Application of Radiolabeled Monoclonal A7 Antibody for Radioimmunotherapy of Human Colon Cancer

2004 Fiscal Year Final Research Report Summary

Application of Radiolabeled Monoclonal A7 Antibody for Radioimmunotherapy of Human Colon Cancer

Research Project

Project/Area Number

13470180

Research Category

Grant-in-Aid for Scientific Research (B)

Allocation Type

Single-year Grants

Section

一般

Research Field

Radiation science

Research Institution

Kanazawa University

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Project Period (FY)

2001 – 2004

Keywords

monoclonal antibody / radioimmunotherapy / colon cancer / radiolabeling / chelating agent / I-131 / Re-186 / Re-188

Research Abstract

Using monoclonal antibody specific for tumor associated antigen expressed on human malignant tumor cells, therapeutic radionuclides can be delivered to the tumor lesion in vivo. For this approach, the stable radiometal chelates is required. Re-186 or Re-188 are expected to be the choice of radionuclide for radioimmunotherapy. We have assessed the conjugation procedure of the MAG3 chelate and HYNIC chelate. The stability of the radiolabel was found to be satisfactory. A monoclonal antibody A7 was used for the project. This antibody recognizes adenocarcinoma related antigen on the variety of human colon cancer cells. The A7 antibody was labeled with Re-186, resulting in the specific activity of greater than 37 MBq/mg. And the immunoreactivity of the labeled antibody was 67%, which is equivalent for that of I-131 labeled

counterpart.
LS180 human colon cancer cells were inoculated to the Balb/c nude mice. In vivo imaging with either I-131 or Re-186 labeled A7 provided well-delineated tumor. Therapy trial study demonstrated that Re-186 A7 delivered 1.6 times higher radiation to the tumor than I-131 A7. Thus, Re-186 antibody should be the attractive modality for radioimmunotherapy.
We have tried to increase the tumor uptake of radiolabeled antibodies by modifying the delivery system to the tumor tissue. The combination usage of angiotensin-II and a kininase inhibitor, enalapril maleate, increased the mouse blood pressure from 95/61 to 153/67. And the tumor uptake was also increased by the factor of 1.62 with little change in normal organ distribution. In conclusions, enhanced tumor uptake was achieved by manipulating hemodynamics and vascular permeability of the tumor tissue and this technique can be applied for effective targeting.

Research Products (10 results)

All | 2004 | 2003 | 2002 | 2001

All | Journal Article

[Journal Article] Optimization of radioimmunotherapy interactions with hyperthermia 2004

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

[Journal Article] Limitations of 99mTc-tetrofosmin in assessing reversal effects of verapamil on multi-drug resistance associated protein 1 (MRP1) function 2004

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

[Journal Article] Reduction of 99mTc-sestamibi and 99mTc-tetrofosmin uptake in MRP-expressing breast cancer cells under hypoxic conditions is independent of MRP function 2003

[Journal Article] Radionuclide cisternography in intracranial hypotension syndrome 2002

[Journal Article] Radioimmunotherapy with 186Re-labeled monoclonal antibody to treat liver metastases of colon cancer cells in nude mice 2002

[Journal Article] Methylxanthine sensitization of human colon cancer cells to 186Re-monoclona antibody 2001

[Journal Article] Methylxanthine sensitization of human colon cancer cells to 186Re-monoclonal antibody 2001

[Journal Article] Experimental radioimmunotherapy with 186Re-MAG3-A7 anti-colorectal cancer monoclonal antibody : comparison with 131I-counterpart 2001

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