The Jackson Laboratory

B6.CE-*Galc* ^{twi} /J

Stock No: **000845** | twitcher

Congenic

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These mice carry a spontaneous mutation at the *Galc* locus characterized by a neurological leukodystrophy.

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GENETIC OVERVIEW

Genetic Background

000664 C57BL/6J

Generation

Galc^{twi}

Allele Type	Gene Symbol	Gene Name
Spontaneous (Null/Knockout)	*Galc*	galactosylceramidase

VIEW GENETICS

RESEARCH APPLICATIONS

Neurobiology Research
Mouse/Human Gene Homologs

VIEW ALL RESEARCH APPLICATIO

Details

Detailed Description

The twitcher mouse is a neurological leukodystrophy mutant first observed in 1976 at The Jackson Laboratory. Initially characterized on a mixed C57BL/6J and CE/J background, a neurological phenotype was first observed by day 30 and homozygotes did not survive beyond three months of age. (Duchen LW, et. al., 1980) Subsequent backcrosses to C57BL/6J and the generation of a full congenic (> 10 backcrosses) shortened the time to onset to approximately 21 days with death by 40 days. Head tremors and decreased body weight are initial clinical indicators and mice are generally less active than unaffected littermates. Muscle weakness in the hindlimbs is a promiment feature with the health of the mutants progressively declining until death. There is a significant lack of myelin in the twitcher CNS, along with astrocytic gliosis. The nerves in the PNS are also demyelinated. The mutant CNS and PNS contain multinucleated, periodic acid-Schiff-positive globoid cells. Electron microscopic analysis shows these cells contain paracrystalline inclusions and twisted tubules.

Galactosylceramidase (GALC) is the enzyme responsible for the initial step of galactosylceramide (or galactocerebroside) degradation. Galactocerebroside is one of the most abundant and unique lipid constituents of the myelin sheath and the twitcher mouse is a useful mutant in which to study myelina tion and myelin metabolism. This substrate of the enzyme GALC, however, does not accumulate in tissues of affected mice (or humans). The pathologies are believed to result from the abnormal accumulation of the cytotoxic metabolite galactosylsphingosine (psychosine), another substrate of GALC that inhibits protein kinase C, that causes myelin-forming cells of the CNS and PNS to dysfunction and undergo apoptosis. Levels of myelin protein mRNAs are normal through postnatal day 20 but decline after day 25, corresponding to the observed pathological demyelinating changes. The data indicate that specific gene expression during myelination appears normal initially. Astrogliosis in the CNS is initiated prior to the appearance of myelin pathologies (as early as postnatal 15) and GFAP mRNA is highly upregulated after day 20, presumably as a response to demyelination. Cytokines are believed to play a major role in the inflammatory responses associated with the disease course. TNF-alpha and IL-6 in the CNS appear to be induced by the pathological condition; reactive astrocytes and microglia contribute to the pathogenic course in the CNS of these mutants.(Taniike et al., 1998; Kobayashi et al., 1980; Suzuki and Suzuki, 1995; LeVine and Brown, 1997; Matsushima et al., 1994).

Development

Control Suggestions

Genetics

Galc^{twi}

Disease/Phenotype

Disease Terms

Research Areas By Phenotype

Mammalian Phenotype Terms by Genotype

References

Technical Support

CONTACT TECHNICAL SUPPORT

Genotyping Protocols
Pyrosequencing:Galc
Sanger sequencing:Galc-SEQ
Sanger sequencing:Galc-SEQ
Genotyping resources and troubleshooting

Appearance
black, tremors
Related Genotype: *a*/*a* *Galc*^{twi}/*Galc*^{twi}

black, unaffected
Related Genotype: *a*/*a* +/?

Citation
When using the twitcher mouse strain in a publication, please cite the originating article(s) and include JAX stock #000845 in your Materials and Methods section.

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