腫瘍内アミノ酸・アミン代謝を利用した癌の内部照射治療薬剤の検索

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Research Project

Project/Area Number	14657212
Research Category	Grant-in-Aid for Exploratory Research
Allocation Type	Single-year Grants
Research Field	Radiation science
Research Institution	Kanazawa University
Principal Investigator	**川井 恵一** 金沢大学, 医学部, 教授 (30204663)
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Project Period (FY)	**2002 – 2004**
Project Status	Completed (Fiscal Year 2004)
Budget Amount *help	**¥3,400,000 (Direct Cost: ¥3,400,000)** Fiscal Year 2004: ¥900,000 (Direct Cost: ¥900,000) Fiscal Year 2003: ¥700,000 (Direct Cost: ¥700,000) Fiscal Year 2002: ¥1,800,000 (Direct Cost: ¥1,800,000)
Keywords	腫瘍内アミン代謝 / 放射性ヨウ素標識薬剤 / 悪性黒色腫 / メラニン生合成 / 含硫アミン誘導体 / 神経芽細胞腫 / カテコールアミン産生 / 偽伝達物質誘導体 / チロシナーゼ基質類似体 / 神経芽細胞質
Research Abstract	本課題研究では、腫瘍細胞で特異的に亢進している代謝機能に親和性を保持し、腫瘍組織への高い集積・滞留と正常組織からの速やかな排泄を示すとともに尿排泄性、代謝安定性を具備する放射性ヨウ素標識化合物の開発を目的として、ヨウ素標識に適した芳香族アミノ酸、アミン類を選択して、各腫瘍系で特異的に亢進している代謝酵素などに親和性を示す放射性医薬品を分子設計し、本医薬品の設計戦略の有用性を評価した。 悪性黒色腫細胞ではメラニン形成が異常に亢進しており、フェノール環を有する含硫アミン誘導体は、メラニン生合成に必須のチロシナーゼとの基質親和性が高いことが報告されている。このメラニン形成に着目し、チロシナーゼ基質類似体であるヨウ素標識人工アミノ酸を合成・評価した結果、黒色腫組織への高い集積及び滞留性が確認され、投与後早期より画像化に必要な対周辺組織比が得られた。そこで、メラニン生合成経路への親和性の向上を期待し、新たに含硫アミン誘導体を合成により得た。放射性ヨウ素標識体(I-PCA)は、高い標識率及び放射化学的純度で得られた。B16黒色腫担癌マウス体内分布において、I-PCAは血中からの消失は非常に早く、早期に体外排泄された。一方、黒色腫組織への集積は軟部組織と比較して高く、組織滞留性も認められ、画像化に必要な対周辺組織比は既に臨床使用されている腫瘍診断薬を上回っていた。 同様に、カテコールアミン産生が異常に亢進している神経芽細胞腫に対し、神経伝達物質に構造の類似した5種類の偽伝達物質誘導体を選択して、その放射性ヨウ素標識に対して培養細胞を用いたスクリーニングを行った。その結果、ノルアドレナリンと同じ1級アミンであり、芳香性水酸基を3位に有する誘導体が、ノルアドレナリンより2.4倍も高い集積性を示したことから、最も可能性の高い腫瘍診断薬であると考えられた。 従って、腫瘍細胞に特徴的な代謝亢進に基づく放射性医薬品の設計戦略の妥当性が示された。

Report (3 results)

2004 Annual Research Report

2003 Annual Research Report

2002 Annual Research Report

Research Products (58 results)

All | 2005 | 2004 | Other

All | Journal Article | Book | Publications

[Journal Article] Time course of discordant BMIPP and thallium uptake after ischemia and reperfusion in a rat model. 2005

[Journal Article] Locoreginal radioimmunotherapy with ^<186>Re-labeled monoclonal antibody in treating small peritoneal carcinomatosis of colon cancer in mice in comparison with ^<131>I-counterpart. 2005

[Journal Article] Inhibitory effects of amino-acid fluids on drug binding to site II of human serum albumin in vitro. 2005

[Journal Article] Transport of ^<99m>Tc-MAG_3 via rat renal organic anion transporter 1. 2004

[Journal Article] Hypoxia as a factor for ^<67>Ga accumulation in tumour cells. 2004

[Journal Article] Optimization of radioimmunotherapy interactions with hyperthermia. 2004

[Journal Article] Transcellular transport of 4-iodo-L-meta-tyrosine via system L across monolayers of kidney epithelial cell line LLC-PK1. 2004

[Journal Article] The radiotoxicity of ^<131>I therapy of thyroid cancer : assessment by micronucleus assay of B lymphocytes. 2004

[Journal Article] Role of brain perfusion single-photon emission tomography in traumatic head injury. 2004

[Journal Article] Single dose planning for radioiodine-131 therapy of Graves' disease. 2004

[Journal Article] Transcellular transport of radioiodinated 3-iodo-α-methyl-L-tyrosine across monolayers of kidney epithelial cell line LLC-PK1. 2004

[Journal Article] Limitations of ^<99m>Tc tetrofosmin in assessing reversal effects of verapamil on the function of multi-drug resistance associated protein 1. 2004

[Journal Article] Renal accumulation and excretion of radioiodinated 3-iodo-α-methyl-L-tyrosine. 2004

[Journal Article] Multifactorial analysis on the short-term side effects occurring within 96 hours after radioiodine-131 therapy for differentiated thyroid carcinoma. 2004

[Journal Article] Improved survival of mice bearing liver metastases of colon cancer cells treated with a combination of radioimmunotherapy and antiangiogenic therapy. 2004

[Journal Article] Detection of cardiomyocyte death in a rat model of ischemia and reperfusion using ^<99m>Tc-labeled annexin V. 2004

[Journal Article] Cerebral blood flow abnormalities induced by transient hypothyroidism after thyroidectomy. -Analysis by Tc-99m-HMPAO and SPM96-. 2004

[Journal Article] Left ventricular ejection and filling rate measurement based on the automatic edge detection method of ECG-gated blood pool single-photon emission tomography. 2004

[Journal Article] Brown adipose tissue : evaluation with ^<201>Tl and ^<99m>Tc-sestamibi dual-tracer SPECT. 2004

[Journal Article] Changes in dopamine D2 receptors and 6-[^<18>F]fluoro-L-3,4-dihydroxy-phenylalanine uptake in the brain in 6-hydroxydopamine lesioned rats. 2004

[Journal Article] ^<227>Th-EDTMP : a potential therapeutic agent for bone metastasis. 2004

[Journal Article] Failure of radioiodine treatment in Graves' disease intentionally caused by a patient : suspected Munchausen syndrome. 2004

[Journal Article] In vitro detection of mdr1 mRNA in murine leukemia cells with 111 In-labeled oligonucleotide. 2004

[Book] PET and Molecular Imaging. State of the Art and Future Perspectives 2004

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URL: https://kaken.nii.ac.jp/grant/KAKENHI-PROJECT-14657212/

Published: 2002-03-31 Modified: 2016-04-21