A copy number variation on human chromosome 16p11.2 is among the most common genetic variations found in autism spectrum disorders. The 16p11 allele has the syntenic 440 kbp region on mouse chromosome 7F3 deleted (between and including *Coro1a* to *Spn*) and also expresses a fluorescent reporter gene (mCherry) under the control of the CAG promoter. These mice may be useful in studying basal ganglia circuitry and the pathophysiology of autism.

Donating Investigator
Jacqueline N Crawley, University of California Davis School of Medicine
Ricardo E Dolmetsch, Stanford University
This strain description is for 16p11<sup>−</sup> mice on a predominantly C57BL/6N genetic background. Because the live colony at The Jackson Laboratory is maintained by breeding B6129SF1/J (Stock No. 101043) with heterozygous 16p11<sup>−</sup> males every generation, the phenotype of the 16p11<sup>−</sup> mice distributed from The Jackson Laboratory Stock No. 025100 could vary from that shown below. We may modify the strain description if necessary as published results become available.

A copy number variation (CNV) on human chromosome 16p11.2 is among the most common genetic variations found in autism spectrum disorders (ASD). Patients with this deletion display motor deficits, speech/language delay, and cognitive impairments, accompanied by ASD, attention deficit hyperactivity disorder (ADHD), seizures, and hearing disorders. Conversely, a duplication of 16p11.2 is associated with schizophrenia. The chromosome 16p11.2 CNV encompasses 26 genes that are highly conserved on mouse chromosome 7F3.

The 16p11<sup>−</sup> allele has the syntenic 440 kbp region on mouse chromosome 7F3 deleted (between and including Coro1a to Sprn) and also expresses a membrane-targeted fluorescent reporter gene (mCherry) under the control of the CAG promoter. Heterozygous mice (16p11<sup>+</sup>) are viable and fertile, but are visibly smaller and leaner with impaired early postnatal survival (see additional breeding notes below). 16p11<sup>−</sup> mice exhibit normal social behavior but show hyperactivity, circling and deficits in movement control, hearing (deaf), and habituation to familiarity. Heterozygotes have anatomical and cellular abnormalities, particularly in cortex and striatum of juvenile mice: abnormalities in the basal ganglia circuitry, elevated dopamine D2 receptor (Drd2+) expressing striatal medium spiny neurons and fewer dopamine-sensitive (Drd1+) neurons in deep layers of cortex. For imaging large-scale anatomical structures, such as white matter tracts, mCherry fluorescence is very strong. For identification of single neuronal cell-bodies, however, immunohistochemical fluorescence might improve the outcome.

The donating investigator reports the following breeding characteristics. Heterozygous females do not take care of their pups. Breeding 16p11<sup>−</sup> animals together never resulted in homozygous pups. To improve pup survival, breeding cages may be supplemented with high-fat chow and fresh fruit (apples and oranges). Removing wildtype littermates by postnatal day 6 reduces food competition and is very effective in improving 16p11<sup>−</sup> pup survivability. Further, 16p11<sup>−</sup> pups benefit from concentrated liquid dietary supplement and vitamin B12 injections (if underweight). Heterozygous mice are usually still runty at standard weaning age, and benefit from delaying wean for up to a week. All weanlings may be provided with fresh fruit supplements until 4 weeks of age. Healthy adults can be maintained on standard rodent chow and water ad libitum. Underweight adults benefit from dietary supplements.

Mice with the mouse chromosome 7F3 region flanked by several loxP and frt sites (16p11<sup>ﬂx</sup>) are available at The Jackson Laboratory as Stock No. 025330.
Genotyping Protocols
Standard PCR: Del(7Coro1a-Spn)Dolm-alternate 1
Genotyping resources and troubleshooting
Breeding Considerations

When maintaining a live colony, the donating investigator routinely breeds wildtype females with heterozygous males. When maintaining a live colony at The Jackson Laboratory, B6129SF1/J (Stock No. 101043) females are bred with heterozygous males every generation.

Heterozygous mice (16p11\(^{+/-}\)) are viable and fertile, but are visibly smaller and leaner with impaired early postnatal survival. The donating investigator reports the following breeding characteristics. Heterozygous females do not take care of their pups. Breeding 16p11\(^{+/-}\) animals together never resulted in homozygous pups. To improve pup survival, breeding cages may be supplemented with high-fat chow and fresh fruit (apples and oranges). Removing wildtype littermates by postnatal day 6 reduces food competition and is very effective in improving 16p11\(^{+/-}\) pup survivability. Further, 16p11\(^{+/-}\) pups benefit from concentrated liquid dietary supplement and vitamin B12 injections (if underweight). Heterozygous mice are usually still runty at standard weaning age, and benefit from delaying wean for up to a week. All weanlings may be provided with fresh fruit supplements until 4 weeks of age. Healthy adults can be maintained on standard rodent chow and water ad libitum. Underweight adults benefit from dietary supplements.

Although the Portmann et al. 2014 Cell Rep 7(4):1077-92 publication describes the mESC used were 129/OLA, the donating laboratory indicates it may have been a different 129 origin. It is not known if the 16p11\(^{+/-}\) mice we received retained the mESC-derived allele(s) at the tyrosinase locus (e.g., Tyr\(^{c}\) and/or Tyr\(^{c-h}\)) that, because it is only ~40 kbp proximal on chromosome 7, would segregate along with the 16p11\(^{+/-}\) region.

Additional Breeding and Husbandry Support

Citation

When using the 16p11.2\(^{-}\) mouse strain in a publication, please cite the originating article(s) and include JAX stock #025100 in your Materials and Methods section.

Animal Health Reports

Facility Barrier Level Descriptions

Production of mice from cryopreserved embryos or sperm occurs in a maximum barrier room, G200

Pricing & Availability

Typically mice are recovered in 10-14 weeks. Contact Customer Service to place an order or for more information.

Domestic Pricing

<table>
<thead>
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<th>SERVICE/PRODUCT</th>
<th>DESCRIPTION</th>
<th>PRICE</th>
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<td>Cryo Recovery</td>
<td>Heterozygous or Wildtype for Del(7Coro1a-Spn)1Dolm</td>
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