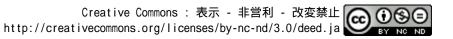
ノックアウトマウスを用いたガラクトース転移酵素 遺伝子群の役割分担の解明

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|-------|----------------------------------|
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2003 Fiscal Year Final Research Report Summary

Elucidation of individual roles of the galactosyl|ransferase gene family using gene knockout mice

Research Project

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| Allocation Type |
| Single-year Grants |
| Section |
| 一般 |
| Research Field |
| Laboratory animal science |
| Research Institution |
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Carbohydrate / Knockout mice / Galactosyltransferase / Selectins / Inflammation / Skin wound healing / Embryonic lethal

Research Abstract

Cell-to-cell, interactions are important for cell growth and differentiation. The interaction through cell surface carbohydrates is one of indispensable mechanisms among them. We have been studying on the role of carbohydrates in vivo by generating a gene knockout mouse deficient in β -1.4-galactosyhransferase-I(β 4GalT-I). β 4GalTs are recently found to form the gene family consisting of 7 genes, which have their own roles.

We analyzed carbohydrate structures of β 4GalT-I KO mice in detail. Contribution of β 4GalT-I gene to the biosynthesis of carbohydrates of various cell types was estimated by measuring Gal residues in the β 1,4-linkage. Next, carbohydrate ligands of selectins, which are known to be synthesized by β 4GalTs and other glycosyltransferases, were analyzed in β 4GalT-I KO mice. Contribution of β 4GalT-I gene to their biosynthesis was also estimated. Furthermore, Inflammatory responses of β 4GalT-I KO mice and the effect of β 4GalT-I deficiency were examined. In addition, the effect of β 4GalT-I deficiency on skin wound healing was examined. Our results indicated that β 4GalT-I plays an important role in the biosynthesis of carbohydrate ligands of selectins and their deficiency results in reduction of inflammatory responses and delayed wound healing in β 4GalT-I KO mice.

While these results were obtained using β 4GalT-I KO mice on mixed genetic backgrounds, we found β 4GalT-I KO mice on inbred background to be lethal during late embryogenesis. Since growth retardation of the placenta rather than the embryo was remarkable several days before its death, the defect of placenta was suggested to be a cause of the embryonic lethality. Since the reason of changeable lethality depending on genetic background might be a compensatory activity by other β 4GalTs, gene knockout mice deficient in another β 4GalT gene were generated. Studies on elucidating the role of these p4GalT genes are in progress.

Research Products (10 results)

| _ | |
|---|----------|
| AI | l Other |
| All Publ | ications |
| [Publications] Kotani, N.et al.: "Knockout of mouse β1,4-galactosyltransferase-1 gene results in a dramatic shift of outer chain moieties of N-glycans from type 2 to type chains in hepatic membrane and plasma glycoproteins."Biochemical Journal. 357. 827-834 (2001) | 21 🗸 |
| [Publications] Asano, M.et al.: "Impaired selectin ligand biosynthesis and reduced inflammatory responses in β -1,4-galactosyltransferase-I-deficient mice." Blood. 102. 1678-1685 (2003) | ~ |
| [Publications] Mori, R.et al.: "Impairment of skin wound healing in β 1,4-galactosyltranseferase-deficient mice with reduced leukocyte recruitment." American Journal of Pathology. 164. 1303-1314 (2004) | ~ |
| [Publications] Kotani, N.et al.: "Polylactosamine synthesis and branch formation of N-glycans in β 1,4- galactosyltransferase-1 deficient mice." Archives of Biochemistry a Biophysics. (In press). (2004) | nd 🗸 |
| [Publications] 浅野雅秀 他:"糖鎖とIgA腎症"Molecular Medicine. 40. 1056-1061 (2003) | ~ |
| [Publications] Kotani, N., Asano, M., Iwakura, Y., Takasaki, S.: "Knockout of mouse β1,4-galactosyltransferase-1 gene results in a dramatic shift of outer chain moieties of N-glycans from type 2 to type 1 chains in hepatic membrane and plasma glycoproteins."Biochemical Journal. 357. 827-834 (2001) | of 🗸 |
| [Publications] Asano, M., Nakae, S., Kotani, N., Shirafuji, N., Nambu, A., Hashimoto, N., Kawashima, H., Hirose, M., Miyasaka, M., Takasaki, S., Iwakura, Y.: "Impaired selectin ligand biosynthesis and reduced inflammatory responses in β-1,4-galactosyltransferase-I-deficient mice."Blood. 102. 1678-1685 (2003) | ~ |
| [Publications] Mori, R., Kondo, T., Nishie, T., Oshima, T., Asano, M.: "Impairment of skin wound healing in β-1,4-galactosyltransferase-deficient mice with reduced leukoc recruitment."American Journal of Pathology. 164. 1303-1314 (2004) | ;yte 💊 |
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| [Publications] Asano, M., Nishie, T., Miyaishi, S.: "Carbohydrates and IgA nephropathy"Molecular Medicine. 40. 1056-1061 (2003) | ~ |
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