試験管内「血液脳関門」モデルの作製と新しい脳特異的輸送担体開発の試み

1994 Fiscal Year Final Research Report Summary

Establishment of an In Vitro Model of "Blood Brain Barrier" and an Attempt with it to Develop a Brain-Specific Transport Vector

Research Project

Project/Area Number

04558024

Research Category

Grant-in-Aid for Developmental Scientific Research (B)

Allocation Type

Single-year Grants

Research Field

物質生物化学

Research Institution

Kanazawa University

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Keywords

blood brain barrier / vascular endothelial cells / pericytes / astroglial cells / advanced glycation endproducts / diabetic microangiopathy / aldosterone / vascular endothelial growth factor

Research Abstract

(1) In the present study, we have established an in vitro model of "blood brain barrier". With vascular endothelial cell, pericyte and astroglial cell co-culture systems, the barrier as well as transport activities selective to brain vessels were reconstituted, which passed polycationic albumin but excluded native albumin or inulin in the physiological polarity. This model would seem to be useful in screeeing substances that could act on the central nervous system and in evaluating their delivery into the brain. The present study has also demonstrated that astroglial cells are capable of "transdifferentiating "non-brain-type endothelial cells into brain-type ones : human umbilical vein endothelial cells co-cultured with astroglial cells did express the brain endothelium-specific genes, including those for gamma-transglutamyl transpeptidase, transferrin receptor and P-glycoprotein, and aquired the anti-inulin barrier propert. Although we failed to develop brain-specific transport vectors, new discoveries (2) that advanced glycation endproducts selectively injure pericytes through interactions with their cell-surface receptors, (3) that endothelial cells and vascular smooth muscle cells possess the devices both for synthesizing and for responding to aldosterone, a steroid implicated in the regulation of blood pressure, and (4) that hypoxia-induced proliferation of vascular cells in mediated by autocrine vascular endothelial growth factor, were made during the course of this study, and we have thus proposed novel mechanisms underlying the development and progression of various human vascular disorders including diabetic microangiopathy, hypertension and angiogenesis.

Research Products (44 results)

All | Other

All | Publications (44 results)

[Publications] Yasuko Kamiya: "Mutations in genes for acetylcholinesterase intensify lethality by acrylamide in Caenorhabditis elegans." Neuroscience letters. 145. 37-39 (1992)

[Publications] Noriko Kimura: "Detection of multiple hormones and their mRNAs in human neuroblastoma cell line NB-1 using in situ hybridization,immunocytochemisty and radioimmunoassay." Virchows Archiv B Cell Pathol.62. 321-327 (1992)

[Publications] Sho-ichi Yamagishi: "Vascular pericytes not only regulate growth, but also preserve prostacyclin-producing ability, and protect against lipid peroxide-induced injury, of co-cultured endothelial cells." Biochem. Biophys. Res. Commun.190. 418-425 (1993)

[Publications] Sho-ichi Yamagishi: "Endothelin 1 mediates endothelium-dependent proliferation of vascular pericytes." Biochem. Biophys. Res.Commun.191. 840-846 (1993)

[Publications] Noriko Kimura: "Multiple hormone gene expression in ganglioneuroblastoma with watery diarrhea hypokalemia and achlorhydria sydrome." Cancer. 71. 2841-2846 (1993)

[Publications] Yasuko Kamiya: "Developmental and pharmacological studies of acetylcholinesterase-defective mutants of Caenorhabditis elegans." Zoological Science. 10. 43-51 (1993)

[Publications] Koji Nata: "Structure determination and evolution of the chicken cDNA and gene encoding prepropancreatic polypeptide" Gene. 130. 183-189 (1993)

[Publications] Haruhiko Hatakeyama: "Vascular Aldosterone:Biosvnthesis and a Link to Angiotensin II-Induced Hypertrophy of Vascular Smooth Muscle Cells." J. Biol. Chem.269. 24316-24320 (1994)

[Publications] Haruhiko Hatakeyama: "Angiotensin II up-regulates the expression of type A endothelin receptor in human vascular smooth'muscle cells" Biochem. and Mol. Biol. Int.34. 127-134 (1994)

[Publications] Shin-ichi Harada: "Mutations in the unc-41 gene cause elevation of acetylcholine levels." Journal of Neurochemistry. 63. 439-446 (1994)

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[Publications] Masahide Kaji: "Antisense oligonucleotides against c-met mRNA inhibit the growth of human gastric cancer cells." Antisense Research and Development. (in press). (1995)

[Publications] Kayo Uchiyama: "Topical fluconazole:high penetration without corneal toxicity." Iens and eye toxicity research. (in press). (1995)

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[Publications] Emi Nakashima: "Reversal of Drug Sensitivity in MDR Subline of P388 Leukemia by Gene-Targeted Antisense Oligonucleotide" J. Pharmaceutical Sciences. (submitted). (1995)

[Publications] Masahide Kaji: "Collegium Internationale Chirurgiae Digestivae" International Proceedings Division MONDUZZIEDITORE, 564 (1994)

[Publications] Hiroshi Yamamoto: "Hypoxia-Induced Proliferation of Vascular Cells and “Vascular VEGF"" Microcirculation Annual (in press), (1995)

[Publications] 加治 正英: "進行胃癌に対する治療戦略 ～遺伝子診断から集学的治療まで～" ソフトサイエンス社, 237 (1995)

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