National Human Genome Research Institute (NHGRI)

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Murine Model of Niemann-Pick Disease Type C

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Key Words

Niemann-Pick Disease Type C, NPC1, Hepatosplenomegaly

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Summary

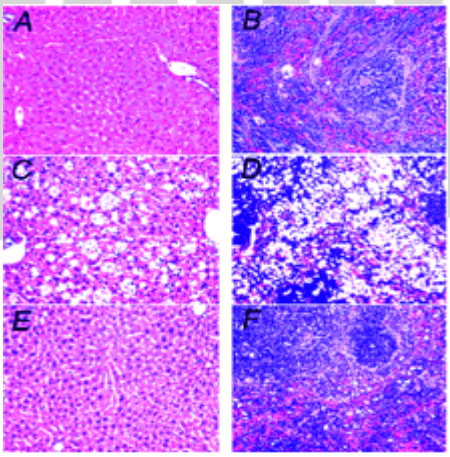
Niemann-Pick Disease Type C (NPC) is caused by mutations in the NPC1 gene. It is an autosomal recessive neurodegenerative disorder, characterized by intracellular accumulation of cholesterol and gangliosides within the endosomal-lysosomal system. Thus, NPC patients generally present with hepatosplenomegaly (enlargement of liver and spleen) and neurological degeneration. While the NPC1-deficient mice recapitulate the phenotype of human patients, these animals die around eight to eleven weeks of age, making them a time-limited model. NHGRI investigators generated three lines of transgenic mice (named **Tg(Npc1)**) carrying a murine wild-type NPC1 gene under the control of mouse prion promoter that targets mainly the central nervous system. Mating these mice with the NPC1 knockout model, rescues the disease effects related to neurologic degeneration, allowing for a normal lifespan. The rescued mice, however, still maintain the visceral defects (namely, hepatosplenomegaly), associated with cholesterol accumulation.

Potential Commercial Applications

The available lines of Tg(Npc1) mice are a useful tool for studying both the visceral disease aspects of Niemann-Pick Disease Type C, such as the enlargement of liver and spleen, and the biology of cholesterol accumulation.

Related Article

Loftus et al., *Rescue of neurodegeneration in Niemann-Pick C mice by a prion-promoter-driven Npc1 cDNA transgene*, 11 Human Molecular Genetics 3107 (2002).
http://hmg.oxfordjournals.org/content/11/24/3107.long



Normal liver **(A)**, normal spleen **(B)**, NPC1-deficient liver **(C)**, NPC1-deficient spleen **(D)**, Tg(Npc1) liver **(E)**, and Tg(Npc1) spleen **(F)**. Npc1-deficient organs show increased macrophage presence and vacuolated cytoplasm in comparison to normal mice. Transgenic mice show some but not full rescue.