Overview

JAXTag™

Also Known As:B6CBA-R6/2 (CAG 120 +/- 5)

These transgenic mice display a progressive neurological phenotype that mimics many of the features of Huntington Disease (HD) in humans, including choreiform-like movements, involuntary stereotypic movements, tremor, and epileptic seizures, as well as nonmovement disorder components, including unusual vocalization. Frequent urination and loss of body weight and muscle bulk occurs through the course of the disease. Neurological developments include Neuronal Intranuclear Inclusions, which contain both the huntingtin and ubiquitin proteins. This line is transgenic for the 5’ end of the human HD gene carrying approximately 120 +/- 5 (CAG)repeat expansions.

Donating Investigator

Gillian P Bates, University College London, Institute of Neurology

GENETIC OVERVIEW

<table>
<thead>
<tr>
<th>Genetic Background</th>
<th>Generation</th>
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<tr>
<td>Stock No: 006494</td>
<td>Tg(HDexon1)62Gpb/3J</td>
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<td>B6CBA-R6/2 (CAG 120 +/- 5)</td>
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<td>Transgenic</td>
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Sized to accommodate orders of up to 10 or more with age range. Ask Customer Service for details.
Important Note
January 2007: alteration in strain name and phenotype. Please see Strain Development for additional information.

Detailed Description
This line is transgenic for the 5' end of the human HD gene carrying approximately 120 +/- 5 (CAG) repeat expansions. The transgene is ubiquitously expressed. Transgenic mice exhibit a progressive neurological phenotype that mimics many of the features of HD, including choreiform-like movements, involuntary stereotypic movements, tremor, and epileptic seizures, as well as nonmovement disorder components, including unusual vocalization. They urinate frequently and exhibit loss of body weight and muscle bulk through the course of the disease. Neurologically they develop Neuronal Intranuclear Inclusions (NII) which contain both the huntingtin and ubiquitin proteins. Previously unknown, these NII have subsequently been identified in human HD patients. The age of onset of HD symptoms is reported to occur between 9 and 11 weeks. Commonly known as the "R6/2" strain.

Transgenic mice develop hyperglycemia by 12 weeks of age with a corresponding decrease in insulin levels. Pancreatic beta cells develop huntingtin inclusions as early as 7 weeks of age, by 12 weeks more than 95% of beta cells have inclusions. Pancreatic alpha and delta cells also exhibit some inclusions (24% and 6% of cells, respectively) by 12 weeks. Pancreatic islets become hypotonic and beta cells are dramatically reduced in number by 12 weeks. Beta cells contain very few insulin secretory vesicles. (Bjorkqvist M., et al. 2005)

The HDexon1 transgene functions as single copy insertion. Sequence analysis identified its insertion site within an intron of the predicted gene Gm12695 on mouse chromosome 4 (chr4:96,409,585-96,414,930 [assembly NCBI 37/mus musculus)
9], and the transgene is flanked by two rearranged sequences that do not contain the full exon 1 encoding DNA (Cowin et al. 2011 PLoS ONE 6(12):e28409). Additionally, a segment of Gram-positive bacterial sequence (likely originating from cloning vector contamination) is inserted just upstream of the HTT promoter that drives the expression of the intact copy. Transgene insertion also resulted in a 5.4 kbp deletion of mouse chromosomal DNA near the integration site (Chiang et al. 2012 Nat Genet. 44(4):390-7). As of January 2017, the function of predicted gene Gm12695 is unknown. It is normally expressed at negligible levels in mouse brain. The transgene insertion (in antisense orientation to Gm12695 transcription) results in increased cortical expression of a partial Gm12695 fragment (exons 8-11) - and this transcript is shown to have significant expression among the extensive network of differentially expressed genes associated with the R6/2 model, including those regulating synaptic transmission, cell signaling and transcription (Jacobsen et al. 2017 Sci Rep. 7:41120).

This strain ships with a JAXTag™ affixed. Learn more about JAXTag™.

General Information for R6/2 transgenic mouse lines:
The R6/2 transgenic mouse lines express a transgene encoding the 5’ end of human HTT with different lengths of CAG repeat expansions. The CAG repeat number is subject to germline and somatic instability, and may expand or contract. The phenotype of R6/2 animals varies greatly as a function of CAG repeat size and, similar to what is observed in humans, R6/2 transgenic mice may exhibit higher incidence of CAG repeat expansion when the transgene is transmitted via paternal inheritance. Interestingly, the copy:phenotype relationship is not linear for R6/2 mice, nor does a large CAG repeat number necessarily lead to an earlier onset and more severe phenotype. Genetic background may also lead to variations in disease severity/progression.

When using lines with unstable CAG repeat length, it is strongly recommended the CAG repeat number be quantified in all the experimental animals - all animals in all experimental groups should carry comparable CAG repeat sizes. CAG repeat sizing of HD mice should be done using high-resolution methods - as assays based on agarose gel electrophoresis typically do not provide sufficient resolution to accurately measure CAG repeat numbers. If labs do not have access to the appropriate equipment for determining CAG repeat length, CAG repeats can be evaluated on a fee-for-service basis by Laragen, Inc.
Genotyping Protocols
Standard PCR: Laragen
Standard PCR: Laragen
Standard PCR: Laragen
Standard PCR: TG(HDexon1), TG(YAC)
Probe: Tg(HDexon1)62Gpb-EP3
Standard PCR: Tg(HDexon1)62Gpb CAG Sizing

Genotyping resources and troubleshooting

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

Breeding Considerations

This strain is a good breeder.

For R6/2 transgenic mice, the CAG repeat number is subject to germline/somatic instability and may expand/contract. For additional information, see “General Information for R6/2 transgenic mouse lines” in our Detailed Description section.

Hemizygous females are not fertile. Hemizygous males have a 3-4 week breeding window so mating scheme should be via multiple females. Also, only about half of the male hemizygotes are fertile. The breeding scheme was: B6CBAF1 females X hemizygous HD62 males, preferably a trio (2 B6CBAF1 females and one hemizygous male). Strain is now maintained by ovarian transplant hemizygote females X B6CBAF1/J males. Both mating schemes are available to the customer, but OT hemi female x B6CBAF1/J is recommended mating scheme. The expected coat color from breeding is Black, Agouti.

Additional Breeding and Husbandry Support

Appearance
black
Related Genotype: a/a

agouti, ataxic, tremors
Related Genotype: A/+ HTT/-

agouti
Related Genotype: A/+?

black, ataxic, tremors
Related Genotype: a/a HTT/-

Citation
When using the B6CBA-R6/2 (CAG 120 +/- 5) mouse strain in a publication, please cite the originating article(s) and include JAX stock #006494 in your Materials and Methods section.

Animal Health Reports
Facility Barrier Level Descriptions

MP13 (Maximum)
**Pricing & Availability**

Sized to accommodate orders of up to 10 or more with age range. Ask Customer Service for details.

**Domestic & International**

Pricing effective for USA, Canada and Mexico shipping destinations

<table>
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<th>AGE</th>
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Terms Of Use

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Licensing Information

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

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