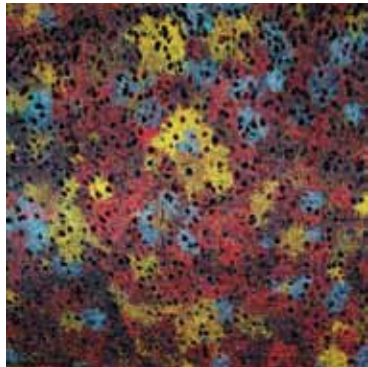
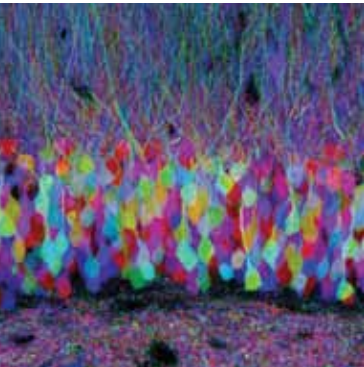
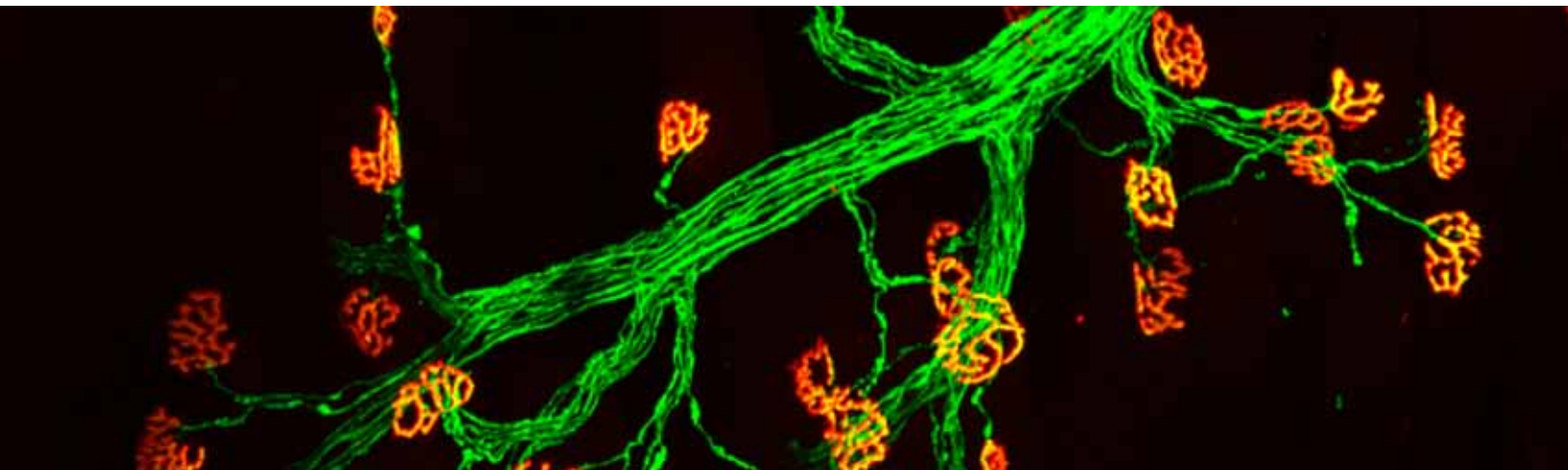


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# Mouse Models for Parkinson's Disease Research

October 2009



*Leading the Search for Tomorrow's Cures*

## Parkinson's Disease Mouse Model Resource

The Parkinson's Disease Mouse Model Resource (PDMMR) is funded by the Michael J. Fox Foundation and an anonymous foundation to provide genetically engineered mice and information useful for their selection and use. The resource also serves as an archive of genetically stable mouse models.

The Repository distributes Parkinson's disease (PD) models that are useful for the study of the basic pathophysiology of PD, and for testing new therapies. Also available are "research tool" strains including transgenics that express marker genes in affected brain regions, and strains with systems for regulating gene expression (e.g. Cre recombinase and tet-inducible promoters) in specific types of neurons.

The Jackson Laboratory has appointed a special research administrator for Parkinson's disease to enhance the distribution of mouse models from the PDMMR. Dr. Michael Sasner will serve as a resource for scientists seeking information about existing models, and also oversee the selection, importation and distribution for new PD models. Scientists with questions or information about potential new strains for distribution can reach Dr. Sasner by email ([mike.sasner@jax.org](mailto:mike.sasner@jax.org)).

## Parkinson's Disease Models

For a current list of all strains, go to [www.jax.org/jaxmice/list/ra1594](http://www.jax.org/jaxmice/list/ra1594)

\* Indicates Strain is Under Development

Gene/Allele/Name	Page	Stock No.	Strain Name
<b>Ache, acetylcholinesterase</b>			
	005987	129-	<i>Ache</i> <sup>tm1Loc</sup> /J
<b>Cacna1a<sup>tg</sup>, calcium channel, voltage-dependent, P/Q type, alpha 1A subunit; tottering</b>			
	000544	B6.D2-	<i>Cacna1a</i> <sup>tg</sup> /J
<b>CDK5R1, cyclin-dependent kinase 5, regulatory subunit 1 (p35)</b>			
	005706	C57BL/6-	Tg(tetO-CDK5R1/GFP)337Lht/J
<b>Chat, choline acetyltransferase</b>			
	008364	B6;129-	<i>Chat</i> <sup>tm1(Cre/Esr1)Nat</sup> /J
<b>COX8A, cytochrome c oxidase subunit 8A (ubiquitous)</b>			
	006618	C57BL/6-	Tg(tetO-COX8A/EYFP)1Ksn/J
<b>cre, cre recombinase</b>			
	008364	B6;129-	<i>Chat</i> <sup>tm1(Cre/Esr1)Nat</sup> /J
	008532	B6;129-	<i>Th</i> <sup>tm1(cre/Esr1)Nat</sup> /J
	008601 *	B6.Cg-	Tg(Th-cre)1Tmd/J
	006660	B6.SJL-	<i>Slc6a3</i> <sup>tm1.1(cre)Bkmm</sup> /J
<b>Csf1<sup>op</sup>, colony stimulating factor 1 (macrophage); osteopetrosis</b>			
	000231	B6;C3Fe a/a-	<i>Csf1</i> <sup>op</sup> /J

Gene/Allele/Name	Page	Stock No.	Strain Name
<b>Dbh, dopamine beta hydroxylase</b>			
	3	009688 *	B6;129- <i>Dbh</i> <sup>tm2(Th)Rpa</sup> <i>Th</i> <sup>tm1Rpa</sup> /J
<b>Dld, dihydrolipoamide dehydrogenase</b>			
	008333	B6;129P2-	<i>Dld</i> <sup>tm1Pl</sup> /J
<b>Drd2, dopamine receptor 2</b>			
	003190	B6.129S2-	<i>Drd2</i> <sup>tm1Low</sup> /J
<b>Drd4, dopamine receptor 4</b>			
	008084	B6.129P2-	<i>Drd4</i> <sup>tm1Dkg</sup> /J
<b>Esr1, estrogen receptor 1 (alpha)</b>			
	004744	B6.129P2-	<i>Esr1</i> <sup>tm1Ksk</sup> /J
<b>GFP, Green Fluorescent Protein</b>			
	008323	B6.Cg-	Tg(Mc4r-MAPT/GFP*)21Rck/J
	008321	B6.Cg-	Tg(Npy-MAPT/GFP*)1Rck/J
	008322	B6.Cg-	Tg(Pomc-MAPT/GFP*)1Rck/J
	005706	C57BL/6-	Tg(tetO-CDK5R1/GFP)337Lht/J
	007677	CB6-	Tg(Gad1-EGFP)G42Zjh/J
	007673	B6.Cg-	Tg(Gad1-EGFP)3Gfng/J
	008324	B6.Cg-	Tg(Pmch-MAPT/GFP*)1Rck/J
	007894	B6.Cg-	Tg(Rgs4-EGFP)4Lvt/J
	006340	STOCK Tg	(Gad1/EGFP)98Agmo/J

# Mouse Models for Parkinson's Disease

Gene/Allele/Name		
Page	Stock No.	Strain Name
<b>Htra2<sup>mn2</sup>, HtrA serine peptidase 2; motor neuron degeneration 2</b>		
	004608	B6(Cg)-Htra2 <sup>mn2</sup> /J
<b>lacZ, beta-galactosidase</b>		
	003139	B6.Cg-Tg(DBHn-lacZ)8Rpk/J
<b>LRRK2, leucine-rich repeat kinase 2, human</b>		
3	009610 *	FVB/N-Tg(LRRK2)1Cjli/J
3	009604 *	FVB/N-Tg(LRRK2*R1441G)135Cjli/J
<b>Mapk10, mitogen activated protein kinase 10</b>		
	004322	B6.129S1-Mapk10 <sup>tm1Flv</sup> /J
<b>MAPT, Mapt, microtubule-associated protein tau</b>		
	008169	B6;C3-Tg(Prnp-MAPT*P301S)PS19Vle/J
	005491	B6.Cg-Mapt <sup>tm1(EGFP)Klt</sup> Tg(MAPT)8cPdav/J
	004807 *	B6.Cg-Psen1 <sup>tm1Mpm</sup> Tg(APP <sup>Swe</sup> ,tauP301L)1Lfa/J
	008323	B6.Cg-Tg(Mc4r-MAPT/GFP*)21Rck/J
	008321	B6.Cg-Tg(Npy-MAPT/GFP*)1Rck/J
	008324	B6.Cg-Tg(Pmch-MAPT/GFP*)1Rck/J
	008322	B6.Cg-Tg(Pomc-MAPT/GFP*)1Rck/J
	003741	B6D2-Tg(Prnp-MAPT)43Vle/J
	004808	STOCK Mapt <sup>tm1(EGFP)Klt</sup> Tg(MAPT)8cPdav/J
<b>Nos2, nitric oxide synthase 2, inducible</b>		
	002609	B6.129P2-Nos2 <sup>tm1Lau</sup> /J
	002596	B6;129P2-Nos2 <sup>tm1Lau</sup> /J
	004684	B6(129P2) Nos2 <sup>tm1Lau</sup> .cht1/J
<b>Park2, PARK2, parkin</b>		
4	007587	129S-Park2 <sup>tm1Rpa</sup> /J
4	006582	B6.129S4-Park2 <sup>tm1Shn</sup> /J
5	009090 *	FVB/NJ-Tg(Slc6a3-PARK2*Q311X)AXw/J
<b>Park7, Parkinson disease (autosomal recessive, early onset) 7</b>		
5	006577	B6.Cg-Park7 <sup>tm1Shn</sup> /J
<b>Parp1, poly (ADP-ribose) polymerase family, member 1</b>		
	002779	129S-Parp1 <sup>tm1Zqw</sup> /J
<b>Pitx3<sup>ak</sup>, paired-like homeodomain transcription factor 3; aphakia</b>		
	000942	STOCK Pitx3 <sup>ak</sup> /2J
<b>PSEN1, Psen1, presenilin 1</b>		
	004807 *	B6.Cg-Psen1 <sup>tm1Mpm</sup> Tg(APP <sup>Swe</sup> ,tauP301L)1Lfa/J
<b>Qk<sup>ak</sup>, quaking</b>		
	000506	B6C3Fe a/a-Qk <sup>ak</sup> /J
	000567	B6.Cg-T <sup>2J</sup> +/+ Qk <sup>ak</sup> /J

Gene/Allele/Name		
Page	Stock No.	Strain Name
<b>Slc6a3, solute carrier family 6 (neurotransmitter transporter, dopamine), member 3; cre, cre recombinase</b>		
	006302	B6;SJL-Slc6a3 <sup>tm1.1(cre)Bkmm</sup> /J
	006660	B6.SJL-Slc6a3 <sup>tm1.1(cre)Bkmm</sup> /J
<b>Snca, SNCA, synuclein, alpha; synuclein, alpha (non A4 component of amyloid precursor)</b>		
6	003692	B6;129X1-Snca <sup>tm1Rosl</sup> /J
6	008132	STOCK Tg(THY1-Snca)M1mSud/J
7	004479	B6;C3-Tg(Prnp-SNCA*A53T)83Vle/J
7	008389	C57BL/6-Tg(THY1-SNCA)1Sud/J
7	008473	B6.Cg-Tg(THY1-SNCA*A30P)M30Sud/J
8	008134 *	B6.Cg-Tg(THY1-SNCA*A30P)TS2Sud/J
8	008135	B6.Cg-Tg(THY1-SNCA*A53T)M53Sud/J
8	008474 *	STOCK Tg(THY1-SNCA*A53T)F53Sud/J
8	008883 *	B6;129-Gt(ROSA)26Sor <sup>tm1(SNCA*A53T)Djmo</sup> /TmdJ
9	008886 *	B6;129-Gt(ROSA)26Sor <sup>tm3(SNCA*E46K)Djmo</sup> /TmdJ
9	008889 *	B6;129-Gt(ROSA)26Sor <sup>tm2(SNCA*119)Djmo</sup> /TmdJ
<b>Snca, Snca, synuclein, alpha; synuclein, beta</b>		
6, 10	006390	B6;129-Snca <sup>tm1Sud</sup> Snca <sup>tm1.1Sud</sup> /J
<b>Snca, Snca, synuclein, alpha; synuclein, beta</b>		
10	008133	B6.129-Snca <sup>tm1Sud</sup> /J
<b>Sncg, synuclein, gamma</b>		
10	008843 *	B6.129P2-Sncg <sup>tm1Vlb</sup> /J
<b>Spp1, secreted phosphoprotein 1</b>		
11	004936	B6.129S6(Cg)-Spp1 <sup>tm1Blh</sup> /J
<b>Th, tyrosine hydroxylase</b>		
11	009688 *	B6;129-Dbh <sup>tm2(Th)Rpa</sup> Th <sup>tm1Rpa</sup> /J
	008532	B6;129-Th <sup>tm1(cre/Esr1)Nat</sup> /J
<b>Tnfrsf1a Tnfrsf1b, tumor necrosis factor receptor superfamily, member 1a and 1b</b>		
	003243	B6;129S-Tnfrsf1a <sup>tm1Imx</sup> Tnfrsf1b <sup>tm1Imx</sup> /J
<b>tTA, tetracycline-controlled transactivator</b>		
	007004	B6.Cg-Tg(Camk2a-tTA)1Mmay/DboJ
	005706	C57BL/6-Tg(tetO-CDK5R1/GFP)337Lht/J
	006618	C57BL/6-Tg(tetO-COX8A/EYFP)1Ksn/J
<b>Ucp2, uncoupling protein 2 (mitochondrial, proton carrier)</b>		
12	005934	B6.129S4-Ucp2 <sup>tm1Lowl</sup> /J
<b>YFP, Yellow Fluorescent Protein</b>		
	006618	C57BL/6-Tg(tetO-COX8A/EYFP)1Ksn/J

# Select Models for Parkinson's Disease Research

<b>Gene/Marker</b> <b>Dbh</b>	<b>Name</b> dopamine beta hydroxylase <b>Common Name(s)</b> DBM; DOPBHY
<b>Allele Symbol/Name</b> <b>Common Name(s)</b>	<b>Dbh<sup>tm2(Th)Rpa</sup>, targeted mutation 1, Richard D Palmiter</b> DBH-TH <sup>-</sup> ; Dbh <sup>Th</sup>
<b>Strain Name</b> <b>Stock Number</b> <b>Phenotype</b>	<b>B6;129-Dbh<sup>tm2(Th)Rpa</sup> Th<sup>tm1Rpa</sup>/J</b> <b>009688</b> Mice heterozygous for both targeted mutations are viable and fertile. Dopamine-deficient (DA-deficient, DA <sup>-/-</sup> , or DD) mice are homozygous for the TH mutant allele and heterozygous for the DBH-TH mutant allele ( <i>Th</i> <sup>-/-</sup> ; <i>Dbh</i> <sup>Th/+</sup> ). While no expression from the TH mutant allele is observed in any tissues (resulting in deficiency of both dopamine (DA) and norepinephrine (NE)), the DBH-TH mutant allele contains the TH coding sequence under the control of the endogenous DBH promoter region and restores TH expression in noradrenergic neurons. DD mice become hypoactive and hypophagic around two weeks of age and usually die before four weeks of age. Treatment with L-DOPA, the product of TH enzymatic activity, rescues size, feeding, and life span. These DD mice may be useful in studying dopaminergic neurobiology (including neurotransmitters, addiction, feeding, learning and memory, catecholamines, and Parkinsonian phenotypes).
<b>Selected Reference(s)</b>	Hnasko TS, Sotak BN, Palmiter RD. 2007. Cocaine-conditioned place preference by dopamine-deficient mice is mediated by serotonin. <i>J Neurosci</i> 27: 12484-8. Zhou Q-Y, Quaife CJ, Palmiter RD. 1995. Targeted disruption of the tyrosine hydroxylase gene reveals that catecholamines are required for mouse fetal development. <i>Nature</i> 374: 640-3. Zhou QY, Palmiter RD. 1995. Dopamine-deficient mice are severely hypoactive, adipsic, and aphagic. <i>Cell</i> 83: 1197-209.
<b>Gene/Marker</b> <b>LRRK2</b>	<b>Name</b> leucine-rich repeat kinase 2
<b>Allele Symbol/Name</b> <b>Common Name(s)</b>	<b>Tg(LRRK2)1Cjli, transgene insertion 1, Chenjian Li</b> WT-OX; TG-WT-OX; BAC WT LRRK2
<b>Strain Name</b> <b>Stock Number</b> <b>General Terms</b>	<b>FVB/N-Tg(LRRK2)1Cjli/J</b> <b>009610</b> Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/CORNELL_IT.htm">www.jax.org/jaxmice/licensing/CORNELL_IT.htm</a> )
<b>Phenotype</b>	Mice hemizygous for the BAC LRRK2 transgene are viable and fertile, with expression of a wild-type human leucine-rich repeat kinase 2 ( <i>LRRK2</i> ) gene directed by its endogenous promoter/enhancer regions on the BAC transgene. These BAC LRRK2 mice (also called WT-OX mice) "overexpress" the wild-type human LRRK2 protein in cortex, cerebellum, striatum and ventral midbrain at an approximately five- to ten-fold greater level than endogenous mouse <i>Lrrk2</i> , and are a control strain for the BAC LRRK2 <sup>R1441G</sup> Parkinson's disease strain (Stock No. 009604). Contrary to the hypokinetic motor deficit of the BAC LRRK2 <sup>R1441G</sup> Parkinson's disease mice, WT-OX mice exhibit slightly increased motor activities compared to nontransgenic wild-type controls.
<b>Selected Reference(s)</b>	Li Y, Liu W, Oo TF, Wang L, Tang Y, Jackson-Lewis V, Zhou C, Gekhman K, Bogdanov M, Przedborski S, Beal MF, Burke RE, Li C. 2009. Mutant LRRK2(R1441G) BAC transgenic mice recapitulate cardinal features of Parkinson's disease. <i>Nat Neurosci</i> 12(7):826-8.
<b>Allele Symbol/Name</b> <b>Common Name(s)</b>	<b>Tg(LRRK2*R1441G)135Cjli, transgene insertion 135, Chenjian Li</b> TG-RP135; LRRK2 <sup>R1441G</sup>
<b>Strain Name</b> <b>Stock Number</b> <b>General Terms</b>	<b>FVB/N-Tg(LRRK2*R1441G)135Cjli/J</b> <b>009604</b> Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/CORNELL_IT.htm">www.jax.org/jaxmice/licensing/CORNELL_IT.htm</a> )
<b>Phenotype</b>	Mice hemizygous for the BAC LRRK2 <sup>R1441G</sup> transgene are viable and fertile, with expression of a mutant form of human leucine-rich repeat kinase 2 (LRRK2*R1441G) associated with autosomal dominant, late-onset Parkinson's disease directed by the endogenous <i>LRRK2</i> promoter/enhancer regions on the BAC transgene. LRRK2 <sup>R1441G</sup> mice from founder line RP135 express the mutant protein in cortex, cerebellum, striatum and ventral midbrain at an approximately five- to ten-fold greater level than endogenous mouse <i>Lrrk2</i> . LRRK2 <sup>R1441G</sup> mice exhibit multiple late-onset and progressive characteristics of Parkinson's disease; including hypokinetic motor deficits (reversible with administration of levodopa or apomorphine [a direct-acting dopamine agonist]), progressive dopaminergic neuron dysfunction and degeneration, axon injury pathology,

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and hyperphosphorylated tau. These LRRK2<sup>R1441G</sup> mice recapitulate the motor behavioral, neurochemical, and histopathological features of Parkinson's disease and represent a robust *in vivo* model for studying the Parkinson's disease pathogenesis and neurodegeneration elicited by the dominant toxic effects of mutant LRRK2<sup>R1441G</sup> expression.

*Selected Reference(s)*

Li Y, Liu W, Oo TF, Wang L, Tang Y, Jackson-Lewis V, Zhou C, Geghman K, Bogdanov M, Przedborski S, Beal MF, Burke RE, Li C 2009. Mutant LRRK2(R1441G) BAC transgenic mice recapitulate cardinal features of Parkinson's disease. *Nat Neurosci* 12(7):826-8.

*Gene/Marker*

**Park2**

**Name** Parkinson disease (autosomal recessive, juvenile) 2, parkin

**Common Name(s)** AR-JP; LPRS2; PDJ; PRKN; Park

*Allele Symbol/Name*

**Park2<sup>tm1Rpa</sup>, targeted mutation 1, Richard D Palmiter**

*Strain Name*

**129S-Park2<sup>tm1Rpa</sup>/J**

*Stock Number*

**007587**

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*Phenotype*

Mice carrying this mutation are viable, fertile, and display no apparent defects or abnormalities. Mutations in the human homolog of this gene are associated with autosomal juvenile parkinsonism, a heritable form of Parkinson's disease.

*Selected Reference(s)*

Perez FA; Palmiter RD 2005. Parkin-deficient mice are not a robust model of parkinsonism. *Proc Natl Acad Sci U S A* 102:2174-9.

*Allele Symbol/Name*

*Common Name(s)*

**Park2<sup>tm1Shn</sup>, targeted mutation 1, Jie Shen**

parkin -/-

*Strain Name*

**B6.129S4-Park2<sup>tm1Shn</sup>/J**

*Stock Number*

**006582**

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*Phenotype*

Homozygous mice are viable and fertile, and exhibit grossly normal brain morphology. Western blot analysis using antibody specific to C-terminal sequences indicates the absence of full length gene product. RT-PCR shows that exon 2 splices to exon 4, skipping exon 3 entirely, resulting in a frame shift and a premature stop codon in exon 5. While EGFP transcripts are present, little parkin-EGFP fusion protein is detectable by Western analysis. Homozygous mice have increased extracellular dopamine concentration in the striatum. Further, medium-sized striatal spiny neurons require greater currents to induce synaptic responses, suggesting a reduction in synaptic excitability in the absence of the endogenous gene. Homozygotes also exhibit deficits in behavioral paradigms sensitive to dysfunction of the nigrostriatal pathway. The numbers of dopaminergic neurons in the substantia nigra, however, are normal up to the age of 24 months, in contrast to the substantial loss of nigral neurons characteristic of Parkinson's disease. Homozygous mice and their isolated cells exhibit mitochondrial dysfunction and impaired protection from oxidative stress. Muscle cells isolated from homozygous mice have defective skeletal muscle mitochondrial homeostasis and increased sensitivity to amyloid-beta toxicity. These mice model the exon 3 deletion mutation most common in human autosomal recessive juvenile parkinsonism (AR-JP) patients and may be useful in studies of Parkinson's disease, dopamine regulation, nigrostriatal function, mitochondrial function, and other neurobiological research.

*Selected Reference(s)*

*In an attempt to offer alleles on well-characterized or multiple genetic backgrounds, alleles are frequently moved to a genetic background different from that on which an allele was first characterized. Mice with this mutation were originally published on a mixed B6;129S4 genetic background. It should be noted that the phenotype could vary from that originally described. The strain description will be modified as published results become available.*

Goldberg MS, Fleming SM, Palacino JJ, Cepeda C, Lam HA, Bhatnagar A, Meloni EG, Wu N, Ackerson LC, Klapstein GJ, Gajendiran M, Roth BL, Chesselet MF, Maidment NT, Levine MS, Shen J. 2003. Parkin-deficient mice exhibit nigrostriatal deficits but not loss of dopaminergic neurons. *J Biol Chem* 278:43628-35.

# Select Models for Parkinson's Disease Research

<b>Gene/Marker</b> <b>PARK2</b>	<b>Name</b> Parkinson disease (autosomal recessive, juvenile) 2, parkin (Human)
<b>Allele Symbol/Name</b> <b>Common Name(s)</b> <b>Promoter</b>	<b>Tg(Slc6a3-PARK2*Q311X)AXwy, transgene insertion A, X William Yan</b> Parkin-Q311X line A; Parkin-Q311X(A); TgA <i>Slc6a3</i> , solute carrier family 6 (neurotransmitter transporter, dopamine), member 3
<b>Strain Name</b> <b>Stock Number</b> <b>General Terms</b>	<b>FVB/NJ-Tg(Slc6a3-PARK2*Q311X)AXwy/J</b> <b>009090</b> Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/UCLA_2.htm">www.jax.org/jaxmice/licensing/UCLA_2.htm</a> )
<b>Phenotype</b>	Hemizygous Parkin-Q311X(A) mice are viable and fertile, with expression of a FLAG-tagged, C-terminal truncated human parkin-Q311X mutation associated with Turkish early-onset Parkinson's disease directed to dopaminergic neurons of the substantia nigra pars compacta (SNc) and ventral tegmentum area (VTA) by the mouse <i>Slc6a3</i> promoter/enhancer sequences. Parkin-Q311X(A) mice (derived from founder line A) have expression of the FLAG-tagged parkin-Q311X protein in dopaminergic neurons at a level that is approximately equivalent to or just below that expected from a heterozygous endogenous parkin allele. Parkin-Q311X(A) mice exhibit multiple late-onset and progressive hypokinetic motor deficits, progressive dopaminergic neuron dysfunction and degeneration, and age-dependent accumulation of proteinase K-resistant endogenous alpha-synuclein. Compared to founder line D, Parkin-Q311X(A) mice have a higher transgene copy number that results in more robust and earlier onset of hypokinetic motor deficits and more significant dopaminergic (DA) neuron degeneration. These Parkin-Q311X(A) mice represent a robust <i>in vivo</i> model for studying the Parkinson's disease pathogenesis and neurodegeneration elicited by the dominant toxic effects of mutant parkin-Q311X expression.
<b>Selected Reference(s)</b>	Lu XH, Fleming SM, Meurers B, Ackerson LC, Mortazavi F, Lo V, Hernandez D, Sulzer D, Jackson GR, Maidment NT, Chesselet MF, Yang XW 2009. Bacterial artificial chromosome transgenic mice expressing a truncated mutant parkin exhibit age-dependent hypokinetic motor deficits, dopaminergic neuron degeneration, and accumulation of proteinase K-resistant alpha-synuclein. <i>J Neurosci</i> 29:1962-76.

<b>Gene/Marker</b> <b>Park7</b>	<b>Name</b> Parkinson disease (autosomal recessive, early onset) 7
<b>Allele Symbol/Name</b> <b>Common Name(s)</b>	<b><i>Park7</i><sup>tm1Shn</sup>, targeted mutation 1, Jie Shen</b> DJ-1 <sup>-</sup>
<b>Strain Name</b> <b>Stock Number</b> <b>General Terms</b>	<b>B6.Cg-Park7<sup>tm1Shn</sup>/J</b> <b>006577</b> Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/BWH2.htm">www.jax.org/jaxmice/licensing/BWH2.htm</a> )
<b>Phenotype</b>	Homozygous mice are viable and fertile. Western blot analysis using antibody specific to C-terminal sequences indicates the absence of full length gene product. Homozygous mice exhibit hypokinesia and nigrostriatal dopaminergic deficits: evoked dopamine overflow in the striatum is reduced (primarily as a result of increased dopamine uptake), nigral neurons (dopaminergic neurons) have abnormal action potential characteristics, and long term depression is absent in medium spiny neurons. Also, D2-receptor mRNA abundance and radioligand binding is normal. Dopaminergic neurons from substantia nigra pars compacta (SNpc) of homozygous mice exhibit significantly higher sensitivity to energy metabolism impairment and nigral dopaminergic neurons are particularly sensitive to Na <sup>+</sup> /K <sup>+</sup> ATPase impairment. These mutant mice may be useful in studies of Parkinson's disease, dopaminergic physiology, nigrostriatal function, locomotor inactivity, and other neurobiological research. <i>In an attempt to offer alleles on well-characterized or multiple genetic backgrounds, alleles are frequently moved to a genetic background different from that on which an allele was first characterized. Mice with this mutation were originally published on a mixed B6;129 genetic background. It should be noted that the phenotype could vary from that originally described. The strain description will be modified as published results become available.</i>
<b>Selected Reference(s)</b>	Goldberg MS, Pisani A, Haburcak M, Vortherms TA, Kitada T, Costa C, Tong Y, Martella G, Tschertner A, Martins A, Bernardi G, Roth BL, Pothos EN, Calabresi P, Shen J. 2005. Nigrostriatal dopaminergic deficits and hypokinesia caused by inactivation of the familial Parkinsonism-linked gene DJ-1. <i>Neuron</i> 45:489-96.

# Select Models for Parkinson's Disease Research

Gene/Marker <b><i>Snca</i></b>	Name <b>synuclein, alpha</b> Common Name(s) NACP; PARK1; PARK4; PD1; alpha-synuclein; alphaSYN
Allele Symbol/Name Common Name(s)	<b><i>Snca</i><sup>tm1Rosl</sup>, targeted mutation 1, Arnon Rosenthal</b> alpha-Syn <sup>-/-</sup> ; alpha-Synko
Strain Name	<b>B6;129X1-<i>Snca</i><sup>tm1Rosl</sup>/J</b>
Stock Number	<b>003692</b>
General Terms	Use of MICE by companies or for-profit entities requires a license prior to shipping. (see <a href="http://www.jax.org/jaxmice/licensing/RINAT.htm">www.jax.org/jaxmice/licensing/RINAT.htm</a> )
Phenotype	Homozygous null mice are viable, fertile, normal in size and do not display any gross abnormalities. No gene product (mRNA or protein) is detected in brain tissue. A wild-type complement of dopamine neurons, fibers and synaptic terminals is present and the overall brain architecture appears to be intact. They suffer from a reduction in total striatal dopamine and exhibit an attenuated locomotor response when given amphetamine. Normal dopamine release is observed upon stimulation of the nigrostriatal terminal with a single electrical pulse. When multiple stimuli are applied however, null mice exhibit an accelerated recovery of dopamine release. A similar acceleration is seen in wild-type mice in the presence of increased extracellular calcium. The phenotype observed in homozygous <i>Snca</i> -null mice suggests that <i>Snca</i> is an activity-dependent negative regulator of dopamine neurotransmission.
Selected Reference(s)	Abeliovich A, Schmitz Y, Farinas I, Choi-Lundberg D, Ho WH, Castillo PE, Shinsky N, Verdugo JM, Armanini M, Ryan A, Hynes M, Phillips H, Sulzer D, Rosenthal A. 2000. Mice lacking alpha-synuclein display functional deficits in the nigrostriatal dopamine system. <i>Neuron</i> 25:239-52.
Allele Symbol/Name Common Name(s)	<b><i>Snca</i><sup>tm1Sud</sup>, targeted mutation 1, Thomas C Sudhof</b> alpha <sup>-</sup>
Strain Name	<b>B6;129-<i>Snca</i><sup>tm1Sud</sup> <i>Sncb</i><sup>tm1.1Sud</sup>/J</b>
Stock Number	<b>006390</b>
General Terms	Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm">www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm</a> )
Phenotype	Mice homozygous for this targeted mutation are viable and fertile and do not display any gross physical or behavioral abnormalities. No protein product from these targeted genes is detected in brain tissue. Overall brain morphology and structure appears normal. No significant changes in the ultrastructure, short- or long-term synaptic plasticity, or in the pool size or replenishment of recycling synaptic vesicles is detected. Dopamine levels in the double targeted mice are decreased by approximately 20%, but dopamine uptake and release from isolated nerve terminals is normal. Serotonin levels are unchanged. This mutant mouse strain represents a model that may be useful in studies of synaptic function and neurodegenerative disease.
Selected Reference(s)	Chandra S, Fornai F, Kwon HB, Yazdani U, Atasoy D, Liu X, Hammer RE, Battaglia G, German DC, Castillo PE, Sudhof TC. 2004. Double-knockout mice for alpha- and beta-synucleins: effect on synaptic functions. <i>Proc Natl Acad Sci U S A</i> 101:14966-71.
Allele Symbol/Name Common Name(s) Promoter	<b>Tg(THY1-<i>Snca</i>)M1mSud, transgene insertion M1m, Thomas C Sudhof</b> M1m; Syn <sup>mtg</sup> <i>THY1</i> , Thy-1 cell surface antigen
Strain Name	<b>STOCK Tg(THY1-<i>Snca</i>)M1mSud/J</b>
Stock Number	<b>008132</b>
Former & Common Name(s)	B6.Cg-Tg(THY1- <i>Snca</i> )1Sud/J; B6.Cg-Tg(THY1- <i>Snca</i> )M1mSud/J
General Terms	Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm">www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm</a> )
Phenotype	Mice hemizygous for this transgene are viable and fertile and do not display any gross physical or behavioral abnormalities, even upon aging. This strain may be useful in studies of presynaptic proteins and synaptic vesicles.
Selected Reference(s)	Chandra S, Gallardo G, Fernandez-Chacon R, Schluter OM, Sudhof TC. 2005. Alpha-synuclein cooperates with CSPalpha in preventing neurodegeneration. <i>Cell</i> 123:383-96.

# Select Models for Parkinson's Disease Research

<i>Gene/Marker</i> <b>SNCA</b>	<i>Name</i> <b>synuclein, alpha (non A4 component of amyloid precursor) (Human)</b>
<i>Allele Symbol/Name</i> <i>Common Name(s)</i> <i>Promoter</i>	<b>Tg(Prnp-SNCA*A53T)83Vle, transgene insertion 83, Virginia M-Y Lee</b> A53T alpha-synuclein PRP; M83; Tg(SNCA)83Vle <i>Prnp</i> , prion protein
<i>Strain Name</i> <i>Stock Number</i> <i>Former &amp; Common Name(s)</i> <i>General Terms</i>	<b>B6;C3-Tg(Prnp-SNCA*A53T)83Vle/J</b> <b>004479</b> B6;C3H-Tg(SNCA)83Vle/J; M83 Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/UPENN.htm">www.jax.org/jaxmice/licensing/UPENN.htm</a> )
<i>Phenotype</i>	Mice homozygous for the transgenic insert are viable and normal in size. These transgenic mice express human A53T variant alpha-synuclein (full-length, 140 amino acid isoform) under the direction of the mouse prion protein promoter. At eight months of age, some homozygous mice develop a progressively severe motor phenotype. Presentation of the phenotype may manifest at 14-15 months of age (on average). Lax grooming, weight loss and diminished mobility precede movement impairment, partial limb paralysis, trembling and inability to stand. Immunohistochemistry analysis of mutants between eight to 12 months of age reveals widely distributed alpha-synuclein inclusions, with dense accumulation in the spinal cord, brainstem, cerebellum and thalamus. The appearance of alpha-synuclein aggregate inclusions parallels the onset of the motor impairment phenotype. Axons and myelin sheaths exhibit progressive ultrastructural degeneration. Immunoelectron microscopy and biochemical analysis show the inclusions in neurons are comprised primarily of 10-16 nm fibrils of alpha-synuclein. The structure, location and onset of the inclusions seen in the mutant mice resemble characteristics seen in human neuronal alpha-synucleinopathies, such as familial Parkinson's Disease. Mice hemizygous for the transgenic insert develop similar phenotypic traits, but onset occurs later, between 22 and 28 months of age. Homozygous mice have a high incidence of nonproductive matings. This mutant mouse strain represents a model that may be useful in studies of Parkinson's Disease.
<i>Selected Reference(s)</i>	Giasson BI, Duda JE, Quinn SM, Zhang B, Trojanowski JQ, Lee VM. 2002. Neuronal alpha-synucleinopathy with severe movement disorder in mice expressing A53T human alpha-synuclein. <i>Neuron</i> 34:521-33.
<i>Allele Symbol/Name</i> <i>Common Name(s)</i> <i>Promoter</i>	<b>Tg(THY1-SNCA)1Sud, transgene insertion 1, Thomas C Sudhof</b> LHS; Syn <sup>htg</sup> <i>THY1</i> , Thy-1 cell surface antigen
<i>Strain Name</i> <i>Stock Number</i> <i>Former &amp; Common Name(s)</i> <i>General Terms</i>	<b>C57BL/6-Tg(THY1-SNCA)1Sud/J</b> <b>008389</b> B6.Cg-Tg(THY1-SNCA*A53T)1Sud/J Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm">www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm</a> )
<i>Phenotype</i>	This transgenic strain carries a human THY1 promoter driving expression of the human synuclein, alpha (SNCA) gene. Levels of expression show a 5-fold increase in the brain and a 10-fold increase in the spinal cord. Hemizygotes are viable and fertile and unlike some similar mutant transgenic lines, do not display any Parkinson-like phenotype upon aging.
<i>Selected Reference(s)</i>	Chandra S, Gallardo G, Fernandez-Chacon R, Schluter OM, Sudhof TC. 2005. Alpha-synuclein cooperates with CSPalpha in preventing neurodegeneration. <i>Cell</i> 123 :383-96.
<i>Allele Symbol/Name</i> <i>Common Name(s)</i> <i>Promoter</i>	<b>Tg(THY1-SNCA*A30P)M30Sud, transgene insertion TS2, Thomas C Sudhof</b> M30 <i>THY1</i> , Thy-1 cell surface antigen
<i>Strain Name</i> <i>Stock Number</i> <i>General Terms</i>	<b>B6.Cg-Tg(THY1-SNCA*A30P)M30Sud/J</b> <b>008473</b> Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm">www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm</a> )
<i>Phenotype</i>	The A30P mutation in this transgenic strain is associated with the development of familial Parkinson's disease. The onset of hind limb mobility problems and a resting tremor phenotype occur around 10 months of age due to a loss of motor neurons. No Lewy body-like pathology has been observed. Extensive cell death in the spinal cord and brain are seen. This strain may be useful in studies of Parkinson's disease. Expression of the transgene

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<p><i>Selected Reference(s)</i></p>	<p>is 5-fold higher in the brain and 10-fold higher in the spinal cord. Hemizygous mice are viable and fertile, and survive to approximately 14 months of age.</p> <p>Chandra S, Gallardo G, Fernandez-Chacon R, Schluter OM, Sudhof TC. 2005. Alpha-synuclein cooperates with CSPalpha in preventing neurodegeneration. <i>Cell</i> 123 :383-96.</p>
<p><i>Allele Symbol/Name</i> <i>Common Name(s)</i> <i>Promoter</i></p>	<p><b>Tg(THY1-SNCA*A30P)TS2Sud, transgene insertion TS2, Thomas C Sudhof</b> TS2 <i>THY1</i>, Thy-1 cell surface antigen</p>
<p><i>Strain Name</i> <i>Stock Number</i> <i>Former &amp; Common Name(s)</i> <i>General Terms</i></p>	<p><b>B6.Cg-Tg(THY1-SNCA*A30P)TS2Sud/J</b> <b>008134</b> B6.Cg-Tg(THY1-SNCA*A30P)1734Sud/J Use of MICE by companies or for-profit entities requires a license prior to shipping. (<a href="http://www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm">www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm</a>)</p>
<p><i>Phenotype</i></p>	<p>The A30P mutation in this transgenic strain is associated with the development of familial Parkinson's disease. The onset of hind limb mobility problems occurs around 12 months of age (sometimes earlier), induced by a loss of motor neurons and associated with the formation of insoluble alpha synuclein aggregates. This strain may be useful in studies of Parkinson's disease. Hemizygous mice are viable and fertile.</p>
<p><i>Selected Reference(s)</i></p>	<p>Chandra S, Gallardo G, Fernandez-Chacon R, Schluter OM, Sudhof TC. 2005. Alpha-synuclein cooperates with CSPalpha in preventing neurodegeneration. <i>Cell</i> 123 :383-96.</p>
<p><i>Allele Symbol/Name</i> <i>Common Name(s)</i> <i>Promoter</i></p>	<p><b>Tg(THY1-SNCA*A53T)M53Sud, transgene insertion M53, Thomas C Sudhof</b> M53; M70A53T <i>THY1</i>, Thy-1 cell surface antigen</p>
<p><i>Strain Name</i> <i>Stock Number</i> <i>Former &amp; Common Name(s)</i> <i>General Terms</i></p>	<p><b>B6.Cg-Tg(THY1-SNCA*A53T)M53Sud/J</b> <b>008135</b> B6.Cg-Tg(THY1-SNCA*A53T)1Sud/J Use of MICE by companies or for-profit entities requires a license prior to shipping. (<a href="http://www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm">www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm</a>)</p>
<p><i>Phenotype</i></p>	<p>Hemizygous transgenic mice are viable and fertile and develop a Parkinson-like phenotype upon aging. Hind limb paralysis due to loss of motor neurons and a resting tremor are initially seen at about six months of age. No Lewy body-like pathology is noted. Cell death in the spinal cord (extensive) and brain are observed.</p>
<p><i>Selected Reference(s)</i></p>	<p>Chandra S, Gallardo G, Fernandez-Chacon R, Schluter OM, Sudhof TC. 2005. Alpha-synuclein cooperates with CSPalpha in preventing neurodegeneration. <i>Cell</i> 123 :383-96.</p>
<p><i>Allele Symbol/Name</i> <i>Common Name(s)</i> <i>Promoter</i></p>	<p><b>Tg(THY1-SNCA*A53T)F53Sud, transgenic insertion F53, Thomas C Sudhof</b> F53 <i>THY1</i>, Thy-1 cell surface antigen</p>
<p><i>Strain Name</i> <i>Stock Number</i> <i>General Terms</i></p>	<p><b>B6.Cg-Tg(THY1-SNCA*A53T)F53Sud/J</b> <b>008474</b> Use of MICE by companies or for-profit entities requires a license prior to shipping. (<a href="http://www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm">www.jax.org/jaxmice/licensing/UTEXSWHHMI.htm</a>)</p>
<p><i>Phenotype</i></p>	<p>These mice are transgenic for the A53T mutation of the human <i>SNCA</i> (synuclein, alpha) gene under the control of a human <i>THY1</i> (thymus cell antigen 1, theta) promoter. Hemizygotes are viable and fertile and develop a Parkinson-like phenotype upon aging. Hind limb paralysis due to loss of motor neurons and a resting tremor are initially seen at about eight months of age. No Lewy body-like pathology is noted. Cell death in the spinal cord (extensive) and brain are observed. Expression of the transgene is 10-fold increased in the brain and 20-fold in the spinal cord.</p>
<p><i>Allele Symbol/Name</i> <i>Common Name(s)</i></p>	<p><b><i>Gt(ROSA)26Sor<sup>tm1(SNCA*A53T)Djmo</sup></i>, targeted mutation 1, Darren Moore</b> ROSA26-Syn-A53T; ROSA26-SynA53TTg</p>
<p><i>Strain Name</i> <i>Stock Number</i> <i>General Terms</i></p>	<p><b>B6;129-Gt(ROSA)26Sor<sup>tm1(SNCA*A53T)Djmo</sup>/TmdJ</b> <b>008883</b> Use of MICE by companies or for-profit entities requires a license prior to shipping. (<a href="http://www.jax.org/jaxmice/licensing/JHU2FPLIC.htm">www.jax.org/jaxmice/licensing/JHU2FPLIC.htm</a>)</p>
<p><i>Phenotype</i></p>	<p>Homozygous ROSA26-Syn-A53T mice are viable and fertile, with the familial Parkinson's disease-associated A53T missense mutant form of human alpha-synuclein (human A53Tα-Syn or SYNA53T) inserted into the</p>

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*Gt(ROSA)26Sor* (ROSA26) locus. Widespread expression of human A53T $\alpha$ -Syn is blocked by an upstream *loxP*-flanked STOP sequence (in the absence of Cre recombinase, no human A53T $\alpha$ -Syn protein is observed in brain regions). When bred to cre expressing mice, the STOP sequence is deleted in the tissues of offspring where Cre recombinase is present; resulting in human A53T $\alpha$ -Syn expression. In particular, Stock No. 008601 B6.Cg-Tg(Th-cre)1Tmd/J may be useful for this application. These ROSA26-Syn-A53T mice allow inducible expression of a human mutation associated with familial Parkinson's disease and may be useful for studying the progressive dopaminergic neurodegeneration of Parkinson's disease and other synucleinopathies, Lewy bodies, and synaptic plasticity.

*Selected Reference(s)* Daher JP, Ying M, Banerjee R, McDonald RS, Dumas Hahn M, Yang L, Beal MF Thomas B, Dawson VL, Dawson TM, Moore DJ. 2009. Conditional transgenic mice expressing C-terminally truncated human alpha-synuclein (alphaSyn119) exhibit reduced striatal dopamine without loss of nigrostriatal pathway dopaminergic neurons. *Mol Neurodegener* 4:34.

*Allele Symbol/Name* ***Gt(ROSA)26Sor<sup>tm1</sup>(SNCA<sup>A53T</sup>)Djmo*, targeted mutation 3, Darren Moore**  
*Common Name(s)* ROSA26-Syn-E46K; ROSA26-SynE46KTg

*Strain Name* **B6;129-Gt(ROSA)26Sor<sup>tm3</sup>(SNCA<sup>E46K</sup>)Djmo/TmdJ**

*Stock Number* **008886**

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*Phenotype* Homozygous ROSA26-Syn-E46K mice are viable and fertile, with the E46K missense mutant form of human alpha-synuclein (human E46K $\alpha$ -Syn or SYNE46K; associated with familial Parkinson's disease, dementia, and visual hallucinations) inserted into the *Gt(ROSA)26Sor* (ROSA26) locus. Widespread expression of human E46K $\alpha$ -Syn is blocked by an upstream *loxP*-flanked STOP sequence (in the absence of Cre recombinase, no human E46K $\alpha$ -Syn protein is observed in brain regions). When bred to cre expressing mice, the STOP sequence is deleted in the tissues of offspring where Cre recombinase is present; resulting in human E46K $\alpha$ -Syn expression. In particular, Stock No. 008601 B6.Cg-Tg(Th-cre)1Tmd/J may be useful for this application. These ROSA26-Syn-E46K mice allow inducible expression of a human mutation associated with familial Parkinson's disease, dementia, and visual hallucinations and may be useful for studying the progressive dopaminergic neurodegeneration of Parkinson's disease and other synucleinopathies, Lewy bodies, and synaptic plasticity.

*Selected Reference(s)* Daher JP, Ying M, Banerjee R, McDonald RS, Dumas Hahn M, Yang L, Beal MF Thomas B, Dawson VL, Dawson TM, Moore DJ. 2009. Conditional transgenic mice expressing C-terminally truncated human alpha-synuclein (alphaSyn119) exhibit reduced striatal dopamine without loss of nigrostriatal pathway dopaminergic neurons. *Mol Neurodegener* 4:34.

*Allele Symbol/Name* ***Gt(ROSA)26Sor<sup>tm2</sup>(SNCA<sup>119</sup>)Djmo*, targeted mutation 2, Darren Moore**  
*Common Name(s)* ROSA26-Syn119; ROSA26-SynCT119Tg; ROSA26-a-synuclein C-terminal truncation variant (Syn119)

*Strain Name* **B6;129-Gt(ROSA)26Sor<sup>tm2</sup>(SNCA<sup>119</sup>)Djmo/TmdJ**

*Stock Number* **008889**

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*Phenotype* Homozygous ROSA26-Syn119 mice are viable and fertile, with the familial Parkinson's disease-associated Syn119 C-terminal truncation of human alpha-synuclein (human  $\alpha$ -Syn119 or SynCT119) inserted into the *Gt(ROSA)26Sor* (ROSA26) locus. Widespread expression of human  $\alpha$ -Syn119 is blocked by an upstream *loxP*-flanked STOP sequence (in the absence of Cre recombinase, no human  $\alpha$ -Syn119 protein is observed in brain regions). When bred to cre expressing mice, the STOP sequence is deleted in the tissues of offspring where Cre recombinase is present; resulting in human  $\alpha$ -Syn119 expression. In particular, Stock No. 008601 B6.Cg-Tg(Th-cre)1Tmd/J may be useful for this application. These ROSA26-Syn119 mice allow inducible expression of a human mutation associated with familial Parkinson's disease and may be useful for studying the progressive dopaminergic neurodegeneration of Parkinson's disease and other synucleinopathies, Lewy bodies, and synaptic plasticity.

*Selected Reference(s)* Daher JP, Ying M, Banerjee R, McDonald RS, Dumas Hahn M, Yang L, Beal MF Thomas B, Dawson VL, Dawson TM, Moore DJ. 2009. Conditional transgenic mice expressing C-terminally truncated human alpha-synuclein (alphaSyn119) exhibit reduced striatal dopamine without loss of nigrostriatal pathway dopaminergic neurons. *Mol Neurodegener* 4:34.

# Select Models for Parkinson's Disease Research

Gene/Marker <b><i>Sncb</i></b>	Name <b>synuclein, beta</b> Common Name(s) <b>betaSYN</b>
Allele Symbol/Name Common Name(s)	<b><i>Sncb</i><sup>tm1Sud</sup>, targeted mutation 1, Thomas C Sudhof</b> BSF
Strain Name Stock Number General Terms	<b>B6.129-<i>Sncb</i><sup>tm1Sud</sup>/J</b> <b>008133</b> Use of MICE by companies or for-profit entities requires a license. ( <a href="http://www.jax.org/jaxmice/licensing/SALKFLP.htm">www.jax.org/jaxmice/licensing/SALKFLP.htm</a> ) Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/UTEXSWHHML.htm">www.jax.org/jaxmice/licensing/UTEXSWHHML.htm</a> )
Phenotype	These mice possess <i>loxP</i> sites on either side of exon 2 of the targeted gene. Mice that are homozygous for this allele are viable, normal in size and do not display any gross physical or behavioral abnormalities, but breed very poorly. Protein levels are normal. When bred to a strain expressing Cre recombinase, this mutant mouse strain may be useful in studies of presynaptic proteins and synaptic vesicles.
Selected Reference(s)	Chandra S, Fornai F, Kwon HB, Yazdani U, Atasoy D, Liu X, Hammer RE, Battaglia G, German DC, Castillo PE, Sudhof TC. 2004. Double-knockout mice for alpha- and beta-synucleins: effect on synaptic functions. <i>Proc Natl Acad Sci U S A</i> 101:14966-71.
Allele Symbol/Name Common Name(s)	<b><i>Sncb</i><sup>tm1.1Sud</sup>, targeted mutation 1.1, Thomas C Sudhof</b> BSR; beta <sup>-</sup>
Strain Name Stock Number General Terms	<b>B6;129-<i>Sncb</i><sup>tm1Sud</sup> <i>Sncb</i><sup>tm1.1Sud</sup>/J</b> <b>006390</b> Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/UTEXSWHHML.htm">www.jax.org/jaxmice/licensing/UTEXSWHHML.htm</a> )
Phenotype	Mice homozygous for this targeted mutation are viable and fertile and do not display any gross physical or behavioral abnormalities. No protein product from these targeted genes is detected in brain tissue. Overall brain morphology and structure appears normal. No significant changes in the ultrastructure, short- or long-term synaptic plasticity, or in the pool size or replenishment of recycling synaptic vesicles is detected. Dopamine levels in the double targeted mice are decreased by approximately 20%, but dopamine uptake and release from isolated nerve terminals is normal. Serotonin levels are unchanged. This mutant mouse strain represents a model that may be useful in studies of synaptic function and neurodegenerative disease.
Selected Reference(s)	Chandra S, Fornai F, Kwon HB, Yazdani U, Atasoy D, Liu X, Hammer RE, Battaglia G, German DC, Castillo PE, Sudhof TC. 2004. Double-knockout mice for alpha- and beta-synucleins: effect on synaptic functions. <i>Proc Natl Acad Sci U S A</i> 101:14966-71.
Gene/Marker <b><i>Sncg</i></b>	Name <b>synuclein, alpha (non A4 component of amyloid precursor)</b>
Allele Symbol/Name Common Name(s)	<b><i>Sncg</i><sup>tm1Vlb</sup>, targeted mutation 1, Vladimir L Buchman</b> TgHSNCG <sup>tm1VLB</sup>
Strain Name Stock Number Phenotype	<b>B6.129P2-<i>Sncg</i><sup>tm1Vlb</sup>/J</b> <b>008843</b> Mice homozygous for this $\gamma$ -synuclein mutant allele are viable and fertile with no obvious abnormalities in development, behavior, or gross morphology of the nervous system. No RNA or protein expression from the targeted gene is observed. Slight upregulation of $\beta$ -synuclein is reported in the midbrain of homozygous mice. Homozygous mice are also resistant to the inflammatory/apoptotic Parkinson's disease-like pathology that results following MPTP neurotoxin administration (the active form of which (MPP <sup>+</sup> ) gains entry into dopaminergic cells via the dopamine transporter (DAT)). These $\gamma$ -synuclein mutant mice may be useful in studying synuclein function in neurodegenerative diseases, such as Parkinson's disease.
Selected Reference(s)	Ninkina N, Papachroni K, Robertson DC, Schmidt O, Delaney L, O'Neill F, Court F, Rosenthal A, Fleetwood-Walker SM, Davies AM, Buchman VL. 2003. Neurons expressing the highest levels of gamma-synuclein are unaffected by targeted inactivation of the gene. <i>Mol Cell Biol</i> 23:8233-45. Senior SL, Ninkina N, Deacon R, Bannerman D, Buchman VL, Cragg SJ, Wade-Martins R. 2008. Increased striatal dopamine release and hyperdopaminergic-like behaviour in mice lacking both alpha-synuclein and gamma-synuclein. <i>Eur J Neurosci</i> 27:947-57.

# Select Models for Parkinson's Disease Research

<p>Gene/Marker <b>Spp1</b></p>	<p>Name <b>secreted phosphoprotein 1</b>  Common Name(s) 44kDa bone phosphoprotein; Apl-1; BNSP; BSPI; Bsp; ETA-1; OP; OPN; OSP; Opnl; Ric; Spp-1; bone sialoprotein 1; minopontin; osteopontin; osteopontin-like protein</p>
<p>Allele Symbol/Name Common Name(s)</p>	<p><b>Spp1<sup>tm1Blh</sup></b>, targeted mutation 1, Brigid L Hogan  Eta-1; OPN<sup>-</sup>; Opn<sup>-</sup>; eta1</p>
<p>Strain Name Stock Number General Terms</p>	<p><b>B6.129S6(Cg)-Spp1<sup>tm1Blh</sup>/J</b>  <b>004936</b>  Use of MICE by companies or for-profit entities requires a license prior to shipping (<a href="http://www.jax.org/jaxmice/licensing/MAINMED.htm">www.jax.org/jaxmice/licensing/MAINMED.htm</a>)</p>
<p>Additional Research Areas Phenotype</p>	<p>Immunology and Inflammation Research; Internal/Organ Research  Mice that are homozygous for the targeted mutation are viable, fertile, normal in size and do not display any gross physical or behavioral abnormalities. No gene product (mRNA) is detected by RT-PCR analysis of embryonic fibroblasts and kidney. Immunohistochemical analysis of kidney and bone tissue also fails to detect gene product (protein). Homozygotes exhibit disorganized ultrastructural wound matrix remodeling and defective macrophage infiltration and accumulation at sites of injury and infection. Experimentally induced hyperoxaluria results in renal tubule deposition of calcium oxalate crystals. Accelerated ectopic calcification mineralization in soft tissues occurs after subcutaneous implantation of glutaraldehyde-fixed aortic valve tissue. Mutant macrophage response to mycobacteria infection and pulmonary granulomatous response and inflammation are impaired. According to a recent publication (Hsieh <i>et al</i> 2006 <i>Cancer Res</i> 2006 66:7119-27), mutant mice treated with a skin chemical carcinogenesis protocol show a marked decrease both in tumor/papilloma incidence and multiplicity compared with wild-type. This mutant mouse strain may be useful in studies of tissue remodeling, wound repair, fibrosis and granulomatous diseases.  <i>All of the characterization of this mutant was performed while the mutant allele was on a mixed 129S6, Black Swiss background. The phenotype of the donated mutant, which is on a congenic C57BL/6 background, may vary.</i></p>
<p>Selected Reference(s)</p>	<p>Liaw L, Birk DE, Ballas CB, Whitsitt JS, Davidson JM, Hogan BL. 1998. Altered wound healing in mice lacking a functional osteopontin gene (spp1). <i>J Clin Invest</i> 101:1468-78.</p>

<p>Gene/Marker <b>Th</b></p>	<p>Name <b>tyrosine hydroxylase</b>  Common Name(s) TYH; The</p>
<p>Allele Symbol/Name Common Name(s)</p>	<p><b>Th<sup>tm1Rpa</sup></b>, targeted mutation 1, Richard D Palmiter  DA<sup>-</sup>, pTH4, TH<sup>-</sup></p>
<p>Strain Name Stock Number Phenotype</p>	<p><b>B6;129-Dbh<sup>tm2(Th)Rpa</sup> Th<sup>tm1Rpa</sup>/J</b>  <b>009688</b>  Mice heterozygous for both targeted mutations are viable and fertile. Dopamine-deficient (DA-deficient, DA<sup>-/-</sup>, or DD) mice are homozygous for the TH mutant allele and heterozygous for the DBH-TH mutant allele (Th<sup>-/-</sup>; Dbh<sup>Th/+</sup>). While no expression from the TH mutant allele is observed in any tissues (resulting in deficiency of both dopamine (DA) and norepinephrine (NE)), the DBH-TH mutant allele contains the TH coding sequence under the control of the endogenous DBH promoter region and restores TH expression in noradrenergic neurons. DD mice become hypoactive and hypophagic around two weeks of age and usually die before four weeks of age. Treatment with L-DOPA, the product of TH enzymatic activity, rescues size, feeding, and life span. These DD mice may be useful in studying dopaminergic neurobiology (including neurotransmitters, addiction, feeding, learning and memory, catecholamines, and Parkinsonian phenotypes).</p>
<p>Selected Reference(s)</p>	<p>Hnasko TS, Sotak BN, Palmiter RD. 2007. Cocaine-conditioned place preference by dopamine-deficient mice is mediated by serotonin. <i>J Neurosci</i> 27: 12484-8.  Zhou Q-Y, Quaife CJ, Palmiter RD. 1995. Targeted disruption of the tyrosine hydroxylase gene reveals that catecholamines are required for mouse fetal development. <i>Nature</i> 374: 640-3.  Zhou QY, Palmiter RD. 1995. Dopamine-deficient mice are severely hypoactive, adipsic, and aphagic. <i>Cell</i> 83: 1197-209.</p>

# Select Models for Parkinson's Disease Research

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Gene/Marker <b>Ucp2</b>	Name <b>uncoupling protein 2 (mitochondrial, proton carrier)</b> Common Name(s) UCPH
Allele Symbol/Name Common Name(s)	<b>Ucp2<sup>tm1Lowl</sup>, targeted mutation 1, Bradford B Lowell</b> Ucp2-
Strain Name	<b>B6.129S4-Ucp2<sup>tm1Lowl</sup>/J</b>
Stock Number	<b>005934</b>
Former & Common Name(s)	B6.129-Ucp2 <sup>tm1Lowl</sup> /J
General Terms	Use of MICE by companies or for-profit entities requires a license prior to shipping. ( <a href="http://www.jax.org/jaxmice/licensing/BETHIS3.htm">www.jax.org/jaxmice/licensing/BETHIS3.htm</a> )
Additional Research Areas	Diabetes and Obesity Research; Metabolism Research; Research Tools: Toxicology Research
Phenotype	Homozygous mice are viable and fertile and do not express full length mRNA in heart, kidney, spleen, white adipose tissue, and pancreatic islets. In splenic mitochondria, endogenous protein was undetectable. When grown under high glucose conditions, cultured pancreatic islet cells from homozygous mice have increased insulin secretion and ATP levels compared to wild-type. Homozygous mice have 18% lower blood glucose levels. Whether fasting or fed, homozygotes have approximately 3-fold greater serum insulin due to increased insulin secretion. Similarly, glucose-stimulated insulin secretion is significantly increased. High fat diet-fed mice or palmitate-treated islets maintain pancreatic glucose responsiveness <i>in vivo</i> and <i>in vitro</i> compared to wild-type. Mitochondria isolated from the dopaminergic mesencephalic nigral cells of homozygous mice have increased reactive oxygen species but lesser mitochondria number and increased sensitivity to MPTP, mimicking Parkinson's disease. This mouse may be useful in studies of diabetes, glucose-dependent metabolism-secretion coupling, aerobic respiration, Parkinson's disease, epilepsy, stroke, and other neurodegenerative diseases.
Selected Reference(s)	Zhang CY, Baffy G, Perret P, Krauss S, Peroni O, Grujic D, Hagen T, Vidal-Puig AJ, Boss O, Kim YB, Zheng XX, Wheeler MB, Shulman GI, Chan CB, Lowell BB. 2001. Uncoupling protein-2 negatively regulates insulin secretion and is a major link between obesity, beta cell dysfunction, and type 2 diabetes. <i>Cell</i> 105:745-55.

## Research Models for Parkinson's Disease

[www.jax.org/jaxmice/research/neurobiology/parkinsons](http://www.jax.org/jaxmice/research/neurobiology/parkinsons)

Links to research models for Parkinson's Disease.

## Neurobiology Research Tools

[www.jax.org/jaxmice/research/neurobiology/tools](http://www.jax.org/jaxmice/research/neurobiology/tools)

View database generated lists for research tools for neurobiology strains either by strain name, including strain description or by promoter, including site of expression.

## Other Related Mouse Model Areas

[www.jax.org/jaxmice/research](http://www.jax.org/jaxmice/research)

Links to the following research areas under Neurobiology Research: Alzheimer's Disease, Amyotrophic lateral sclerosis (ALS) Disease, Huntington's Disease, and Spinal Muscular Atrophy (SMA) Disease.

## Donate a Strain to The Jackson Laboratory Repository

[www.jax.org/grc](http://www.jax.org/grc)

This site describes the benefits you receive for donating a strain, and provides a web submission form.

## JAX® Mice Database

[www.jax.org/jaxmice](http://www.jax.org/jaxmice)

A searchable database containing information related to mouse phenotype, strain construction, husbandry, genotyping protocols and relevant citations.

## Resource Manuals

[www.jax.org/jaxmice/literature](http://www.jax.org/jaxmice/literature)

Resource manuals are available many topics: Breeding strategies, Cancer, Genetic background, JAX® Mice Research Tool Strains, Neurobiology. For a full listing of manuals available or to request a copy of these manuals please go to our online literature request form ([www.jax.org/jaxmice/literature](http://www.jax.org/jaxmice/literature)).

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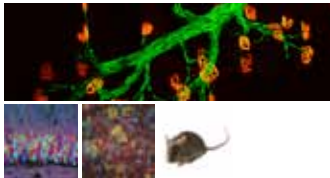
[www.jax.org/jaxmice/newstrains](http://www.jax.org/jaxmice/newstrains)

We distribute hundreds of new mouse models each year. The supply of mice from strains that have recently been released for distribution may be limited. See our website for further information.

## New Strains Under Development

[www.jax.org/jaxmice/interestlist](http://www.jax.org/jaxmice/interestlist)

You can see which strains are under development by research area or by gene symbol. Each year, nearly 300 new mouse models become available from The Jackson Laboratory. See our website for further information



1. Top: Motor neurons in the lateral gastrocnemus of B6.Cg-Tg(Thy1-YFP)16Jrs/J (Stock Number 003709) are seen as green, acetylcholine receptors on the muscle are labeled with bungarotoxin in red. Courtesy of Dr. Rob Burgess, The Jackson Laboratory.
2. Bottom left: B6;CBA-Tg(Thy1-Brainbow1.0)Mlch/J (Stock Number 007910) Neurons are labelled in the dentate gyrus. Courtesy of Dr. Jean Livet, Harvard University. Livet *et al.*, *Nature* 450: 56 (2007).
3. Bottom right: B6.Cg-Tg(Thy1-Brainbow1.1)Mlch/J (Stock Number 007911) Astrocytes are labelled in the cortex. Courtesy of Dr. Jean Livet, Harvard University. Livet *et al.*, *Nature* 450: 56 (2007).