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Pharmacy and Pharmacology

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Biopharmaceutics

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◆ 研究概要

- ・血液網膜関門の輸送機能解析と網膜への薬物送達
- ・生体内関門組織における生理機能及び輸送機能解明

◆ 原 著

- 1) Hosoya K., Minamizono A., Katayama K., Terasaki T., and Tomi M.: Vitamin C transport in oxidized form across the rat blood-retinal barrier. *Invest. Ophthalmol. Vis. Sci.*, 45:1232-1239, 2004.
- 2) Hori S., Ohtsuki S., Hosoya K., Nakashima E., and Terasaki T.: A pericyte-derived angiopoietin-1 multimeric complex induces occludin gene expression in brain capillary endothelial cells through Tie-2 activation in vitro. *J. Neurochem.*, 89:503-513, 2004.
- 3) Nakashima T., Tomi M., Katayama K., Tachikawa M., Watanabe M., Terasaki T., and Hosoya K.: Blood-to-retina transport of creatine via creatine transporter (CRT) at the rat inner blood-retinal barrier. *J. Neurochem.*, 89:1454-1461, 2004.
- 4) Deguchi Y., Naito Y., Ohtsuki S., Miyakawa Y., Morimoto K., Hosoya K., Sakurada S., and Terasaki T.: Blood-brain barrier permeability of novel [D-Arg²]dermorphin (1-4) analogues: transport property is related to the slow onset of antinociceptive activity in the central nervous system. *J. Pharmacol. Exp. Ther.*, 310:177-184, 2004.
- 5) Ohtsuki S., Takizawa T., Takanaga H., Hori S., Hosoya K., and Terasaki T.: Localization of organic anion transporting polypeptide 3 (oatp3) in mouse brain parenchymal and capillary endothelial cells. *J. Neurochem.*, 90:743-749, 2004.
- 6) Tomi M., Abukawa H., Nagai Y., Hata T., Takanaga H., Ohtsuki S., Terasaki T., and

Hosoya K.: Retinal selectivity of gene expression in rat retinal versus brain capillary endothelial cell lines by differential display analysis. *Mol. Vis.*, 10:537-543, 2004.

- 7) Fernandes R., Carvalho A. L., Kumagai A., Seica R., Hosoya K., Terasaki T., Murta J., Pereira P., and Faro C.: Downregulation of retinal GLUT1 in diabetes by ubiquitinylation. *Mol. Vis.*, 10:618-628, 2004.
- 8) Hosoya K., Tomi M., Takayama M., Komokata Y., Nakai D., Tokui T., Nishimura K., Ueda M., Obinata M., Hori S., Ohtsuki S., Amidon G. L., and Terasaki T.: Transporter mRNA expression in a conditionally immortalized rat small intestine epithelial cell line (TR-SIE). *Drug Metabol. Pharmacokinet.*, 19:264-269, 2004.
- 9) Shiiki T., Ohtsuki S., Kurihara A., Naganuma H., Nishimura K., Tachikawa M., Hosoya K., and Terasaki T.: Brain insulin impairs amyloid- β (1-40) clearance from rat brain. *J. Neurosci.*, 24:9632-9637, 2004.
- 10) Tomi M., and Hosoya K.: Application of magnetically isolated rat retinal vascular endothelial cells for the determination of transporter gene expression levels at the inner blood-retinal barrier. *J. Neurochem.*, 91:1244-1248, 2004.

◆ 総 説

- 1) Hosoya K., Hori S., Ohtsuki S., and Terasaki T.: A new in vitro model for blood-cerebrospinal fluid barrier transport studies: an immortalized choroid plexus epithelial cell line derived from the tsA58 SV40 large T-antigen gene transgenic rat. *Adv. Drug Deliv. Rev.*, 56:1875-1885, 2004.

◆ 学会報告

- 1) 中島寿久, 登美斉俊, 立川正憲, 渡辺雅彦, 寺崎哲也, 細谷健一: 内側血液網膜関門におけるc-reatine輸送機能変動解析. 日本薬学会第124年会, 2004, 3, 大阪.
- 2) 大嶋祐貴, 登美斉俊, 片山和憲, 細谷健一: 血液網膜関門におけるestradiol 17- β glucuronide排出輸送機構の解析. 日本薬学会第124年会, 2004, 3, 大阪.
- 3) 南園明人, 登美斉俊, 片山和憲, 寺崎哲也, 細谷健一: Streptozotocin誘発糖尿病ラットにおけ

- る網膜へのvitamin C輸送能の変動解析. 日本薬学会第124年会, 2004, 3, 大阪.
- 4) 登美斉俊, 南園明人, 細谷健一: 磁気標識抗CD31抗体を用いた網膜血管内皮細胞の単離. 日本薬学会第124年会, 2004, 3, 大阪.
 - 5) Hosoya K., Nakashima T., Katayama K., Tachikawa M., Watanabe M., Terasaki T., and Tomi M.: CRT as a system responsible for the transport of creatine at the inner blood-retinal barrier. Annual meeting of the Association for Research in Vision and Ophthalmology, 2004, 4, Fort Lauderdale, USA.
 - 6) Leal E. C., Aveleira C., Sa M., Serra A., Castilho A., Terasaki T., Hosoya K., Cunha-Vaz J., and Ambrosio A. F.: Rat retinal endothelial cell dysfunction induced by hyperglycemia and oxidative stress: additive effects? Annual Meeting of the Association for Research in Vision and Ophthalmology, 2004, 4, Fort Lauderdale, USA.
 - 7) Fernandes R., Carvalho A. L., Kumagai A. K., Seica R., Hosoya K., Terasaki T., Murta J., Pereira P., and Faro C.: Downregulation of retinal GLUT1 in diabetes by the ubiquitin proteasome pathway. Annual meeting of the Association for Research in Vision and Ophthalmology, 2004, 4, Fort Lauderdale, USA.
 - 8) Tomi M., Minamizono A., and Hosoya K.: Magnetically isolation and characterization of rat retinal vascular endothelial cells (RVEC). 2nd Pharmaceutical Science World Congress, 2004, 5, Kyoto.
 - 9) Hosoya K., Ohshima Y., Katayama K., and Tomi M.: Efflux transport of estradiol 17- β glucuronide across the blood-retinal barrier: a study employing microdialysis in rats. 2nd Pharmaceutical Science World Congress, 2004, 5, Kyoto.
 - 10) Nakashima T., Tomi M., Katayama K., Tachikawa M., Watanabe M., Terasaki T., and Hosoya K.: Creatine transport mechanisms at the inner blood-retinal barrier. 2nd Pharmaceutical Science World Congress, 2004, 5, Kyoto.
 - 11) Deguchi Y., Naito Y., Ohtsuki S., Miyakawa Y., Morimoto K., Hosoya K., Sakurada S., and Terasaki T.: Blood-brain barrier permeability of novel [D-Arg²]dermorphin (1-4) analogues: transport property is related to the slow onset of antinociceptive activity in the central nervous system. 2nd Pharmaceutical Science World Congress, 2004, 5, Kyoto.
 - 12) 中村元気, 登美斉俊, 片山和憲, 細谷健一: 条件的不死化ラット網膜Müller細胞株におけるvitaminC輸送機構の解析. 日本薬学会北陸支部第110回例会, 2004, 7, 金沢.
 - 13) 新井可南子, 登美斉俊, 片山和憲, 細谷健一: 条件的不死化ラット網膜毛細血管内皮細胞株におけるcholine輸送機構の解析. 日本薬学会北陸支部第110回例会, 2004, 7, 金沢.
 - 14) 北出直久, 横田徳子, 登美斉俊, 片山和憲, 細谷健一: 条件的不死化ラット網膜毛細血管内皮細胞株におけるsystem γ^+ 輸送系の解析. 日本薬学会北陸支部第110回例会, 2004, 7, 金沢.
 - 15) 登美斉俊: 条件的不死化内側網膜関門およびMüller細胞株の樹立と網膜へのシスチン輸送機構解明への応用, 第29回製剤セミナー, 2004, 7, 木更津.
 - 16) Deguchi Y., Miyakawa Y., Sakurada S., Naito Y., Morimoto K., Ohtsuki S., Hosoya K., and Terasaki T.: In vivo and in vitro study on blood brain barrier transport of a novel μ 1-specific opioide, TAPA. International Symposium for Opioid and Pain-related Peptide in Sendai, 2004, 7, Sendai.
 - 17) Deguchi Y., Naito Y., Ohtsuki S., Miyakawa Y., Morimoto K., Sakurada S., Hosoya K., and Terasaki T.: Blood-brain barrier permeability of [D-Arg²]dermorphin (1-4) analogues, ADAB and ADAMB, is related to the slow onset of antinociceptive activity in the central nervous system. International Symposium for Opioid and Pain-related Peptide in Sendai, 2004, 7, Sendai.
 - 18) Hosoya K., Nakashima T., Katayama K., Tachikawa M., Watanabe M., Terasaki T., and Tomi M.: Role of creatine transporter (CRT) at the inner blood-retinal barrier. AAPS annual meeting and exposition, 2004, 11, Baltimore, USA.
 - 19) Hosoya K., and Tomi M.: Retinal vascular

endothelial cell purification method for the determination of mRNA expression at the inner blood-retinal barrier. AAPS annual meeting and exposition, 2004, 11, Baltimore, USA.

- 20) Nakashima T., Tomi M., Katayama K., Tachikawa M., Watanabe M., Terasaki T., and Hosoya K.: Creatine biosynthesis is catalyzed by GAMT in retinal Müller cells. 第19回日本薬物動態学会年会, 2004, 11, 金沢.
- 21) Tomi M., Ohshima Y., Katayama K., and Hosoya K.: Expression and function of organic anion transporting polypeptide 2 (oatp2) at the inner blood-retinal barrier. 第19回日本薬物動態学会年会, 2004, 11, 金沢.
- 22) Nakamura G., Tomi M., Katayama K., and Hosoya K.: Vitamin C transport in retinal Müller cells. 第19回日本薬物動態学会年会, 2004, 11, 金沢.
- 23) Arai K., Tomi M., Katayama K., and Hosoya K.: Functional characterization of choline transport system in retinal capillary endothelial cells. 第19回日本薬物動態学会年会, 2004, 11, 金沢.
- 24) Kitade N., Yokota N., Tomi M., Katayama K., and Hosoya K.: L-Arginine transport in retinal capillary endothelial cells. 第19回日本薬物動態学会年会, 2004, 11, 金沢.
- 25) 細谷健一, 中島寿久, 立川正憲, 寺崎哲也, 渡辺雅彦, 登美斉俊: クレアチンの網膜移行性と合成. 第26回生体膜と薬物の相互作用シンポジウム, 2004, 11, 東京.
- 26) 杉田貴弘, 大嶋祐貴, 登美斉俊, 細谷健一: Microdialysis法を用いた血液網膜関門からの dehydroepiandrosterone sulfate 排出輸送機構の解析. 日本薬学会北陸支部第111回例会, 2004, 12, 金沢.

◆ その他

- 1) 細谷健一, 南園明人, 片山和憲, 寺崎哲也, 登美斉俊: 血液脳関門における vitamin C 輸送機構. 科学技術振興機構 (JST) 戦略的創造研究推進事業 (CREST) 「脳を守る」シンポジウム, 2004, 1, 東京.
- 2) 登美斉俊: 血液脳関門の claudin-5 制御による脳へのドラッグデリバリーは可能か? ファルマシア, 40:165, 2004.

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◆ 著 書

- 1) Carstens E., and Kuraishi Y.: Animal models of itch: scratching away at the problem. In: "Itch: Basic Mechanisms and Therapy (Basic and Clinical Dermatology)". Eds. Gil Yoshipovitch, Francis McGlone, Alan B. Fleischer and Malcolm W. Greaves, Marcel Dekker Inc., New York, USA, 35-50, 2004.
- 2) Andoh T., and Kuraishi Y.: Substans P and Itch. In: "Itch: Basic Mechanisms and Therapy (Basic and Clinical Dermatology)". Eds. Gil Yoshipovitch, Francis McGlone, Alan B. Fleischer and Malcolm W. Greaves, Marcel Dekker Inc., New York, USA, 89-97, 2004.
- 3) 佐々木 淳, 倉石 泰: 急性帯状疱疹痛と一酸化窒素. オピオイド研究の進歩と展望 鎮痛薬・オピオイドペプチド研究会編, ネオメディカル, 厚木市, 112-117, 2004.

◆ 原 著

- 1) Andoh T., and Kuraishi Y.: Direct action of immunoglobulin G on primary sensory neurons through Fc gamma receptor I. FASEB J. 18: 182-184 and FASEB J Express Article 10.1096/fj.02-1169fj, 2004.
- 2) Andoh T., Al-Akeel A., Tsujii K., Nojima H., and Kuraishi Y.: Repeated treatment with the traditional medicine Unsei-in inhibits substance P-induced itch-associated responses through downregulation of the expression of nitric oxide synthase 1 in mice. J. Pharmacol. Sci. 94:207-210, 2004.
- 3) Kuraishi Y., Takasaki I., Nojima H., Shiraki K., and Takahata H.: Effects of the suppression of acute herpetic pain by