

Answer 1:

Bibliographic Information

Influence of ondansetron on the antitumor activity and lung toxicity of bleomycin. Suddek, Ghada M.; Salem, Hatem A.; Ahmed, Wafaa A.; Badary, Osama A.; Gameil, Nariman M.; El-Kashef, Hassan A. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Mansoura University, Egypt. *Journal of Basic & Applied Sciences* (2008), 4(1), 33-44. Publisher: University of Karachi, Educational Forum, CODEN: JBASBR ISSN: 1814-8085. Journal written in English. CAN 149:24522 AN 2008:464657 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Bleomycin (BLM) is well known by its antitumor activity both in vitro and in vivo. However, pulmonary fibrosis has been considered the dose limiting toxicity of the drug. Moderate nausea and vomiting occur in virtually all patients taken BLM. Ondansetron (OND) is a highly selective 5-HT₃ receptor antagonist with significant antiemetic activity. This study was conducted to investigate the effect of OND administration on the antitumor and lung toxicity of BLM. The antitumor activity was evaluated both in vitro and in vivo using Ehrlich ascites carcinoma (EAC) cells. Ondansetron did not alter the antitumor effect of BLM in vitro or in vivo. The lung toxicity of BLM was evidenced by decrease in the body wt., increase in the lung/body wt. ratio, decrease in the response of pulmonary arterial rings to 5-HT and increase in the contractility of tracheal smooth muscles induced by ACh. The toxicity was also confirmed biochem. by marked increases in hydroxyproline and lipid peroxidn. in rat lung and the decrease in GSH level. Pretreatment with ondansetron decreased lipid peroxidn. and normalized GSH level and hence enhanced the percent survival of rats. The results of the present study indicate that OND did not modify the antitumor effect of BLM but ameliorated the increase in some biochem. markers assocd. with BLM-induced lung toxicity.

Answer 2:

Bibliographic Information

Site-Specific Drug Delivery by Photochemical Internalization Enhances the Antitumor Effect of Bleomycin. Berg, Kristian; Dietze, Andreas; Kaalhus, Olav; Hogset, Anders. Departments of Radiation Biology, The Norwegian Radium Hospital, Montabello, Norway. *Clinical Cancer Research* (2005), 11(23), 8476-8485. Publisher: American Association for Cancer Research, CODEN: CCRE4 ISSN: 1078-0432. Journal written in English. CAN 144:376253 AN 2005:1260090 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

PURPOSE: Photochem. internalization is under development for improving macromol. therapy by inducing photochem. damage to endocytic vesicles. This damage leads to the release of therapeutic macromols. entrapped in endocytic vesicles into the cytosol. The macromols. may in this way be able to interact with therapeutic targets instead of being degraded by lysosomal hydrolases. Bleomycin is used in several std. cancer chemotherapy regimens. Its hydrophilic and relatively large chem. structure limits its ability to penetrate membrane structures, which causes the accumulation of bleomycin in endocytic vesicles. The purpose of this study was to evaluate the therapeutic potential of aluminum phthalocyanine disulfonate (AIPcS2a)-based photochem. delivery of bleomycin. **Exptl. Design:** Three tumors of different origin were grown s.c. in BALB/c (nu/nu) mice. The photosensitizer AIPcS2a and bleomycin were systemically administered and the tumor area was exposed to red light when the tumor vol. had reached 100 mm³. The tumor vol. was measured frequently after treatment and the time for the tumor vol. to reach 800 to 1,000 mm³ was selected as the end point. **RESULTS:** The photochem. delivery of bleomycin induced a delayed tumor regrowth, and in two out of three tumor models, lead to 60% complete response, whereas no complete responses were seen after treatment with bleomycin alone. A statistical model to assess synergism was established. Combination of the photochem. treatment and bleomycin was found to induce a synergistic delay in tumor growth. **CONCLUSION:** AIPcS2a-based photochem. internalization of bleomycin induces a synergistic inhibition of tumor growth in three different tumor models. This treatment combination should be further considered for clin. utilization.

Answer 3:

Bibliographic Information

Indium-111-bleomycin complex in squamous cell cancer xenograft tumors of nude mice. Jaaskela-Saari, Hilikka A.; Grenman, Reidar; Ramsay, Hans A.; Tarkkanen, Jussi; Paavonen, Timo; Kairemo, Kalevi J. A. Department of Otorhinolaryngology-Head and Neck Surgery, Helsinki University Central Hospital, Helsinki, Finland. *Cancer Biotherapy & Radiopharmaceuticals* (2005), 20(4), 426-435. Publisher: Mary Ann Liebert, Inc., CODEN: CBRAFJ ISSN: 1084-9785. Journal written in English. CAN 144:269612 AN 2005:1019034 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Introduction: Labeling of bleomycin with Auger-emitter Indium-111 increases cytotoxicity in squamous cell cancer (SCC) cell lines, as we have reported earlier. In this study, we investigated whether ¹¹¹InBLMC is toxic and effective in vivo among SCC-xenografted mice. The influence of ¹¹¹InBLMC on the squamous cell carcinoma cell cycle stimulated interest. **Materials and methods:** In an animal expt., 10 SCC-xenografted mice were used, two for demonstrating targeting in gamma-camera images, eight for i.p. receiving NaCl, BLM, or ¹¹¹InBLMC as therapy. After a 2-wk follow-up, the tumors were analyzed for proliferation (mitoses, Ki-67). DNA flow cytometric anal. was carried out from tumor samples and three UT-SCC cell lines. **Results:** Tumors were obsd. on gamma-camera images in xenografted mice after a ¹¹¹InBLMC injection. The UT-SCC-19A-xenografted mouse had a T/non-T uptake of 7.54 at 4 h after the injection. At the end of the therapeutic trial, the mice were alive. In spite of a small no. of animals, our findings indicate that BLM and ¹¹¹InBLMC seem to be more effective than NaCl in reducing tumor size. The proliferative activity was strong in BLM and in ¹¹¹InBLMC groups, indicating regrowth of the tumors. In DNA anal., the percentages of cells in the G2/M-phases increased after exposure to BLM and particularly to ¹¹¹InBLMC in all three cell lines. **Conclusions:** The effect of BLM is preserved after the adding of Auger-emitter In-111. Tumor-seeking ¹¹¹InBLMC can be administered safely at tumor-decreasing concns. in xenograft head and neck cancers. To demonstrate the antitumor effect of ¹¹¹InBLMC, the expts. should be extended to include a larger no. of mice. BLM, and esp. ¹¹¹InBLMC, seems to induce alteration in the cell cycle by producing a G2/M block. The verification of the result requires repeated in vitro expts.

Answer 4:

Bibliographic Information

Effects and possible anti-tumor immunity of electrochemotherapy with bleomycin on human colon cancer xenografts in nude mice. Zheng, Min-Hua; Feng, Bo; Li, Jian-Wen; Lu, Ai-Guo; Wang, Ming-Liang; Hu, Wei-Guo; Sun, Ji-Yuan; Hu, Yan-Yan; Ma, Jun-Jun; Yu, Bao-Ming. Department of General Surgery, Ruijin Hospital, Shanghai Minimally Invasive Surgery Center, Shanghai Institute of Digestive Surgery, Shanghai Second Medical University, Shanghai, Peop. Rep. China. *World Journal of Gastroenterology* (2005), 11(16), 2426-2430. Publisher: World Journal of Gastroenterology, CODEN: WJGAF2 ISSN: 1007-9327. Journal written in English. CAN 143:205923 AN 2005:501137 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

AIM: To evaluate the anti-tumor effects and possible involvement of anti-tumor immunity of electrochemotherapy (ECT) employing electroporation and bleomycin in human colon cancer xenografts in nude mice, and to establish the exptl. basis for clin. application of ECT. **METHODS:** Forty nude mice, inoculated s.c. human colon cancer cell line LoVo for 3 wk, were allocated randomly into four groups: B+E+ (ECT), B+E- (administration of bleomycin alone), B-E+ (administration of elec. pulses alone), and B-E- (no treatment). Tumor vols. were measured daily. The animals were killed on the 7th d, the wts. of xenografts were measured, and histologies of tumors were evaluated. Cytotoxicity of spleen natural killer (NK) and lymphokine-activated killer (LAK) cells was then assessed by lactic dehydrogenase release assay. **RESULTS:** The mean tumor vol. of group B+E+ was statistically different from the other three groups after the treatment ($F = 36.80, P < 0.01$). There was one case of complete response, seven cases of partial response (PR) in group B+E+, one case of PR in group B+E- and group B-E+ resp., and no response was obsd. in group B-E-. The difference of response between group B+E+ and the other three groups was statistically significant ($\eta^2 = 25.67, P < 0.01$). Histol., extensive necrosis of tumor cells with considerable vascular damage and inflammatory cells infiltration were obsd. in group B+E+. There was no statistical difference between the cytotoxicity of NK and LAK cells in the four treatment groups. **CONCLUSION:** ECT significantly enhances the chemosensitivity and effects of chemotherapy in human colon cancer xenografts in nude mice, and could be a kind of

novel treatment modality for human colon cancer. The generation of T-cell-dependent, tumor-specific immunity might be involved in the process of ECT.

Answer 5:

Bibliographic Information

Clonogenic assay with established human tumour xenografts: correlation of in vitro to in vivo activity as a basis for anticancer drug discovery. Fiebig, H. H.; Maier, A.; Burger, A. M. Oncotest GmbH, Institute for Experimental Oncology, Freiburg, Germany. *European Journal of Cancer* (2004), 40(6), 802-820. Publisher: Elsevier Science Ltd., CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 141:342988 AN 2004:284718 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Pluripotent cells can be grown in clonogenic assays. The tumor stem-cell fraction, which accounts for <0.4% of the total cells, and which is considered the most relevant cell type in the development of metastases and recurrences, is able to divide and to form colonies in a semisolid matrix (agar or methylcellulose). Major applications of the tumor clonogenic assay (TCA) are chemosensitivity testing of tumors and xenografts, and for assessments within drug discovery programs. Of crit. relevance for the usefulness of the TCA is whether it can predict sensitivity or resistance towards clin. used agents. When we compared the response of human tumors established as xenografts in nude mice in the TCA in vitro to that of the clin. response, 62% of the comparisons for drug sensitivity, and 92% of the comparisons for drug resistance were correct. The same percentage of true/false observations was found when tumors were tested after serial passage in nude mice in the TCA in vitro and their response compared to in vivo activity in corresponding xenografts (60% and 90%, resp.). The highest correct predictive values were, however, found when the clin. response of tumors was compared to their explants established in the nude mouse and treated in vivo. Of 80 comparisons performed, we obsd. a correct prediction for tumor resistance in 97% and for tumor sensitivity in 90%. In our opinion, the TCA with established human tumor xenografts has an important role in current drug discovery strategies. We therefore included the TCA as secondary assay in our approach to anticancer drug discovery and found that a no. of novel agents were active; these are now in advanced preclin. development or clin. trials. Thus, the tumor clonogenic assay has proven predictive value in the chemosensitivity testing of std. and exptl. anticancer drugs.

Answer 6:

Bibliographic Information

Development of human lymphoma/leukemia xenograft models in immune-deficient mice for evaluation of potential anticancer agents. Dykes, D. J.; Hollingshead, M. G.; Camalier, R. F.; Waud, W. R.; Mayo, J. G. Southern Research Institute, Birmingham, AL, USA. *Contributions to Oncology* (1999), 54(Relevance of Tumor Models for Anticancer Drug Development), 295-304. Publisher: S. Karger AG, CODEN: COONEV ISSN: 0250-3220. Journal written in English. CAN 133:217399 AN 2000:242563 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Eleven human lymphoma/leukemia cell lines were assessed as in vivo xenograft models in severe combined immunodeficient (SCID) mice. In prepn. for efficacy evaluations of new antitumor agents, all eleven cell lines have been characterized for sensitivity to known clin. useful agents. The lines included in the study represent a variety of diseases including T-cell, myelogenous, and lymphoblastic leukemias, as well as histiocytic, B-cell and Burkitt's lymphomas. The selected agents for this study were representative of various chem. classes. Addnl., growth studies were performed including comparisons in athymic nude mice. These studies were designed to det. s.c. tumor vol. doubling times, graft success, latent growth periods, and other characteristics necessary to effectively implement and interpret anticancer efficacy evaluations. The various tumor lines used proved to be good models for chemotherapy trials. In the chemotherapy trials, considerable independent chemotherapeutic profiles were obsd. but there were also some similarities among the various histol. types.

Answer 7:

Bibliographic Information

Antitumor activity of bleomycin A6 against human nasopharyngeal cancer in cell culture and in nude mice. Guan, Zhong; Ye, Hui; Peng, Jieren; Yang, Xiaoping. Sun Yat-sen Memory Hospital, Sun Yat-sen University of Medical Sciences, Canton, Peop. Rep. China. *Guangdong Yixue* (1998), 19(5), 326-327. Publisher: Guangdongsheng Yixue Qingbao Yanjiuso, CODEN: GUYIEG ISSN: 1001-9448. Journal written in Chinese. CAN 129:298013 AN 1998:506878 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Cytotoxicity of bleomycin A6 on human nasopharyngeal carcinoma cell line SUNE-1 in culture and in nude mice xenografted with SUNE-1 cells was studied. MTT method demonstrated that the IC50 of bleomycin A6 was 1.45 µg/mL in vitro. The in vitro inhibition rate was 84.3 and 88.9% at the dosage of 10 and 15 mg/kg, resp. The results suggest that bleomycin A6 possesses antitumor activity against human nasopharyngeal carcinoma in vitro and in vivo.

Answer 8:

Bibliographic Information

Antiangiogenic chemotherapeutic agents: characterization in comparison to their tumor growth inhibition in human renal cell carcinoma models. Schirner, Michael; Hoffmann, Jens; Menrad, Andreas; Schneider, Martin R. Research Laboratories of Schering AG, Berlin, Germany. *Clinical Cancer Research* (1998), 4(5), 1331-1336. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 129:103876 AN 1998:328200 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The mechanism of action of anticancer chemotherapeutic agents is mainly thought to be due to a direct inhibition of tumor cell proliferation. The enhanced endothelial cell proliferation rate in tumor specimens raised the question of whether therapeutic effects of chemotherapeutic agents might be at least partially attributed to inhibition of tumor angiogenesis. In the present study, we investigated the potential effects of chemotherapeutic agents on human renal carcinoma angiogenesis with the alginate implantation model in mice. For the first time, we also compared results from the angiogenesis model with the inhibitory effects on growth of s.c. xenografts in nude mice. Vincristine and bleomycin exerted strong inhibition of tumor angiogenesis in both carcinoma lines close to the level of the std. antiangiogenic agent O-chloroacetyl-carbamyl-fumagillol (AGM-1470; T/C 22%). Adriamycin reduced angiogenesis of Caki-2 cells (T/C 33%) but had no effect on Caki-1 angiogenesis (T/C 137%). Etoposide and 5-fluorouracil reduced Caki-1 tumor angiogenesis but had no effect on Caki-2. Despite antiangiogenic effects in both carcinoma lines, vincristine, bleomycin, and AGM-1470 significantly reduced only the growth of fast-growing Caki-1 s.c. xenografts but not the slow-growing Caki-2. Antivascular effects by bleomycin and AGM-1470 were also shown by a decrease of microvessel d. in nude mouse xenografts. Our findings suggest that chemotherapeutic agents may exert inhibition of tumor angiogenesis, which could be exploitable by combination therapy of fast-growing tumors. The resistance of the slow-growing Caki-2 carcinoma against acute angiogenesis inhibition indicates a need for well-tolerated angiogenesis inhibitors. Our results also suggest the use of fast-growing s.c. xenografts for demonstrating growth inhibition by antiangiogenic compds. Further characterization of antiangiogenic compds. considered for clin. application should, however, have its focus on slow-growing tumors, which are not accessible for most therapeutic strategies.

Answer 9:

Bibliographic Information

A new approach to treating pancreatic cancer. Dev, S. B.; Nanda, G. S. Genetronics, Inc., San Diego, CA, USA. Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1996), 23rd 693-694. Publisher: Controlled Release Society, Inc., CODEN: PCRMEY ISSN: 1022-0178. Journal written in English. CAN 125:211990 AN 1996:522381 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Electrochemotherapy, which combines chemotherapeutic agents (bleomycin) with pulsed elec. field was used to treat human pancreatic tumors xenografted onto nude mice.

Answer 10:

Bibliographic Information

The effect of tirapazamine (SR-4233) alone or combined with chemotherapeutic agents on xenografted human tumors. Lartigau, E.; Guichard, M. Laboratoire de Radiobiologie, Institut Gustave Roussy, Villejuif, Fr. British Journal of Cancer (1996), 73(12), 1480-1485. Publisher: Stockton, CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 125:157937 AN 1996:471337 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Recent data have shown that the in vitro and in vivo cytotoxicity of bioreductive drugs could be significantly increased when combined with chemotherapy drugs such as cisplatin, depending on the timing of administration. The aim of this study was to define the toxicity (animal lethality) and the activity (growth delay assay, excision assay) of a bioreductive drug, tirapazamine, alone and combined with chemotherapy agents (5-FU, VP16, bleomycin dacarbazine (DTIC) and cisplatin) on nude mice bearing xenografted human tumors: a rectal carcinoma (HRT18) and a melanoma (Na11+). Animal lethality was markedly increased when tirapazamine at the LD 10% was combined with the other drugs. For the HRT18 tumor, the combination of tirapazamine and bleomycin significantly increased the delay of regrowth compared with bleomycin alone and was more cytotoxic than tirapazamine alone. For the Na11 + tumors the combination of tirapazamine with VP16 significantly increased tumor doubling time compared with the controls or VP16 alone. The combination of tirapazamine and VP16 was more cytotoxic than VP16 alone. When compared with cisplatin or tirapazamine alone, there was a significant decrease in plating efficiency when tirapazamine and cisplatin were given at the same time, but not when tirapazamine was given 3 h before cisplatin. In conclusion, tirapazamine was shown to be cytotoxic against clonogenic human tumor cells. Its efficacy in vivo may depend on its combination with already active chemotherapy drugs on the tumor model used. The timing of administration may be less important than previously thought.

Answer 11:

Bibliographic Information

Experimental studies on therapeutic effect of rat monoclonal antibody-bleomycin A6 conjugate against human colorectal cancer. Deng, Y. C.; Zhen, Y. S.; Zheng, S.; Jiang, M. Inst. Med. Biotechnol., Chin. Acad. Medical Sci., Beijing, Peop. Rep. China. Yaoxue Xuebao (1993), 28(6), 410-15. CODEN: YHHPAL ISSN: 0513-4870. Journal written in Chinese. CAN 119:195203 AN 1993:595203 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Bleomycin A6 (A6), a single component of bleomycin complex, is highly active against human colon and cecum cancer cells in vitro and xenografts in nude mice. R19, a rat monoclonal antibody against human cecum cancer Hce-8693 cells, was linked to A6. R19-A6 conjugate retained complete activity of McAb R19 and 10% activity of A6. As detd. by clonogenic assay with human cecum cancer Hce-8693 cells for 1h exposure. The 50% inhibitory concn. (IC50) values for R19-A6, A6 and M3-A6 (conjugate if irrelevant Mc-A6) were 0.019, 1.05 and 1.00 $\mu\text{mol/L}$, resp. The effect of the conjugate R19-A6 was 55-fold stronger than that of free A6 and 53-fold than

irrelevant conjugate M3-A6. Clonogenic assay with human colon cancer HT-29 cells showed that the IC₅₀ values were 0.078 μmol/L and 4.0 μmol/L for R19-A6 and free A6, resp. The cytotoxicity to Hce-8693 and HT-29 cells was markedly blocked by unconjugated McAb R19 but not by irrelevant McAb MARK-3. The R19-A6 conjugate exerted 90% inhibition on the growth of cecum cancer Hce-8693 xenografts in nude mice, whereas equiv. dosed of free A6, R19 plus A6 mixt. and M3-A6 showed 52%, 34% and 48% inhibition, resp. Histopathol. examn. showed no toxic changes in the heart, lung, liver, kidney and bone marrow in the R19-A6 conjugate treated animals. These results suggest that the conjugate of R19 and A6 shows selective cytotoxicity to target human colon and cecum cancer cells and is highly effective against cecum cancer xenografts in nude mice with more remarkable tumor growth inhibition than free A6 at equiv. dose level.

Answer 12:

Bibliographic Information

Chemosensitivity testing of xenografted squamous cell carcinomas of the head and neck region. Elprana, D.; Kuijpers, W.; Wessels, J. M. C.; Wagener, D. J. T.; Van den Broek, P. Dep. Otorhinolaryngol., Univ. Hosp. Nijmegen, Nijmegen, Neth. *Anticancer Research* (1992), 12(6B), 2229-9. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 118:225085 AN 1993:225085 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Eight squamous carcinomas from the head and neck region were established as xenograft lines in nude mice and tested for their sensitivity to the antineoplastic drugs bleomycin and cisplatin. Tumor vol., histol., DNA flow cytometry and mitotic activity were used as parameters. One out of the 8 tumors appeared to be highly sensitive to bleomycin, while three other tumors were sensitive to both bleomycin and cisplatin. These observations are in good correlation with the reported data in patients. All chemosensitive tumors showed regrowth after the cytotoxic drug treatment had been completed. No change was seen in the chemosensitivity of other features of the regrown tumors, not even after repeated exposure to the drugs. Comparison of the tumor vol. with the other parameters applied indicated that the tumor vol. of squamous cell carcinomas was not always a reliable parameter for testing chemosensitivity, because of the important contribution of keratin to the tumor vol. It is concluded that addnl. parameters such as histol. examn., DNA flow cytometry or mitotic activity are necessary in order to draw reliable conclusions on xenografts with a large avital component. In addn., DNA flow cytometry has proved to be very useful for the rapid screening of drug sensitivity.

Answer 13:

Bibliographic Information

Inhibitory effect of bleomycin A6 on human colon cancer xenografts in nude mice. Deng, Yongchuan; Zhen, Yongsu; Zheng, Shu; Xue, Yuchuan. Inst. Med. Biotechnol., Chin. Acad. Sci., Beijing, Peop. Rep. China. *Zhongguo Yixue Kexueyuan Xuebao* (1990), 12(5), 335-40. CODEN: CIHPDR ISSN: 1000-503X. Journal written in Chinese. CAN 115:149850 AN 1991:549850 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Bleomycin A6 was found to be highly active against established human cancer cell lines derived from colon cancer (HT-29) and cecum cancer (Hce-8693), as evaluated by clonogenic assay. These human cancer cells were serially transplanted in nude mice. At a tolerable dosage level, bleomycin A6 exerted remarkable growth inhibition on human colon cancer HT-29 and cecum cancer Hce-8693 xenografts (approx. 90% inhibition). No histopathol. changes were found in the organs of treated animals. Compared on the basis of equitoxic doses (1/9 LD₅₀), bleomycin A6 exerted much stronger growth inhibition against colon cancer HT-29 xenografts in nude mice than 5-fluorouracil and mitomycin C, with inhibition rates of 82%, 12% and 53%, resp. More extensive necrosis was found in tumors treated with bleomycin A6 than in those treated with mitomycin C or 5-fluorouracil. The ratio values of non-necrotic tumor tissue to whole tumor tissue for bleomycin A6, mitomycin C, and 5-fluorouracil were 0.33, 0.65, and 0.57, resp. These observations indicate that bleomycin A6 is a potent antitumor agent against colon cancer xenografts and may be useful in human colon cancer chemotherapy.

Answer 14:

Bibliographic Information

Experimental studies on the antitumor activity of monoclonal antibody - bleomycin A6 conjugate against human liver cancer.

Peng, Z.; Zhen, Y. S. Inst. Med. Biotechnol., Chin. Acad. Med. Sci., Beijing, Peop. Rep. China. Yaoxue Xuebao (1991), 26(5), 331-5. CODEN: YHHPAL ISSN: 0513-4870. Journal written in Chinese. CAN 115:84954 AN 1991:484954 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Bleomycin A6 (A6), a single component of bleomycin complex, is highly active against human liver cancer cells in vitro and xenografts in nude mice. A6 was conjugated to monoclonal antibody H111 directed against human hepatoma BEL - 7402 cells, using Dextran T40 as an intermediate. The conjugate consisted of a coupling molar ratio of 1:264 for H111 and A6, and retained 6.3% of A6 activity. As detd. by clonogenic assay with hepatoma BEL - 7402 cells exposed to the agents for 1 h, the IC90 values for H111-A6 conjugate, free A6 and M3-A6 conjugate (an irrelevant conjugate) were 0.17, 17 and 7 $\mu\text{mol/L}$, resp. The cytotoxicity of Hill-A6 conjugate to target cells was markedly blocked by unconjugated H111 but not by irrelevant monoclonal antibody M3. The H111-A6 conjugate exhibited 78% inhibition on the growth of hepatoma BEL-7402 xenografts in nude mice, whereas the equiv. doses of free A6, M3-A6 conjugate and H111 plus A6 mixt. showed approx. 30% inhibition. Histopathol. examn. showed no toxic changes in the liver, lung, kidney and bone marrow in the H111-A6 conjugate-treated animals. These results suggest that the conjugate of monoclonal antibody and bleomycin A6 exhibits specific cytotoxicity to target liver cancer cells and the conjugate is highly effective against liver cancer xenografts in nude mice with more marked tumor inhibition than free A6 at comparable dose levels.

Answer 15:

Bibliographic Information

Antitumor activity of bleomycin A6 against human liver cancer in cell culture and in nude mice. Jiang, Min; Zhen, Yongsu. Inst. Med. Biotechnol., Chin. Acad. Med. Sci., Beijing, Peop. Rep. China. Yaoxue Xuebao (1987), 22(12), 881-5. CODEN: YHHPAL ISSN: 0513-4870. Journal written in Chinese. CAN 108:87730 AN 1988:87730 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Bleomycin A6 was highly active against human nasopharyngeal, stomach, and liver cancer cell lines in vitro, as evaluated by the clonogenic assay. I.p. injection of bleomycin A6 at a tolerable dose also markedly inhibited human liver cancer xenografted in nude mice. Bleomycin A6 may be clin. useful in the treatment of hepatoma.

Answer 16:

Bibliographic Information

Sensitivity to antineoplastic agents of squamous cell carcinoma of the uterine cervix xenografted into nude mice.

Kawabata, Masakiyo; Hosokawa, Hitoshi; Kato, Kiyoshi; Izumi, Rikuichi. Fac. Med., Toyama Med. Pharm. Univ., Toyama, Japan. Gan to Kagaku Ryoho (1987), 14(11), 3058-63. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 108:68479 AN 1988:68479 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The efficacies of 5 antineoplastic agents (cisplatin, mitomycin, doxorubicin, 5-fluorouracil, and bleomycin) were tested against carcinoma of the human uterine cervix xenografted into nude mice in order to search for effective combination chemotherapy. The

responses to cisplatin and mitomycin were the highest. Thus, combination chemotherapies involving cisplatin and mitomycin are recommended for the treatment of squamous cell carcinoma of the uterine cervix.

Answer 17:

Bibliographic Information

Experimental studies on heterotransplantation of human squamous cell carcinoma in nude mice and sensitivity test for anticancer agents. Sakamoto, Tomoji. Dent. Coll., Hiroshima Univ., Hiroshima, Japan. Hiroshima Daigaku Shigaku Zasshi (1987), 19(1), 1-13. CODEN: HUDJAN ISSN: 0046-7472. Journal written in Japanese. CAN 107:228638 AN 1987:628638 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor effect of the chemotherapeutic agents bleomycin, peplomycin, mitomycin C, cisplatin, 5-fluorouracil, and methotrexate against human squamous cell carcinoma was evaluated in nude mice heterotransplanted with the human carcinoma. Results indicated that the sensitivity test for anticancer agents in nude mice is closely related to their clin. effectiveness. The true pos. and neg. antitumor effects of the drugs tested were 60 and 100%, resp.

Answer 18:

Bibliographic Information

Therapeutic effect of 5-aza-2'-deoxycytidine in human head and neck tumor xenografts. Braakhuis, Boudewijn J. M.; Leyva, Albert; Pinedo, Herbert M.; Snow, Gordon B. Dep. Otolaryngol., Free Univ. Hosp., Amsterdam, Neth. Editor(s): Rygaard, Joergen. Immune-Defic. Anim. Biomed. Res., Int. Workshop Immune-Defic. Anim., 5th (1987), Meeting Date 1985, 380-3. Publisher: Karger, Basel, Switz CODEN: 55YNAL Conference written in English. CAN 107:108921 AN 1987:508921 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

In nude mice bearing xenografts of human head and neck tumors, 5-aza-5'-deoxycytidine retarded tumor growth, in some cases more effectively than vincristine, methotrexate, bleomycin, or 5-fluorouracil.

Answer 19:

Bibliographic Information

The effect of continuous bleomycin infusion on the growth and cell kinetics of heterotransplanted squamous cell carcinoma of the head and neck. Wahlberg, Peter; Wennerberg, Johan; Alm, Per; Bioerklund, Anders; Trope, Claes. Dep. Oto-Rhino-Laryngol., Univ. Hosp., Lund, Swed. Anticancer Research (1987), 7(1), 55-8. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 107:401 AN 1987:400401 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The schedule-dependent effect of bleomycin (BLM) on human squamous cell carcinoma (SCC) was investigated in mice, using a xenografted SCC line originating from the head and neck region. A total dose of 200 mg BLM/kg was administered according to 1 of 3 different schedules: (a) 1 single i.p. injection; (b) i.p. injection every 4 h for 7 days; and (c) continuous s.c. administration for 7 days via osmotic mini-pump. Both the single-dose treatment and iterated injections caused significant retardations of tumor growth, and continuous infusion had a more pronounced effect, almost completely retarding the increase in tumor vol.; these differences in effect

in between the treatment schedules were not, however, statistically significant. The effect of continuous BLM infusion on the cell cycle phase distribution and histopathol. picture was also recorded. During the 1st 3 days of infusion, there was an accumulation of cells in the G0/G1-phase, paralleled by a depletion of cells in S-phase. This was followed by a normalization during the rest of the infusion period, concomitant with a transient increase of the cells in the G2-phase. Histopathol., there were no changes during the 1st 4 days. A swelling of the cytoplasm could then be seen, and after 7 days, scattered groups of necrotic cells were obsd. which later formed necrotic foci. It is noteworthy that the major perturbances in cell cycle phase distribution preceded both the retardation of tumor vol. growth and the histopathol. changes.

Answer 20:

Bibliographic Information

Xenografts in pharmacologically immunosuppressed mice as a model to test the chemotherapeutic sensitivity of human tumors. Floersheim, G. L.; Bieri, A.; Chioldetti, Nicole. Zent. Lehre Forsch., Kantonssp., Basel, Switz. International Journal of Cancer (1986), 37(1), 109-14. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 104:81665 AN 1986:81665 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A human tumor xenograft model using pharmacol. immunosuppressed mice was assessed for its suitability to test preclinically the sensitivity of colorectal carcinomas, bone sarcomas and melanomas against anticancer agents. Beside ionizing radiation, 14 cytotoxic drugs including 5-fluorouracil (5-FU) [51-21-8], dimethylmyleran (DMM) [55-93-6], cytosine arabinoside [147-94-4], cyclophosphamide [50-18-0], melphalan [148-82-3], mitomycin C [50-07-7], adriamycin [23214-92-8], bleomycin [11056-06-7], etoposide [33419-42-0], vinblastine [865-21-4], cisplatin [15663-27-1], procarbazine [671-16-9], DTIC [4342-03-4], and BCNU [154-93-8] were assayed. Ionizing radiation, 5-FU and DMM were also applied at LDs followed by bone-marrow rescue high-dose therapy. Four colon carcinomas responded poorly to most of the agents but one tumor displayed marked sensitivity to BCNU. LDs of radiation, 5-FU and DMM and cyclophosphamide and by an osteosarcoma to the latter drug. No strong effects were seen against melanomas. LDs of DMM induced the best regression of one colon carcinoma. In general, the superiority of high-dose therapy for solid human tumors compared to maximally tolerated doses was demonstrated. Individual carcinomas of the same type displayed different drug sensitivity.

Answer 21:

Bibliographic Information

Continuous infusion versus intermittent bolus injection of bleomycin in a human embryonal testicular cancer xenograft. Osieka, Rainhardt; Glatte, Peter; Schmidt, Carl Gottfried. Westdsch. Tumorzent., Universitaetsklinik. Essen, Essen, Fed. Rep. Ger. Cancer Treatment Reports (1984), 68(5), 799-801. CODEN: CTRRDO ISSN: 0361-5960. Journal written in English. CAN 100:185450 AN 1984:185450 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

In congenitally athymic mice in whom human embryonal testicular cancer xenografts were placed, there was no difference between the antitumor activity of bleomycin [11056-06-7] given by continuous i.v. infusion and that of bleomycin given by intermittent i.v. injection.

Answer 22:

Bibliographic Information

Chemotherapy of human yolk sac tumor heterotransplanted in nude mice. Sawada, Masumi; Matsui, Yoshiaki; Okudaira, Yoshio. Res. Inst. Microb. Dis., Osaka Univ., Suita, Japan. JNCI, Journal of the National Cancer Institute (1983), 71(6),

1221-5. CODEN: JJIND8 ISSN: 0198-0157. Journal written in English. CAN 100:96258 AN 1984:96258 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The chemotherapeutic effects of cis-diamminedichloroplatinum [15663-27-1] plus vinblastine [865-21-4] plus bleomycin [11056-06-7] (PVB) on 3 human yolk sac tumors (YST-1, YST-2, and YST-3) of the ovary, which were heterotransplanted into BALB/c nude mice, were compared with the effects of vincristine+actinomycin D+cyclophosphamide (VAC), the combination currently favored for treatment of yolk sac tumors. Both PVB and VAC significantly reduced the tumor vol. of all the treated tumors. The mean wts. of tumors in animals treated with PVB or VAC were, in percent of the mean tumor wt. in untreated animals: 1.3 and 1.6 for YST-1, 2.5 and 3.3 for YST-2, and 5.5 and 2.7 for YST-3, resp. A strong correlation was noted between tumor vol. and α -fetoprotein level in the sera of mice bearing YST-1 or TST-2 tumors.

Answer 23:

Bibliographic Information

Evaluation of new radiopharmaceuticals for tumor localization: the value of the human tumor xenograft. Taylor, D. M. Inst. Genet. Toxicol., Kernforschungszent. Karlsruhe, Karlsruhe, Fed. Rep. Ger. Med. Radionuclide Imaging Proc. Int. Symp. (1981), Meeting Date 1980, 1 519-26. Publisher: IAEA, Vienna, Austria CODEN: 48APAJ Conference written in English. CAN 97:51906 AN 1982:451906 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The uptake and deposition of ^{67}Ga citrate, ^{57}Co bleomycin and 3 other radiopharmaceuticals were compared in 9 human tumor lines growing as xenografts in immune-deprived CBA/LAC mice, and in 5 long-established, transplantable mouse tumor lines. There are no major differences between the xenografts and the transplanted murine tumors as far as the pattern of radionuclide uptake and deposition is concerned. Consequently, the human tumor xenograft system appears to offer no real advantages over the transplanted rodent tumor for the general screening of potential new tumor-localizing agents. However, since the xenografts retain the essential human biochem. characteristics of the original tumor, including its response to chemo- or radiotherapy, the system may be of considerable value for the more detailed investigation of new agents which show good tumor-localizing potential in rodent tumors, esp. for the evaluation of the functional information about the tumor and its response to treatment which may be obtained by scanning techniques in addn. to the static image.

Answer 24:

Bibliographic Information

Effects of bleomycin and pepleomycin on the xenografted human uterine carcinomas in nude mice. Hayakawa, Kenichi; Matsui, Yoshiaki; Sawada, Masumi; Nishiura, Haruhiko; Okudaira, Yoshio; Sugawa, Tadashi. Res. Inst. Microb. Dis., Osaka Univ., Osaka, Japan. Gan to Kagaku Ryoho (1980), 7(7), 1228-37. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 93:230958 AN 1980:630958 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Effects of bleomycin [11056-06-7] and pepleomycin [68247-85-8] on human uterine carcinomas xenographted to nude mice (BALB/cnu/nu) were examd. from the aspects of morphol., growth, and DNA synthesis of tumor tissue. Both bleomycin and pepleomycin remarkably suppressed the tumor growth and DNA synthesis in AD-5 and CC-2 tumors. Morphol. changes were obsd. by light and electron microscope. Effects on the lung were also obsd. Pepleomycin produced less lung injury than did bleomycin.

Answer 25:

Bibliographic Information

Electroporation therapy: a new approach for the treatment of head and neck cancer. Hofmann G A; Dev S B; Dimmer S; Nanda G S Genetronics, Inc., San Diego, CA 92121, USA. gah@cts.com IEEE transactions on bio-medical engineering (1999), 46(6), 752-9. Journal code: 0012737. ISSN:0018-9294. (CLINICAL TRIAL); (CLINICAL TRIAL, PHASE I); (CLINICAL TRIAL, PHASE II); Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 10356882 AN 1999285370 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Electroporation can deliver exogenous molecules like drugs and genes into cells by pulsed electric fields through a temporary increase in cell membrane permeability. This effect is being used for the treatment of cancer by intratumoral injection of low dosage of an otherwise marginally effective chemotherapeutic drug, bleomycin. Application of a pulsed electric field results in substantially higher uptake of the drug and enhanced killing of the cancer cells than is possible by conventional methods. The MedPulser, a new treatment system for local electroporation therapy (EPT) of head and neck tumors was developed and is described in this paper. EPT with bleomycin has been found to be very effective in killing cancer cells in vitro, in mouse tumor xenografts in vivo, and in tumors in humans. Ten head and neck cancer patients with recurring or unresponsive tumors were enrolled in a Phase I/II clinical trial. Treatment of the entire tumor mass in each of eight patients resulted in five complete responses confirmed by biopsy and MRI, and three partial responses (> or = 50% shrinkage). Two additional patients who received partial treatment of their tumor mass had local response where treated, but no overall lesion remission. Duration of the complete responses ranges from 2-10 months to date. All patients tolerated the treatment well with no significant local or systemic adverse effects.

Answer 26:

Bibliographic Information

Chemotherapy-radiation interactions in human cervix carcinoma xenografts. Tonkin K S; Kelland L R; Steel G G Radiotherapy Research Unit, Institute of Cancer Research, Sutton, Surrey, UK British journal of cancer (1988), 58(6), 738-41. Journal code: 0370635. ISSN:0007-0920. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 2465016 AN 89134673 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The combination of irradiation and four agents of clinical interest in the treatment of cervix carcinoma (bleomycin, etoposide, cisplatin and ifosfamide) have been investigated using two human cervix carcinoma xenografts in nude mice. As a model of clinical brachytherapy regimes, radiation was administered at a continuous low dose rate of 5 cGy min⁻¹ to a total dose of 9 or 12 Gy. No substantial enhancement in tumour growth delay over that observed for radiation alone was observed with bleomycin, etoposide or cisplatin. Ifosfamide, however, led to substantial additional growth delay, an effect which was lost when irradiation was administered at a higher dose rate of 70 cGy min⁻¹. As dose-rates of around 5 cGy min⁻¹ allow greater repair of radiation damage than at the higher dose-rate without significant cell cycling or repopulation, it is possible that ifosfamide may act as an inhibitor of repair processes in this model. It would be of interest to evaluate the role of ifosfamide and brachytherapy regimes in the clinical treatment of carcinoma of the cervix.