

疾患モデル,カルニチン欠損マウスの培養細胞系での 評価検討

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1997 Fiscal Year Final Research Report Summary

Evaluation of disease model traits in cultured cells derived from carnitine deficient JVS mice

Research Project

Project/Area Number

08458274

Research Category

Grant-in-Aid for Scientific Research (B)

Allocation Type

Single-year Grants

Section

一般

Research Field

Laboratory animal science

Research Institution

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Project Period (FY)

1996 – 1997

Keywords

mice / animal model / fatty liver / sperm / cardiac hypertrophy / transporter / carnitine / cultured cells

Research Abstract

JVS mice which are homozygous for recessive mutant gene *jvs* exhibit various pathological syndromes, such as fatty liver, hyperanmonemia, cardiac hypertrophy, reduced fertility in males, and abnormal ; expression of genes related to urea cycle enzymes. In this project we attempt to assess the basis of these syndromes in primary cultured cells or established cell lined from the JVS embryos.















Although we have newly made following findings, it is concluded that various specific syndromes in the JVS mice are difficult to predict from cultured cells from the JVS embryos or new born pups. It seems that further elaborated methods for cell or tissue culture are needed to assess the syndrome in vivo.


1. In enlarged heart muscle some muscle cells have an enlarged nucleus and the increased mitochondria.
2. As seen in sliced kidney, primary cultured embryonic cells and established fibroblastic cells are less active in uptake of free carnitine. The carnitine uptake in vitro is depend on gene dose of mutant gene *jvs*.
3. Although spermatogenesis in JVS is apparently morphologically normal, it seems that the maturation process in epididymus is impaired, and it resulted in partial sterility in JVS male mice.
4. Cold-Induced thermogenesis in JVS was blunted even in the most general condition of laboratory animal room and that the blunted thermogenesis was partially improved with L-carnitine supplement.
5. Volume distribution of free carnitine after ³H-labeled carnitine administration (oral or iv) was significantly reduced and the concentration of free carnitin various organs except brain relative to that of plasma is also lower compared normal controls and bioavailability of free carnitine after oral administration of carnitine in JVS was about 50% of normal control value.


Research Products (18 results)


All Other


All Publications (18 results)

- [Publications] N.Hashimoto: "Gene-dose effect on carnitine transport activity in embryonic fibroblasts of JVS mice as a model of human carnitine transporter deficiency" *Biochem.Pharmacol.*55(in press). (1998) 
- [Publications] I.Narama: "Heterogeneity of histopathologic features in the congenitally carnitine-deficient juvenile visceral steatosis(JVS)mouse." *Biomed.Res.* 18. 247-255 (1997) 
- [Publications] M.Kaido: "Mitochondrial abnormalities in a murine model of primary carnitine deficiency." *European Neurology.* 38. 302-309 (1997) 
- [Publications] M.Kuwajima: "Characteristics of cardiac hypertrophy in the juvenile visceral steatosis mouse with systemic carnitine deficiency." *J.Mol.Cell.Cardiol.*(in press). 
- [Publications] M.Kuwajima: "Carnitine transport defect in fibroblast of juvenile visceral steatosis(JVS)mice." *Biochem.Biophys.Res.Commun.*223. 233-287 (1996) 
- [Publications] K.Okita: "Definition of the locus responsible for systemic carnitine deficiency with in a 1.6cM region of a 1.6cM region of mouse chromosome 11 by detailed linkage analysis." *Genomics.* 33. 289-291 (1996) 
- [Publications] R.Uenaka: "Increased expression of carnitine palmitoyltransferase I gene is repressed by administration of carnitine in the heart of carnitine deficient juvenile visceral steatosis mice" *J.Biochem.*119. 533-540 (1996) 
- [Publications] K.Hotta: "Altered expression of carnitine palmitoyltransferase II in liver,muscle and heart of mouse strain with juvenile visceral steatosis." *Biochem.Biophys.Acta.* 1289. 131-134 (1996) 
- [Publications] K.Hotta: "Disordered expression of glycolytic and gluconeogenic liver enzymes of juvenile visceral steatosis mice with systemic carnitine deficiency." *Diabetes Res.Clin.Pract.*32. 117-123 (1996) 
- [Publications] M.Kuwajima, et al.: "Characteristics of cardiac hypertrophy in the juvenile visceral steatosis mouse with systemic carnitine deficiency" *J.Mol.Cell.Cardiol.*(in press). 
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- [Publications] M.Kaido, et al.: "Mitochondrial abnormalities in a murine model of primary carnitine deficiency." *European Neurology.* 38 (4). 302-309 (1997) 
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