Tremor and reduced lifespan (*trls*): a spontaneous missense mutation in Hcn2

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Mutation (allele) symbol: *Hcn2*^{trls}

Mutation (allele) name: tremor and reduced lifespan

Gene symbol: *Hcn2*

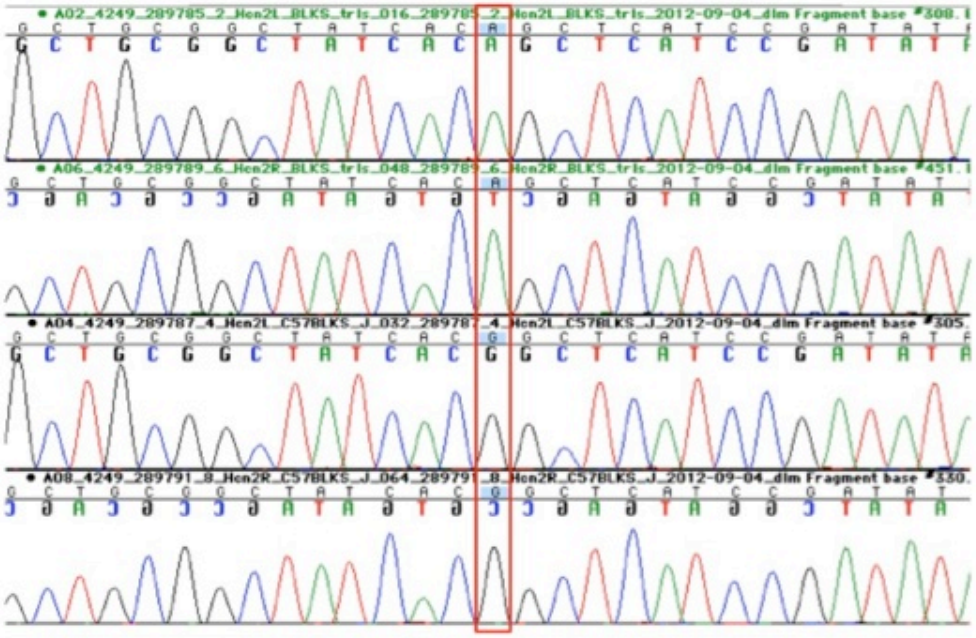
Strain of origin: BKS.Cg-*Dock7*^{m} +/+ *Lepr*^{db}/J

Current strain name: BKS(Cg)-*Hcn2*^{trls}/GrsrJ

Stock #005898 (jaxmice.jax.org)

Phenotype categories: neurological

The tremor and reduced lifespan mutation arose spontaneously at The Jackson Laboratory, and was characterized by Richard Samples et al. Whole exome sequencing was performed to identify candidate coding mutations in the mapped region. Briefly, genomic DNA was enriched for coding sequence by hybridization-based capture with probes representing 54 Mb of annotated coding sequence. The enriched DNA was then sequenced using the Illumina HiSeq high throughput sequencing platform. A single nucleotide polymorphism was found on Chromosome 10 in Hcn2. Primers were generated that produce a 628 base pair product spanning the predicted mutation: Hcn2 Left (GGGCATCACTTTCTTCAAGG) and Hcn2 Right (GACTTTAGTCCCACCCAAGC). Sequence analysis of one mutant genomic DNA samples compared to genomic DNA from one control animals confirmed a single nucleotide transition from G to A at position 79187525 (NCBI build 37, mm9) in *Hcn2*. This is a missense mutation and causes an amino acid change from arginine to glutamine at protein position 315 (See Chromatogram and sequence below).



Comparison of DNA sequence chromatograms of the *Hcn2*^{trls} homozygote and control sequence. The red boxed region corresponds to the green and blue boxed regions shown in the sequence image.

Control

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CAACACGGAG ATCATCCTGG ACCCCGAGAA GATAAAGAAG
 N  T  E   I  I  L  D   P  E  K   I  K  K
AAGTACTTGC GTACGTGGTT CGTGGTGGAC TTCGTGTCAT
K  Y  L  R  T  W  F   V  V  D   F  V  S  S
CCATCCCGGT GGACTACATC TTCCTCATAG TGGAGAAGGG
  I  P  V   D  Y  I   F  L  I  V   E  K  G
AATCGACTCC GAGGTCTACA AGACAGCGCG TGCTCTGCGC
 I  D  S   E  V  Y  K   T  A  R   A  L  R
ATCGTGCGCT TCACCAAGAT CCTCAGTCTG CTGCGGCTGC
I  V  R  F   T  K  I   L  S  L   L  R  L  L
TGCGGCTATC ACGGCTCATC CGATATATCC ACCAGTGGGA
  R  L  S   R  L  I   R  Y  I  H   Q  W  E
AGAG
 E
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Mutant

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CAACACGGAG ATCATCCTGG ACCCCGAGAA GATAAAGAAG
 N  T  E   I  I  L  D   P  E  K   I  K  K
AAGTACTTGC GTACGTGGTT CGTGGTGGAC TTCGTGTCAT
K  Y  L  R  T  W  F   V  V  D   F  V  S  S
CCATCCCGGT GGACTACATC TTCCTCATAG TGGAGAAGGG
  I  P  V   D  Y  I   F  L  I  V   E  K  G
AATCGACTCC GAGGTCTACA AGACAGCGCG TGCTCTGCGC
 I  D  S   E  V  Y  K   T  A  R   A  L  R
ATCGTGCGCT TCACCAAGAT CCTCAGTCTG CTGCGGCTGC
I  V  R  F   T  K  I   L  S  L   L  R  L  L
TGCGGCTATC ACAGCTCATC CGATATATCC ACCAGTGGGA
  R  L  S   Q  L  I   R  Y  I  H   Q  W  E
AGAG
 E
```

A portion of the protein coding region of *Hcn2*. The Control DNA sequence and its amino acid translation are shown on the left, and the *Hcn2*^{trls} mutation DNA and its translation on the right. A single nucleotide transition is enclosed by a green box in the mutant sequence and a blue box in the control sequence. The mutation is predicted to change amino acid 315 from arginine to glutamine. This change is indicated by a red box in the control and the mutant sequences.