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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雑誌名	平成15(2003)年度 科学研究費補助金 基盤研究(B)研究成果報告書概要
巻	2001　2003
ページ	2p.
発行年	2005-04-18
URL	http://doi.org/10.24517/00063483

2003 Fiscal Year Final Research Report Summary

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

Research Project

Project/Area Number

13480280

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)

2001 – 2003

Keywords

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(β4GalT-I). β4GalTs are recently found to form the gene family consisting of 7 genes, which have their own roles.
We analyzed carbohydrate structures of β4GalT-I KO mice in detail. Contribution of β4GalT-I gene to the biosynthesis of carbohydrates of various cell types was estimated by measuring Gal residues in the β1,4-linkage. Next, carbohydrate ligands of selectins, which are known to be synthesized by β4GalTs and other glycosyltransferases, were analyzed in β4GalT-I KO mice. Contribution of β4GalT-I gene to their biosynthesis was also estimated. Furthermore, Inflammatory responses of β4GalT-I KO mice

and the effect of β4GalT-I deficiency were examined. In addition, the effect of β4GalT-I deficiency on skin wound healing was examined. Our results indicated that β4GalT-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 β4GalT-I KO mice.
While these results were obtained using β4GalT-I KO mice on mixed genetic backgrounds, we found β4GalT-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 β4GalTs, gene knockout mice deficient in another β4GalT gene were generated. Studies on elucidating the role of these p4GalT genes are in progress.

Research Products (10 results)

All | Other

All | Publications

[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 1 chains in hepatic membrane and plasma glycoproteins."Biochemical Journal. 357. 827-834 (2001)

[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 β1,4-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 β1,4- galactosyltransferase-1 deficient mice."Archives of Biochemistry and Biophysics. (In press). (2004)

[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)

[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 leukocyte recruitment."American Journal of Pathology. 164. 1303-1314 (2004)

[Publications] Kotani, N., Asano.M., Inoue, M., Iwakura, Y., Takasaki, S.: "Polylactosamine synthesis and branch formation of N-glycans in β1,4-galactosyltransferase-1 deficient mice."Archives of Biochemistry and Biophysics. (In press). (2004)

[Publications] Asano, M., Nishie, T., Miyaishi, S.: "Carbohydrates and IgA nephropathy"Molecular Medicine. 40. 1056-1061 (2003)

URL: https://kaken.nii.ac.jp/report/KAKENHI-PROJECT-13480280/134802802003kenkyu_seika_hokoku_

Published: 2005-04-18