Title: *GLB1*-Related Disorders *GeneReview* Animal Model
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Note: The following information is provided by the authors and has not been reviewed by *GeneReviews* staff.

Ex vivo gene therapy in β-gal-/- mice using genetically modified bone marrow resulted in increased β-galactosidase enzyme activity in multiple brain regions and reduced GM1 ganglioside accumulation [Sano et al 2005].

Additional studies using viral vectors expressing β-galactosidase in β-gal-/- mice have also been reported.

- In the first study, intravenous administration of a recombinant adenovirus encoding β-galactosidase at 24 to 48 hours of life showed reduced GM1-ganglioside accumulation compared to the β-gal-/- controls and β-galactosidase positive staining in the brain [Reviewed in Brunetti-Pierri & Scaglia 2008].
- In the second study, lateral ventricular injection of a recombinant AAV2/1 viral vector containing *GLB1* to neonatal bgal-/- mice prevented neurodegenerative changes. At age three months, treated mice had normal brain neurochemistry and histology [Reviewed in Brunetti-Pierri & Scaglia 2008].
- In a third study using AAV2/1-β–gal, direct injection into the thalamus and deep cerebellar nuclei of adult mice showed increased survival [Baek et al 2010].

Based on the findings in the Baek et al [2010] mouse study above, a cat model was evaluated. The natural GM1 gangliosidosis cat model demonstrates disease onset at 3.5 months and reaches a humane end point by seven months. AAV2/1 or AAV2/rh8 vectors with feline βgal cDNA were injected into the thalamus or deep cerebellar nuclei at 8 to 12 weeks of age. Treated cats survived to 28.3 months without clinical evidence of disease. Furthermore, in the treated cats, brain lesions normalized on MRI [McCurdy et al 2012 and personal communication with Douglas R. Martin].

References

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