

Answer 1:

Bibliographic Information

Targeting therapy against pancreatic carcinoma using a monoclonal antibody and its derivatives. Otsuji, Eigo; Kuriu, Yoshiaki; Toma, Atsushi; Okamoto, Kazuma; Yamagishi, Hisakazu. Department of Surgery, Kyoto Prefectural University of Medicine, Kawaramachi Hirokoji Kamigyo-ku Kyoto, Japan. Recent Research Developments in Cancer (2002), 4(Pt. 2), 745-751. Publisher: Transworld Research Network, CODEN: RRDCCP Journal written in English. CAN 142:409398 AN 2005:86928 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Despite the introduction of several dozen anti-neoplastic drugs, conventional chemotherapy for pancreatic cancer remains disappointing. Recent research has been directed toward the use of monoclonal antibody-drug conjugates for solid tumors. In this study, we used the monoclonal antibody A7 (Mab A7) to target the anti-tumor drug neocarzinostatin (NCS) to pancreatic carcinoma cells. Mab A7 was produced in a hybridoma that was established by cell hybridization between a murine myeloma cell line and the spleen cells of a mouse immunized against a human colon carcinoma. In immunohistol. and animal expts., Mab A7 reacted with human pancreatic carcinomas. However, Mab A7 does not react immunohistochem. with normal pancreatic tissues. NCS was conjugated covalently to Mab A7 (A7-NCS) by SPDP (N-succinimidyl-3-(2-pyridyldithio)-propionate) method. A7-NCS showed greater in vivo antitumor effects on the growth of pancreatic carcinoma than NCS alone. In order to decrease the human anti-mouse antibody (HAMA) response following the administration of murine Mabs, we developed chimeric (human/mouse) Fab fragments of Mab A7 (chA7Fab). ChA7Fab was also conjugated to NCS by the SPDP method, and its applicability as a carrier of NCS for the treatment of human pancreatic carcinoma was examd. The distribution of chA7Fab-NCS was examd. and compared with that of A7-NCS. One hour after administration, greater amts. of chA7Fab-NCS than of A7-NCS accumulated in the tumor. ChA7Fab-NCS cleared more rapidly from the blood than did A7-NCS. Because more than 70% of the administered NCS was inactivated by the serum within 120 min, chA7Fab may be able to carry a large quantity of a short-acting anti-cancer drug such as NCS. In an in vivo therapeutic study using chA7Fab-NCS, the anti-tumor effect of chA7Fab-NCS was greater than that of A7-NCS and tumor growth was completely suppressed after the administration of chA7Fab-NCS.

These results suggest that chA7Fab may be a useful carrier of NCS for targeting therapy against human pancreatic carcinoma and has a lower potential to induce a HAMA response.

Answer 2:

Bibliographic Information

Biodistribution of neocarzinostatin conjugated to chimeric Fab fragments of the monoclonal antibody A7 in nude mice bearing human pancreatic cancer xenografts. Otsuji, Eigo; Yamaguchi, Toshiharu; Yamaoka, Nobuki; Taniguchi, Katsunori; Kato, Makoto; Kotani, Tatsuya; Kitamura, Kazuya; Takahashi, Toshio. 1st Dep. Surg., Kyoto Prefect. Univ. Med., Hirokoji, Japan. Japanese Journal of Cancer Research (1994), 85(5), 530-5. CODEN: JJCREP ISSN: 0910-5050. Journal written in English. CAN 121:194830 AN 1994:594830 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

In this study, we conjugated chimeric Fab fragments of the monoclonal antibody (MAb) A7, which reacts with pancreatic cancers, to the antitumor drug neocarzinostatin (chA7Fab-NCS) and i.v. injected 125I-labeled chA7Fab-NCS into nude mice bearing a human pancreatic cancer xenograft. We compared the tumor localization of 125I-labeled chA7Fab-NCS with that of conventional 125I-labeled A7-NCS, which was produced by conjugation of MAb A7 and NCS. 125I-Labeled chA7Fab-NCS accumulated in the tumor earlier than 125I-labeled A7-NCS, and significantly larger amts. of 125I-labeled chA7Fab-NCS had accumulated in the tumor 1 h after injection. The results suggest that chA7Fab may be a suitable carrier for NCS in immunotargeting therapy against pancreatic cancer.

Answer 3:

Bibliographic Information**Intratumoral administration of neocarzinostatin conjugated to monoclonal antibody A7 in a model of pancreatic cancer.**

Otsuji, Eigo; Yamaguchi, toshiharu; Yamaoka, Nobuki; Kitamura, Kazuya; Yamaguchi, Nozomi; Takahashi, Toshio. 1st Dep. Surg., Kyoto Prefect. Univ. Med., Kyoto, Japan. *Journal of Surgical Oncology* (1993), 53(4), 215-19. CODEN: JSONAU ISSN: 0022-4790. Journal written in English. CAN 119:240985 AN 1993:640985 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The authors investigated the following in athymic nude mice with xenografts of a human pancreatic carcinoma: 1) clearance of the murine monoclonal antibody A7 from the carcinoma; and 2) the antitumor effect of neocarzinostatin conjugated to MAb A7 (A7-NCS) on the carcinoma following intratumoral injection. Compared with 125I-labeled normal mouse IgG, a significantly larger amt. of 125I-labeled A7 remained in the tumor after intratumoral injection. Neocarzinostatin conjugated to MAb A7 showed a greater antitumor activity against human pancreatic cancer than neocarzinostatin alone after intratumoral administration. The conjugate completely suppressed tumor growth macroscopically during the expt. Tumor tissue in mice became necrotic 32 days after injection with A7-NCS. These observations suggest that the intratumoral injection of A7-NCS offers promise in treating pancreatic carcinoma.

Answer 4:

Bibliographic Information**Local administration of monoclonal antibody-drug conjugate: a new strategy to reduce the local recurrence of colorectal cancer.**

Kitamura, Kanuya; Takahashi, Toshio; Kotani, Tatsuya; Miyagaki, Takuya; Yamaoka, Nobuki; Tsurumi, Hiroshi; Noguchi, Akinori; Yamaguchi, Toshiharu. 1st Dep. Surg., Kyoto Prefect Univ. Med., Kyoto, Japan. *Cancer Research* (1992), 52(22), 6323-8. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 118:435 AN 1993:435 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This report investigates the application of monoclonal antibody A7 and its drug conjugate in locally controlling colorectal cancer. The exptl. protocol consisted of local retention, lymphatic delivery, normal organ distribution, systemic toxicity, and tumoricidal effects. When 125I-labeled monoclonal antibody (Mab) A7 was injected into the pelvis and the thigh of Balb/c mice, a high local retention unrelated to antigen-antibody interaction was obsd. at the injected site for 24 h after injection. An anal. of local retention properties related to antigen-antibody interaction, conducted by intratumorally or peritumorally injecting 125I-Mab A7 into the tumor-bearing athymic nude mice, revealed a significantly higher tumor localization of Mab A7 in comparison to i.v. injection. 125I-Mab A7 accumulated to a great extent in the ipsilateral regional lymph node but not in the contralateral regional lymph node. Normal organ accumulation of Mab A7 was lower in the locally injected group than in the i.v. injected group. Intratumoral injection of Mab A7-neocarzinostatin (A7-NCS) led to the complete remission of established tumor in 5 of 6 antigen-pos. xenograft-bearing mice but exhibited a complete remission in only 1 of 6 antigen-neg. xenograft-bearing mice. A single local injection of A7-NCS inhibited tumor development in 12 of 16 and 5 of 15 antigen-pos. tumor-bearing mice and antigen-neg. tumor-bearing mice, resp., whereas neither a systemic injection of A7-NCS and NCS nor a local injection of NCS and saline had a notable inhibitory effect on tumor development. Systemic toxicity of NCS was markedly reduced when it was locally administered in the antibody-conjugated form. These findings indicate that local injection of immunoconjugate is a promising new field for controlling the local recurrence of colorectal cancer.

Answer 5:

Bibliographic Information**In vivo distribution of neocarzinostatin conjugated with antihuman colon cancer-monoclonal antibody.**

Masuda, Tetsuzo. Sch. Med., Akita Univ., Akita, Japan. *Akita Igaku* (1985), 12(3), 469-80. CODEN: AKIGDV ISSN: 0386-6106. Journal written in Japanese. CAN 105:126932 AN 1986:526932 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

When antihuman colon cancer-monoclonal antibody A 7-neocarzinostatin (NCS) conjugate, normal mouse IgG-NCS conjugate, or free NCS was given i.p. and i.v. into nude mice transplanted with human colon cancer, blood NCS concns. lasted longer following the A 7-NCS conjugate or IgG-NCS conjugate than following free NCS; NCS was accumulated more selectively in the colon cancer xenograft following the A 7-NCS conjugate than following the IgG-NCS conjugate and free NCS. Thus, the selective cytotoxicity of NCS might be enhanced by conjugating it with monoclonal antibody A 7, making the A 7-NCS conjugate a useful specific cytotoxic agent against human colon cancer.

Answer 6:

Bibliographic Information

The effect of intravenous and intra-tumoural chemotherapy using a monoclonal antibody-drug conjugate in a xenograft model of pancreatic cancer. Otsuji E; Yamaguchi T; Tsuruta H; Yata Y; Nishi H; Okamoto K; Taniguchi K; Kato M; Kotani T; Kitamura K; + First Department of Surgery, Kyoto Prefectural University of Medicine, Japan
European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology (1995), 21(1), 61-5. Journal code: 8504356. ISSN:0748-7983. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 7851556 AN 95154473 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

In order to investigate the efficacy of the intra-tumoural administration of an anticancer drug-monoclonal antibody conjugate in athymic nude mice bearing xenografts of a human pancreatic carcinoma, we examined the clearance of the murine monoclonal antibody A7 from the xenografts after intravenous or intra-tumoural administration and measured the antitumour effect of neocarzinostatin conjugated to MAb A7 following intravenous or intra-tumoural injection. Compared with 125I-labelled normal mouse IgG, a larger amount of 125I-labelled A7 remained in the tumour after both intravenous and intra-tumoural injection, and a significantly larger amount of 125I-labelled A7 remained in the tumour after intra-tumoural injection than that after intravenous injection. Moreover, a larger amount of 125I-labelled A7-NCS localized in the tumour after intra-tumoural injection than that after intravenous injection. Neocarzinostatin conjugated to MAb A7 showed greater activity against human pancreatic cancer than neocarzinostatin alone after both intravenous and intra-tumoural administration. Tumour growth was suppressed completely by the intra-tumoural administration of A7-NCS at a dose that did not suppress tumour growth via the intravenous route. These observations suggest that the intra-tumoural injection of neocarzinostatin conjugated to MAb A7 offers promise in treating pancreatic carcinoma.