Amplification of Targeting of Radiolabel led Antibody by Overcoming Tumor Hypoxia

2001 Fiscal Year Final Research Report Summary

Amplification of Targeting of Radiolabel led Antibody by Overcoming Tumor Hypoxia

Research Project

Project/Area Number

10670838

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Radiation science

Research Institution

Kanazawa University

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1998 – 2000

Keywords

radioimmunotherapy / radiosensitivity / tumor hypoxia / hypoxia avid tracer / hypoxia imaging / neoangiogenesis

Research Abstract

Objectives: Hypoxia is known to increase resistance to radiation therapy. Moreover, hypoxia induced after certain anticancer drugs initiates neoangiogenesis in tumor tissues resulting in the first step of distant metastases. Therefore, it is clinically important to assess tumor hypoxia as an indicator of radio- and chemotherapeutic effect as well as a prognosis factor. In hypoxic tissues, 4,9-diaza-3, 3, 10, 10-tetramethyl dodecan-2, 11-dione bisoxime (HL91) is designed to accumulate and retained. In this study, we have attempted to evaluate Tc-99m-HL91 as a tumor targeting agent comparing with Tl-201, a flow dependent tumor-seeking agent.
Methods: P388 mouse leukemia, Lewis lung cancer (LLC) and B-16 melanoma cells were used either for in vitro cell binding assay (CBA) or pharmakokinetic studies in tumor xenografted mouse models. CBA was performed under hypoxic condition and compared to normoxic incubation. The biodistribution was assessed at 15, 60, 120

and 180 min after administratio n of Tc-99m-HL91 and Tl-201. Imaging studies were also performed with both tracers.
Results: Under normoxic condition %binding to P388 of Tc-99m-HL91 was low throughout the study (2.4 ± 0.11 % at 20 min and 3.7 ± 0.14% at 240 min), whereas under hypoxic condition %binding was increased with time (2.8 ± 0.11 % at 20 min and 40.4 ± 0.91% at 240 min). The biodistribution study showed comparable tumor uptake to B-16 between both tracers (HL91: 3.1% at 15 min, 2.7% at 180 min vs. Tl-201: 2.5%, 3.2%, respectively). However, the background activity of Tc-99m HL91 is lower than Tl-201 (muscle: HL91: 3.2% at 15 min, 0.8% at 180 min vs. Tl-201: 4.9%, 7.0%, respectively). The transplanted LLC and B-16 tumors were clearly visible with Tc-99m-HL91 and distribution pattern in the tumor was discordant with Tl-201.
Conclusion: Tc-99m-HL91 preferentially accumulates into hypoxic cells and is not flow dependent. Therefore, Tc-99m-HL91 can be used to detect tumor localization and provide the information on status of tumor hypoxia, which is distinctively different from Tl-201.▲ Less

Research Products (6 results)

All Other

All Publications

[Publications] 横山邦彦: "がんのアイソトープ内用療法"癌と化学治療. 26. 768-774 (1999)

[Publications] Seigo Kinuya: "Early response of tumor to radiotherapy should be assessed by both uptake and retention of single phofor tracer"Nuclear Medicine Communication. 20. 581-588 (1999)

[Publications] 横山邦彦: "癌のラジオアイソトープ内用療法の利用の現状と展望"Isotope News. 5. 2-7 (1999)

[Publications] Seigo Kinuya: "Efficacy, toxicity and mode of interacion of combiantion radio-immunotherapy with 5Fu in cdon cancer xuiografts"J Cancer Research Clinical Oncology. 125. 630-636 (1999)

[Publications] 横山邦彦: "センチネルリンパ節の核医学的検出法"Jpn J Breast Cancer. 15. 40-44 (2000)

[Publications] Seigo Kinuya: "Pharmacological intervention with angiotensenII and kinase inhibitor inhances efficacy of radio immunoltherapy"J Nucl Med. 41. 1244-1249 (2000)

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