Overview

This strain provides a broadly used model for severe infantile Niemann Pick Type C1, but unlike human NPC1, no neurofibrillary tangles are found. This null allele has a slightly later onset and decreased severity on this BALB background relative to homozygotes on a C57BL/6 congenic background or homozygotes for the Npc1<sup>spm</sup> allele on a C57BLKS/J background, but this model is more severe than the C57BL/6J-Npc1<sup>m1N</sup>/J model.

Our preclinical efficacy testing services offer scientific expertise and an array of target-based and phenotype-based outcome measures, both in vivo and at endpoint, for flexible study designs and assay development in mouse models of Niemann Pick Type C. See our full service platform.

RESEARCH APPLICATIONS

Mouse/Human Gene Homologs
Neurobiology Research
Sensorineural Research
Reproductive Biology Research
Metabolism Research
Internal/Organ Research
Cardiovascular Research
NPC1 is a transmembrane protein with a sterol-sensing domain that is essential for intracellular transport of unesterified cholesterol out of the endolysosomal compartment to the cytosol. It is primarily localized to late endosomes and lysosomes, but also cycles through the Golgi apparatus. Defects in this gene cause Niemann-Pick Disease Type 1C, in which failed lipid metabolism leads to accumulation of cholesterol and fatty acids in all tissues, with pronounced consequences in spleen, liver, lungs, lymph nodes, thymus, bone marrow and brain. Mice homozygous for the spontaneous $Npc1^{m1N}$ mutation on the BALB/cNctr background have neuronal accumulation of unesterified cholesterol and gangliosides by birth, develop axonal spheroids beginning at approximately 3 weeks of age, progressive weight loss, progressive cerebellar ataxia with onset beginning at approximately 6 weeks of age, microgliosis, and neurodegeneration that is pronounced in the thalamus and Purkinje cells. Purkinje cells show progressive, patterned degeneration from rostral to caudal beginning with zebrin II negative Purkinje cells. Cerebellar sections showed a normal number of Purkinje cells at 30 days of age, by 50 days most were gone from lobules I-III, and by 70 days they only remained in lobule X, but Bergman glia, oligodendrocytes, and granules cells remained intact in all lobules at 70 days of age (Ko et al., 2005). By 40 days of age the brains of homozygotes are significantly smaller than normal. The average reported lifespan is approximately 9-11 weeks. Loss of glia in the corpus callosum precedes the loss of Purkinje cells, and neuroinflammation in BALB/cNctr-$Npc1^{m1N}$/J homozygotes involves atypical microglia (Cougnoux et al., 2018) that are present by 9 days of age and in significant numbers by 22 days of age (Reid et al., 2004). Hypomyelination of the corpus callosum, anterior commissure, and cerebral cortex is found by 10 days of age and progresses, although the optic tract, brainstem, cerebellar white matter, external capsule and optic nerves remain well myelinated. Although premyelinating oligodendrocytes are plentiful at 10 days of age, there is a significant diminution in mature oligodendrocytes at 20 days of age (Takikita et al., 2004). Hyperphosphorylation of tau was found in extracts from BALB/cNctr-$Npc1^{m1N}$/J homozygous cerebrum and cerebellum, but no neurofibrillary tangles were detected (Treiber-Held et al., 2003). Hovakimyan et al. (2013) found highly disrupted olfactory epithelium, abnormal olfactory nerve morphology, increased activated microglia in the olfactory epithelium, loss of olfactory neurons and impaired olfactory response to phenylethyl alcohol, hydrogen sulfide, and carbon dioxide in homozygotes by 10 weeks of age, with less severe changes already evident by 35 days of age. Mitochondrial membrane potential and ATP level are lower than normal in tissues from homozygotes, and the mitochondria of the brain are smaller and more rounded than normal with translucent matrices and irregular cristae. Addition of ATP to culture medium allows the neurite extension and sprouting that is normally diminished in neurons from homozygotes, indicating that the deterioration of neurite outgrowth in homozygous brains stems from inadequate ATP (Yu et al., 2005).

Non-neuronal tissues are also severely affected resulting in hepatosplenomegaly, micronodularity and increased mass of the lungs, and reproductive defects. Histology of the lung of homozygotes on a BALB/c background at 70 days of age found thickened intra-alveolar septae, enlarged lamellar bodies in type II pneumocytes, accumulation of surfactant with increased phospholipid and cholesterol content, and clusters of large foamy alveolar macrophages and vascular-filled leukocytes (Roszell et al., 2013). $Npc1^{m1N}$ homozygous females are infertile, with underdeveloped ovarian follicles, but transplanting
ovaries from homozygotes to wild-type hosts permits ovulation and formation of corpora lutea (Gevry et al., 2004). On this BALB background homozygous males are also infertile and fail to fertilize even zona-free eggs in IVF (Fan et al., 2006), although males on a mixed BALB x 129 background are reportedly fertile (Erickson et al., 2002). Npc1^<sup>m1N</sup>/+ heterozygotes on this BALB/cNctr background have also been found to display elevated cholesterol levels and decreased ATP in the cerebrum and cerebellum, loss of 25-30% of Purkinje cells, and hyperphosphorylation of tau all in very old mice, 104-106 weeks of age, but not at 24 or 40 weeks of age (Yu et al., 2005).

This model of the Niemann-Pick Type C1 lysosomal storage disease is an early onset model that is more severe than the Npc1^<sup>m1N</sup> model but less severe than when this Npc1^<sup>m1N</sup> allele is backcrossed to congenicity onto the C57BL/6 background. Metabolomic profiles from liver extracts of homozygotes at 49 days of age showed a more significant increase in accumulation of ceramides, sphingomyelins, sphingoid bases, gangliosides, free cholesterol, and oxysterols on the congenic C57BL/6J background relative to homozygotes on a BALB/c background. The impact of genetic background was less severe in brain metabolomic profiles in which congenic C57BL/6J homozygotes accumulate more ceramide, lactosylceramide, and 3B,5a,6B-cholestan-triol compared with homozygotes on the BALB/c background (Praggastis et al., 2015). Axonal spheroids are highly concentrated in the fimbria on the C57BL/6 congenic background (Walkley and Suzuki, 2004). The Npc1^<sup>m1N</sup> allele is a null allele; Western blot of liver extracts from homozygotes at 30 and 75 days of age failed to detect NPC1 protein, whereas small amounts of NPC1 were identified in Npc1^<sup>m1N</sup> homozygotes at each timepoint assessed between 30 and 120 days of age (Maue et al., 2011). Purkinje cell loss at 6 weeks of age in Npc1^<sup>m1N</sup> homozygotes was reported to be equivalent to the loss found at 9 weeks of age in Npc1^<sup>m1N</sup> homozygotes (Maue et al., 2011) and the demyelination phenotype is less severe in Npc1^<sup>m1N</sup> homozygotes. Npc1^<sup>m1N</sup> homozygotes have bred before becoming debilitated, but Npc1^<sup>m1N</sup> must be maintained from heterozygous breeders. The C57BLKS/J-Npc1^<sup>m1N</sup> model displays a faster, more severe Purkinje cell loss than do these Npc1^<sup>m1N</sup> homozygotes on the BALB/c background, but survive approximately 15 days longer than this model (Sama et al., 2003).
Genotyping Protocols
Separated PCR: Npc1
Standard PCR: Npc1Alternate1
Separated MCA: Npc1

Genotyping resources and troubleshooting

Dietary Information
LabDiet® 5K52 formulation (6% fat)

Breeding Considerations

When maintaining a live colony, heterozygous mice may be intercrossed or bred to wildtype siblings. Homozygotes are sterile.

Additional Breeding and Husbandry Support

Mating System

Wild-type x Heterozygote
Heterozygote x Wild-type

Appearance

albino, ataxic, tremors
Related Genotype: a/a Tyrp1\textsuperscript{b} /Tyrp1\textsuperscript{b} Tyr\textsuperscript{c} /Tyr\textsuperscript{c} Npc1\textsuperscript{m1N} /Npc1\textsuperscript{m1N}

albino, unaffected
Related Genotype: a/a Tyrp1\textsuperscript{b} /Tyrp1\textsuperscript{b} Tyr\textsuperscript{c} /Tyr\textsuperscript{c} Npc1\textsuperscript{m1N} + or +/+ 

Citation

When using the Niemann Pick type C1 NIH mouse strain in a publication, please cite the originating article(s) and include JAX stock #003092 in your Materials and Methods section.

Animal Health Reports

Facility Barrier Level Descriptions

FGB29 (Standard)

Pricing & Availability

Live mice available in varying quantities. Ask Customer Service for details.

Available

<table>
<thead>
<tr>
<th>AGE</th>
<th>SEX</th>
<th>GENOTYPE</th>
<th>PRICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approx 4-8 weeks</td>
<td>Female</td>
<td>Heterozygous for Npc1\textsuperscript{m1N}</td>
<td>$255.00</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>Heterozygous for Npc1\textsuperscript{m1N}</td>
<td>$255.00</td>
</tr>
<tr>
<td>Approx 4-8 weeks</td>
<td>Female</td>
<td>Wild-type for Npc1\textsuperscript{m1N}</td>
<td>$78.51</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>Wild-type for Npc1\textsuperscript{m1N}</td>
<td>$78.51</td>
</tr>
</tbody>
</table>
## BREEDER PAIR

<table>
<thead>
<tr>
<th>SEX</th>
<th>GENOTYPE</th>
<th>PRICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>Heterozygous for Npc1&lt;sup&gt;mtN&lt;/sup&gt;</td>
<td>$333.51</td>
</tr>
<tr>
<td>Male</td>
<td>Wild-type for Npc1&lt;sup&gt;mtN&lt;/sup&gt;</td>
<td>$333.51</td>
</tr>
<tr>
<td>Female</td>
<td>Wild-type for Npc1&lt;sup&gt;mtN&lt;/sup&gt;</td>
<td>$333.51</td>
</tr>
<tr>
<td>Male</td>
<td>Heterozygous for Npc1&lt;sup&gt;mtN&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

## PAYMENT TERMS AND CONDITIONS

Terms are granted by individual review and stated on the customer invoice(s) and account statement. These transactions are payable in U.S. currency within the granted terms. Payment for services, products, shipping containers, and shipping costs that are rendered are expected within the payment terms indicated on the invoice or stated by contract. Invoices and account balances in arrears of stated terms may result in The Jackson Laboratory pursuing collection activities including but not limited to outside agencies and court filings.

## THE JACKSON LABORATORY'S GENOTYPE PROMISE

The Jackson Laboratory has rigorous genetic quality control and mutant gene genotyping programs to ensure the genetic background of JAX® Mice strains as well as the genotypes of strains with identified molecular mutations. JAX® Mice strains are only made available to researchers after meeting our standards. However, the phenotype of each strain may not be fully characterized and/or captured in the strain data sheets. Therefore, we cannot guarantee a strain’s phenotype will meet all expectations. To ensure that JAX® Mice will meet the needs of individual research projects or when requesting a strain that is new to your research, we suggest ordering and performing tests on a small number of mice to determine suitability for your particular project. We do not guarantee breeding performance and therefore suggest that investigators order more than one breeding pair to avoid delays in their research.

---

**Terms Of Use**

**TERMS OF USE**

General Terms and Conditions

**LICENSING INFORMATION**

Phone: 207-288-6470  
Email: TechTran@jax.org  

JAX® Mice, Products & Services Conditions of Use

"MICE" means mouse strains, their progeny derived by inbreeding or crossbreeding, unmodified derivatives from mouse strains or their progeny supplied by The Jackson Laboratory ("JACKSON"). "PRODUCT(S)" means biological materials supplied by JACKSON, and their derivatives. "SERVICES" means projects conducted by JACKSON for other parties that may include but are not limited to the use of MICE or PRODUCTS. "RECIPIENT" means each recipient of MICE, PRODUCTS, or SERVICES provided by JACKSON including each institution, its employees and other researchers under its control. MICE or PRODUCTS shall not be: (i) used for any purpose other than internal research, (ii) sold or otherwise provided to any third party for any use, or (iii) provided to any agent or other third party to provide breeding or other services. Acceptance of MICE, PRODUCTS or SERVICES from JACKSON shall be deemed as agreement by RECIPIENT to these conditions, and departure from these conditions requires JACKSON's prior written authorization.

**No Warranty**
MICE, PRODUCTS AND SERVICES ARE PROVIDED "AS IS". JACKSON EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS, IMPLIED, OR STATUTORY, WITH RESPECT TO MICE, PRODUCTS OR SERVICES, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR ANY WARRANTY OF NON-INFRINGEMENT OF ANY PATENT, TRADEMARK, OR OTHER INTELLECTUAL PROPERTY RIGHTS.

Credit for PRODUCTS or SERVICES
In case of dissatisfaction for a valid reason and claimed in writing by a purchaser within ninety (90) days of receipt of, PRODUCTS or SERVICES, JACKSON will, at its option, provide credit or replacement for the PRODUCT received or the SERVICES provided; JACKSON makes no other representations and this shall be the exclusive remedy of the purchaser. Please note specific policy for live mice.

Animal Care and Use for SERVICES
Consistent with the requirement for a written understanding regarding animal care and use, the JACKSON Animal Care and Use Committee will review the animal care and use protocol(s) associated with any SERVICES to be performed at JACKSON, and JACKSON shall have ultimate responsibility and authority for the care of animals while on site or in JACKSON custody.

No Liability
In no event shall JACKSON, its trustees, directors, officers, employees, and affiliates be liable for any causes of action or damages, including any direct, indirect, special, or consequential damages, arising out of the provision of MICE, PRODUCTS, or SERVICES, including economic damage or injury to property and lost profits, and including any damage arising from acts or negligence on the part of JACKSON, its agents or employees. Unless prohibited by law, in purchasing or receiving MICE, PRODUCTS, or SERVICES from JACKSON, purchaser or recipient, or any party claiming by or through them, expressly releases and discharges JACKSON from all such causes of action or damages, and further agrees to defend and indemnify JACKSON from any costs or damages arising out of any third party claims.

MICE, PRODUCTS or SERVICES are to be used in a safe manner and in accordance with all applicable governmental rules and regulations.

The foregoing represents the General Terms and Conditions applicable to JACKSON's MICE, PRODUCTS or SERVICES. In addition, special terms and conditions of sale of certain MICE, PRODUCTS, or SERVICES may be set forth separately in JACKSON web pages, catalogs, price lists, contracts, and/or other documents, and these special terms and conditions shall also govern the sale of these MICE, PRODUCTS and SERVICES by JACKSON, and by its licensees and distributors.

Acceptance of delivery of MICE, PRODUCTS or SERVICES shall be deemed agreement to these terms and conditions. No purchase order or other document transmitted by purchaser or recipient that may modify the terms and conditions hereof, shall be in any way binding on JACKSON, and instead the terms and conditions set forth herein, including any special terms and conditions set forth separately, shall govern the sale of MICE, PRODUCTS or SERVICES by JACKSON.

Related Strains

All

By Allele

By Gene

By Collection

All Related Strains