

Answer 1:

Bibliographic Information

Inhibition of human tumor xenograft growth in nude mice by a conjugate of monoclonal antibody LA22 to epidermal growth factor receptor with anti-tumor antibiotics mitomycin C. Shao, Wei; Zhao, Shan; Liu, Zhaofei; Zhang, Jianzhong; Ma, Shujun; Sato, J. Denry; Zhang, Peng; Tong, Mei; Han, Jiping; Wang, Yan; Bai, Dongmei; Wang, Fan; Sun, Le. Welson Pharmaceuticals, Inc., Ellicott City, MD, USA. *Biochemical and Biophysical Research Communications* (2006), 349(2), 816-824. Publisher: Elsevier, CODEN: BBRCA9 ISSN: 0006-291X. Journal written in English. CAN 145:348071 AN 2006:967353 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Anti-EGFR monoclonal antibodies LA22 and Erbitux bind to different epitopes of EGFR. The chemimmunoconjugates of MMC with LA22 or Erbitux were prepd., and in vitro cytotoxicity assays with A549 cells showed that LA22-MMC was much more potent than Erbitux or Erbitux-MMC. Viabilities of A549 cells treated with LA22-MMC, Erbitux or Erbitux-MMC were 35%, 94%, and 81%, resp. Immunoscintigraphy of xenografts of human A431 and A549 cells in nude mice both showed that 125I-labeled-LA22-MMC enriched in tumor sites prominently. Most importantly, in vivo assays showed LA22-MMC was significantly more effective than free drug MMC in the treatment of s.c. xenografts of human A431 cells in nude mice (83% inhibition for LA22-MMC and 30% for MMC). We concluded that LA22-MMC could be a very potent drug for treatment of solid tumors.

Answer 2:

Bibliographic Information

Growth inhibition of human hepatocellular carcinoma xenograft in nude mice by combined treatment with human cytokine-induced killer cells and chemotherapy. Shi, Ming; Yao, Li; Wang, Fusheng; Lei, Zhouyun; Zhang, Bing; Li, Wenliang; Liu, Jingchao; Tang, Zirong; Zhou, Guangde. Division of Biological Engineering, Beijing Institute of Infectious Disease, the 302 Hospital of PLA, Beijing, Peop. Rep. China. *Zhonghua Zhongliu Zazhi* (2004), 26(8), 465-468. Publisher: Zhongguo Yixue Kexueyuan, Zhongguo Xiehe Yike Daxue, Zhongliu Yanjiuso, Zhongliu Yiyuan, CODEN: CCLCDY ISSN: 0253-3766. Journal written in Chinese. CAN 144:466311 AN 2005:1280394 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The inhibitory effects of cytokine-induced killer (CIK) cells alone, chemotherapeutic drug alone, and CIK cells combined with chemotherapeutic drug on the growth of hepatocellular carcinoma (HCC) cells transplanted in nude mice were compared. Peripheral blood mononuclear cells (PBMC) collected from five healthy donors by blood cell separator were incubated in vitro to induce CIK cells in the presence of interferon-gamma (IFN- γ), IL-2 and anti-CD3 monoclonal antibody (mAb). The phenotype of CIK cells was characterized by flow cytometric anal. BEL-7402 HCC cells were inoculated s.c. to nude mice. On day 5, at the inoculation site were injected normal saline (group 1), CIK cells (3×10^7 and 6×10^7 , group 2 and 3), mitomycin-C (MMC 80 μ g in 0.2 mL, group 4), and CIK cells combined with MMC (group 5), resp. The percentage of CD3+, CD3+CD8+, CD3+CD56+, CD25+ cells increased from 64.0%, 28.0%, 7.8%, and 9.1% to 94.7%, 67.7%, 61.3%, and 84.0% resp. after cytokine induction. The percentage of CD3+ and CD3+CD8+ cells remained at high levels during incubation period, but that of CD25+ and CD3+CD56+ cells peaked resp. on day 7 and 13 and then declined. During the 90-day observation, the tumor formation rates were 100%, 70.0%, 80.0%, 70.0% and 66.7%; and the mouse survival rates were 10.0%, 60.0%, 40.0%, 50.0% and 75.0%, resp. from group 1 to group 5. Compared to the other groups, in the combined therapy group of mice, not only the tumor grew slowly and but also showed more marked tissue necrosis. The growth inhibitory effect on human HCC transplanted in nude mice of combined CIK cells and MMC treatment is more potent than that of CIK cells or MMC alone.

Answer 3:

Bibliographic Information

Targeted therapy against Bcl-2-related proteins in breast cancer cells. Emi, Manabu; Kim, Ryungsa; Tanabe, Kazuaki; Uchida, Yoko; Toge, Tetsuya. Department of Surgical Oncology, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima, Japan. *Breast Cancer Research* (2005), 7(6), R940-R952. Publisher: BioMed Central Ltd., CODEN: BRCRFS ISSN: 1465-542X. <http://breast-cancer-research.com/content/pdf/bcr1323.pdf> Journal; Online Computer File written in English. CAN 144:403854 AN 2005:1215059 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Introduction Bcl-2 and Bcl-xL confer resistance to apoptosis, thereby reducing the effectiveness of chemotherapy. We examd. the relationship between the expression of Bcl-2 and Bcl-xL and chemosensitivity of breast cancer cells, with the aim of developing specific targeted therapy. Methods Four human breast cancer cell lines were examd., and the effects of antisense (AS) Bcl-2 and AS Bcl-xL phosphorothioate oligodeoxynucleotides (ODNs) on chemosensitivity were tested in vitro and in vivo. Chemosensitivity was evaluated by the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide) assay, and the antitumor effect was assessed in vivo by the success of xenograft transplantation into athymic mice. Results Treatment with AS Bcl-2 and Bcl-xL ODNs resulted in a sequence-specific decrease in protein expression, compared with controls. Treatment of BT-474, ZR-75-1, and MDA-MB-231 cells with AS Bcl-2 increased chemosensitivity to doxorubicin (DOX), mitomycin C (MMC), paclitaxel (TXL), and docetaxel (TXT). Transfection of the Bcl-2 gene into MDA-MB-453 cells decreased sensitivity to DOX and MMC. Treatment of MDA-MB-231, BT-474, and ZR-75-1 cells with AS Bcl-xL increased chemosensitivity to DOX, MMC and taxanes to a smaller extent than AS Bcl-2. This occurred in the setting of increased Bax and cleaved poly(ADP-ribose) polymerase, as well as decreased Bcl-2 and pAkt. AS Bcl-2 ODNs induced splenomegaly in assocn. with increased serum IL-12, which was attenuated by methylation of the CpG motifs of AS Bcl-2; however, methylated CpG failed to negate the increased antitumor effect of AS Bcl-2. Bcl-2 and Bcl-xL, to a smaller extent, are major determinants of chemosensitivity in breast cancer cells. Conclusion Targeted therapy against Bcl-2 protein with the use of AS ODNs might enhance the effects of chemotherapy in patients with breast cancer.

Answer 4:

Bibliographic Information

Antitumor efficacy of lidamycin on hepatoma and active moiety of its molecule. Huang, Yun-Hong; Shang, Bo-Yang; Zhen, Yong-Su. Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, Peop. Rep. China. *World Journal of Gastroenterology* (2005), 11(26), 3980-3984. Publisher: World Journal of Gastroenterology, CODEN: WJGAF2 ISSN: 1007-9327. Journal written in English. CAN 144:80720 AN 2005:1035266 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Aim: To study the in vitro and in vivo antitumor effect of lidamycin (LDM) on hepatoma and the active moiety of its mol. Methods: MTT assay was used to det. the growth inhibition of human hepatoma BEL-7402 cells, SMMC-7721 cells and mouse hepatoma H22 cells. The in vivo therapeutic effects of lidamycin and mitomycin C were detd. by transplantable hepatoma 22 (H22) in mice and human hepatoma BEL-7402 xenografts in athymic mice. Results: In terms of IC50 values, the cytotoxicity of LDM was 10 000-fold more potent than that of mitomycin C (MMC) and adriamycin (ADM) in human hepatoma BEL-7402 cells and SMMC-7721 cells. LDM mol. consists of two moieties, an aproprotein (LDP) and an enediyne chromophore (LDC). In terms of IC50 values, the potency of LDC was similar to LDM. However, LDP was 105-fold less potent than LDM and LDC to hepatoma cells. For mouse hepatoma H22 cells, the IC50 value of LDM was 0.025 nmol/L. Given by single i.v. injection at doses of 0.1, 0.05 and 0.025 mg/kg, LDM markedly suppressed the growth of hepatoma 22 in mice by 84.7%, 71.6% and 61.8%, resp. The therapeutic indexes (TI) of LDM and MMC were 15 and 2.5, resp. By 2 iv. injections in two expts., the growth inhibition rates by LDM at doses of 0.1, 0.05, 0.025, 0.00625 and 0.0125 mg/kg were 88.8-89.5%, 81.1-82.5%, 71.2-74.9%, 52.3-59.575%, and 33.3-48.3%, resp. In comparison, MMC at doses of 5, 2.5, and 1.25 mg/kg inhibited tumor growth by 69.7-73.6%, 54.0-56.5%, and 31.5-52.2%, resp. Moreover, in human hepatoma BEL-7402 xenografts, the growth inhibition rates by LDM at doses of 0.05 mg/kg x2 and 0.025 mg/kg x2 were 68.7% and 27.2%, resp. However, MMC at the dose of 1.25 mg/kg x2 showed an inhibition rate of 34.5%. The inhibition rate of tumor growth by LDM was higher than that by MMC at the tolerated dose. Conclusion: Both LDM and its chromophore LDC display extremely potent cytotoxicity to hepatoma cells. LDM shows a remarkable therapeutic efficacy against murine and human hepatomas in vivo.

Answer 5:

Bibliographic Information

Effect of Mitomycin C and Vinblastine on FDG Uptake of Human Non-small-Cell Lung Cancer Xenografts in Nude Mice.

Tian, Mei; Zhang, Hong; Higuchi, Tetsuya; Oriuchi, Noboru; Inoue, Tomio; Endo, Keigo. Dep. Nucl. med. and Diagnostic Radiol., Gunma Univ. Sch. Med., Gunma, Japan. *Cancer Biotherapy & Radiopharmaceuticals* (2004), 19(5), 601-605. Publisher: Mary Ann Liebert, Inc., CODEN: CBRAFJ ISSN: 1084-9785. Journal written in English. CAN 142:273277 AN 2004:991809 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This study was designed to preliminarily evaluate the use of positron emission tomog. (PET) with [18F]-2-fluoro-2-deoxy-D-glucose (FDG) for monitoring chemotherapy effects, using a nude-mouse model of human non-small-cell lung cancer (NSCLC), the Lu-99 cell line. Tumor-FDG uptakes and vols. were measured after administrating a single dose of mitomycin (MMC) and vinblastine (VLB) and then compared these for a nontherapy group. A significant redn. in tumor vol. after either chemotherapy occurred and assocd. with significantly lower FDG uptake values than the control group ($p < 0.001$), as early as day 1. These observations suggest that FDG-PET may be useful for noninvasively monitoring the effects of cancer chemotherapy.

Answer 6:

Bibliographic Information

Fluoxetine inhibits multidrug resistance extrusion pumps and enhances responses to chemotherapy in syngeneic and in human xenograft mouse tumor models.

Peer, Dan; Dekel, Yaron; Melikhov, Dina; Margalit, Rimona. Department of Biochemistry, the George S. Wise Life Science Faculty, Tel Aviv University, Tel Aviv-Jaffa, Israel. *Cancer Research* (2004), 64(20), 7562-7569. Publisher: American Association for Cancer Research, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 141:343083 AN 2004:858494 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Multidrug resistance (MDR) operated by extrusion pumps such as P-glycoprotein and multidrug-resistance-assocd.-proteins, is a major reason for poor responses and failures in cancer chemotherapy. MDR modulators (chemosensitizers) were found among drugs approved for noncancer indications and their derivs. Yet toxicity, adverse effects, and poor soly. at doses required for MDR reversal prevent their clin. application. Among newly designed chemosensitizers, some still suffer from toxicity and adverse effects, whereas others progressed to clin. trials. Diversities among tumors and among MDR pumps indicate a need for several clin. approved MDR modulators. Here we report for the first time that fluoxetine (Prozac), the well-known antidepressant, is a highly effective chemosensitizer. In vitro, fluoxetine enhanced (10- to 100-fold) cytotoxicity of anticancer drugs (doxorubicin, mitomycin C, vinblastine, and paclitaxel) in drug-resistant but not in drug-sensitive cells (5 and 3 lines, resp.). Fluoxetine increased drug accumulation within MDR-cells and inhibited drug efflux from those cells. In vivo, fluoxetine enhanced doxorubicin accumulation within tumors (12-fold) with unaltered pharmacokinetics. In four resistant mouse tumor models of both syngeneic and human xenograft, combination treatment of fluoxetine and doxorubicin generated substantial ($P < 0.001$) improvements in tumor responses and in survivals (2- to 3-fold). Moreover, fluoxetine reversed MDR at doses that are well below its human safety limits, free of the severe dose-related toxicity, adverse effects, and poor soly. that are obstacles to other chemosensitizers. This low-dose range, together with the findings reported here, indicate that fluoxetine has a high potential to join the arsenal of MDR reversal agents that may reach the clinic.

Answer 7:

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 8:

Bibliographic Information

Genome-wide cDNA microarray screening to correlate gene expression profiles with sensitivity of 85 human cancer xenografts to anticancer drugs. Zembutsu, Hitoshi; Ohnishi, Yasuyuki; Tsunoda, Tatsuhiko; Furukawa, Yoichi; Katagiri, Toyomasa; Ueyama, Yoshito; Tamaoki, Norikazu; Nomura, Tatsuji; Kitahara, Osamu; Yanagawa, Rempei; Hirata, Koichi; Nakamura, Yusuke. Laboratory of Molecular Medicine, Human Genome Center, Institute of Medical Science, The University of Tokyo, Tokyo, Japan. *Cancer Research* (2002), 62(2), 518-527. Publisher: American Association for Cancer Research, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 136:395496 AN 2002:108259 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

One of the most crit. issues to be solved in regard to cancer chemotherapy is the need to establish a method for predicting efficacy or toxicity of anticancer drugs for individual patients. To identify genes that might be assocd. with chemosensitivity, we used a cDNA microarray representing 23,040 genes to analyze expression profiles in a panel of 85 cancer xenografts derived from nine human organs. The xenografts, implanted into nude mice, were examd. for sensitivity to nine anticancer drugs (5-fluorouracil, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-1-(2-chloroethyl)-1-nitrosourea hydrochloride, adriamycin, cyclophosphamide, cisplatin, mitomycin C, methotrexate, vincristine, and vinblastine). Comparison of the gene expression profiles of the tumors with sensitivities to each drug identified 1,578 genes whose expression levels correlated significantly with chemosensitivity; 333 of those genes showed significant correlation with two or more drugs, and 32 correlated with six or seven drugs. These data should contribute useful information for identifying predictive markers for drug sensitivity that may eventually provide "personalized chemotherapy" for individual patients, as well as for development of novel drugs to overcome acquired resistance of tumor cells to chem. agents.

Answer 9:

Bibliographic Information

Detection of mitomycin C-DNA adducts in human breast cancer cells grown in culture, as xenografted tumors in nude mice, and in biopsies of human breast cancer patient tumors as determined by ^{32}P -postlabeling. Warren, Amy J.; Mustra, David J.; Hamilton, Joshua W. Department of Pharmacology and Toxicology, Dartmouth Medical School, Hanover, NH, USA. *Clinical Cancer Research* (2001), 7(4), 1033-1042. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 136:31365 AN 2001:363657 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Mitomycin C (MMC) is a DNA crosslinking agent that has been used in cancer chemotherapy for >20 yr. However, little is known either qual. or quant. about the relationship between formation and repair of specific MMC-DNA adducts and specific biol. outcomes. The goal of this study was to examine formation and removal of specific MMC-DNA adducts in breast cancer cells using a ^{32}P -postlabeling assay in relation to cytotoxicity and other biol. end points. MMC-DNA adducts were measured in cultured human metastatic MDA-MB-435 cells, in the same cells xenografted as a mammary tumor in nude mice, and in metastatic tumor biopsies obtained from human breast cancer patients undergoing MMC-based therapy. MMC adducts corresponding to the CpG interstrand cross-link, the MMC-G bifunctional monoadduct, and two isomers of the MMC-G monofunctional monoadduct were detected in most samples. Despite similarities in the overall patterns of adduct formation, there were substantial differences between the cultured cells and the in vivo tumors in their adduct distribution profile, kinetics of adduct formation and removal, and relationship of specific adduct levels to cytotoxicity, suggesting that the in vivo microenvironment (e.g., degree of oxygenation, pH, activity of oxidoreductases, and other factors) of breast cancer cells may significantly modulate these parameters.

Answer 10:

Bibliographic Information

Activity of boanmycin against colorectal cancer. Deng, Yong Chuan; Zhen, Yong Su; Zheng, Shu; Xue, Yu Chuan. Cancer Institute, Medical School, Zhejiang University, Hangzhou, Peop. Rep. China. *World Journal of Gastroenterology* (2001), 7(1), 93-97. Publisher: World Journal of Gastroenterology, CODEN: WJGAF2 ISSN: 1007-9327. Journal written in English. CAN 135:174776 AN 2001:155070 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A study was conducted in which a human colorectal tumor xenograft model in nude mice and the orthotopic model of murine colon cancer was used to clarify the antitumor effect of boanmycin comparison with that of mitomycin C and 5-fluorouracil, drugs commonly used in clinics against colorectal cancer. The effect of BAM against colorectal cancer was detd. It was also examd. whether the organ microenvironment could influence the response of a murine colon cancer to systemic therapy with BAM. Results demonstrated that, using the orthotopic implantation technique, murine adenocarcinoma CT-26 can successfully produce an aggressive tumor which retained the morphol. biol. characteristics of the donor tumor and metastasized to the mesenteric glands. BAM inhibited tumor growth on CT-26 implanted into the cecum and s.c more than 5-fluorouracil and mitomycin C at the equitoxic dose. Moreover, the inhibitory effect BAM on the growth of CT-26 tumor was higher at the cecum than at the s.c site in mice, which implicates that BAM may have an organ-specific effect.

Answer 11:

Bibliographic Information

Effects of mitomycin C and carboplatin pretreatment on multidrug resistance-associated P-glycoprotein expression and on subsequent suppression of tumor growth by doxorubicin and paclitaxel in human metastatic breast cancer-xenografted nude mice. Ihnat, Michael A.; Nervi, Angela M.; Anthony, Stephen P.; Kaltreider, Ronald C.; Warren, Amy J.; Pesce, Carrie A.; Davis, Stacey A.; Lariviere, Jean P.; Hamilton, Joshua W. Department of Pharmacology and Toxicology, Dartmouth Medical School, Hanover, NH, USA. *Oncology Research* (1999), 11(7), 303-310. Publisher: Cognizant Communication Corp., CODEN: ONREE8 ISSN: 0965-0407. Journal written in English. CAN 133:344264 AN 2000:517393 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Mitomycin C and carboplatin each suppressed cell P-glycoprotein levels in human MDA-MB-435 cells xenografted as solid tumors into the lateral mammary fat pads of female nude mice, with a similar time course as had previously been obsd. in cell culture. Pretreatment of the mice with mitomycin C or carboplatin 48-72 h prior to receiving either doxorubicin or paclitaxel caused a greater redn. of tumor growth rate than did either of the latter agents alone or given simultaneously. These data suggest that a combination chemotherapy regimen consisting of a DNA crosslinking agent given to modulate the multidrug-resistant phenotype, followed by a 2nd cytotoxic agent, may be an effective treatment for human patients with de novo or late-stage-acquired multidrug-resistant malignancies.

Answer 12:

Bibliographic Information

Antitumor activity and novel DNA-self-strand-breaking mechanism of CNDAC (1-(2-C-cyano-2-deoxy- β -D-arabino-pentofuranosyl)cytosine) and its N4-palmitoyl derivative (CS-682). Hanaoka, Kenji; Suzuki, Masako; Kobayashi, Tomowo; Tanzawa, Fumie; Tanaka, Kazuo; Shibayama, Takahiro; Miura, Shinichi; Ikeda, Tomoko; Iwabuchi, Haruo; Nakagawa, Akihiko; Mitsuhashi, Yoshihiro; Hisaoka, Masashi; Kaneko, Masakatsu; Tomida, Akihiro; Wataya, Yusuke; Nomura, Tatsuji; Sasaki, Takuma; Matsuda, Akira; Tsuruo, Takashi; Kurakata, Shinichi. Biological Research Laboratories, Sankyo Co., Ltd., Tokyo, Japan. International Journal of Cancer (1999), 82(2), 226-236. Publisher: Wiley-Liss, Inc., CODEN: IJCNW ISSN: 0020-7136. Journal written in English. CAN 131:266648 AN 1999:438485 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

We have studied the antitumor activity and the novel DNA-self-strand-breaking mechanism of CNDAC (1-(2-C-cyano-2-deoxy- β -D-arabino-pentofuranosyl)cytosine) and its N4-palmitoyl deriv. (CS-682). In vitro, CS-682 showed strong cytotoxicity against human tumor cells comparable with that of CNDAC; both compds. displayed a similar broad spectrum. In vivo, however, orally administered CS-682 showed a more potent activity against human tumor xenografts than CNDAC, 5'-deoxy-5-fluorouridine, 5-fluorouracil and 2',2'-difluorodeoxycytidine. Moreover, CS-682 was effective against various human organ tumor xenografts at a wide dose range and with low toxicity, and was effective against P388 leukemic cells resistant to mitomycin-C, vincristine, 5-fluorouracil or cisplatin in syngeneic mice. CNDAC, an active metabolite of CS-682, had a prolonged plasma half-life after repeated oral administrations of CS-682 but not after oral administrations of CNDAC itself. This difference may partially explain the higher antitumor activity of CS-682 relative to CNDAC. In both CNDAC- and CS-682-treated carcinoma cells, CNDAC 5'-triphosphate (CNDACTP) was generated and incorporated into a DNA strand. High performance liq. chromatog. (HPLC) and mass spectrometric anal. of the nucleosides prepd. by digestion of the DNA from the CNDAC-treated cells detected ddCNC (2'-C-cyano-2',3'-didehydro-2',3'-dideoxycytidine), which was shown to be generated only when the self-strand-breakage of CNDACTP-incorporated DNA occurred. The cytotoxicity of CNDAC was completely abrogated by the addn. of 2'-deoxycytidine and was low against cells with decreased deoxycytidine kinase. Our results suggest that CNDAC is converted to CNDACMP by deoxycytidine kinase and that the resulting CNDACTP incorporated into a DNA strand as CNDACMP may induce DNA-self-strand-breakage. This novel DNA-self-strand-breaking mechanism may contribute to the potent antitumor activity of CS-682.

Answer 13:

Bibliographic Information

Interferon γ increases the antitumor activity of mitomycin C against human colon cancer cells in vitro and in vivo. Ishihara, Masami; Kubota, Tetsuro; Watanabe, Masahiko; Kawano, Yukio; Narai, Shin; Yasui, Nobutaka; Otani, Yoshihide; Teramoto, Tatsuo; Kitajima, Masaki. Department of Surgery, School of Medicine, Keio University, Tokyo, Japan. Oncology Reports (1999), 6(3), 621-625. Publisher: Oncology Reports, CODEN: OCRPEW ISSN: 1021-335X. Journal written in English. CAN 131:97102 AN 1999:285763 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A combined antitumor activity of mitomycin C (MMC) and interferon γ -1a (IFN- γ) was evaluated to be synergistic by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide assay and human tumor xenografts/severe combined immunodeficient (SCID) mouse system using colon cancer cell lines. The exptl. metastasis of WiDr cells in SCID mouse was inhibited by MMC and IFN- γ with their synergism. Intracellular uptake of MMC in WiDr cells in vitro was significantly increased by IFN- γ , suggesting the mode of synergism of these agents. This model may also partly explain the antitumor activity of combined MMC, 5-fluorouracil and interleukin-2 treatment on hepatic metastasis of colon cancer.

Answer 14:

Bibliographic Information

Cisplatin and mitomycin C combination chemotherapy against human pancreatic cancer xenografts transplanted in nude mice. Tomikawa, Moriaki. School of Medicine, Department of Surgery, Keio University, Japan. Keio Igaku (1998), 75(6), T537-T545. Publisher: Keio Igakkai, CODEN: KEIGAS ISSN: 0368-5179. Journal written in Japanese. CAN 130:246421 AN 1999:16181 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Cisplatin and mitomycin C combination chemotherapy inhibited human pancreatic cancer xenografts transplanted in nude mice. The in vitro studies also indicated that the combination chemotherapy is clin. useful for treatment of pancreatic cancer.

Answer 15:

Bibliographic Information

Efficacy of MGI 114 (6-hydroxymethylacylfulvene, HMAF) against the mdr1/gp170 metastatic MV522 lung carcinoma xenograft. Kelner, M. J.; McMorris, T. C.; Estes, L.; Samson, K. M.; Bagnell, R. D.; Taetle, R. Department of Pathology, University of California San Diego Medical Center, San Diego, CA, USA. European Journal of Cancer (1998), 34(6), 908-913. Publisher: Elsevier Science Ltd., CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 129:170166 AN 1998:400146 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Illudins are a novel class of agents with a chem. structure entirely different from current chemotherapeutic agents. A new semisynthetic deriv., HMAF, is markedly effective in a variety of lung, breast and colon carcinoma xenograft models. This analog, MGI 114, is currently in phase I human clin. trials, and is scheduled for 2 different phase II trials. To det. if MGI 114 could be effective in vivo against mdr tumor cells, we generated an mdr1/gp170-pos. clone of the metastatic MV522 human lung carcinoma line by transfecting a eukaryotic expression vector contg. the cDNA encoding for the human gp170 protein. This MV522/mdr1 daughter line retained the metastatic ability of parental cells. The parental MV522 xenograft is mildly responsive in vivo to mitomycin C and paclitaxel, as evidenced by partial tumor growth inhibition and a small increase in life span, whereas MV522/mdr1 xenografts were resistant to these agents. In contrast to mitomycin C and paclitaxel, MGI 114 produced xenograft tumor regressions in 32 of 32 animals and completely eliminated tumors in more than 30% of MV522/mdr1 tumor-bearing mice. Thus, MGI 114 should be effective in vivo against mdr1/gp170-pos. tumors.

Answer 16:

Bibliographic Information

Chemosensitivity of human pancreatic cancer cell lines serially transplanted in nude mouse. Tomikawa, Moriaki; Kubota,

Tetsuro; Takahashi, Shin; Matsuzaki, Shinjiro Wilson; Kitajima, Masaki. Department of Surgery, School of Medicine, Keio University, Tokyo, Japan. *Anticancer Research* (1998), 18(2A), 1059-1062. Publisher: Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 129:156567 AN 1998:396377 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Pancreatic cancer frequently recurs or metastasizes even after apparently curative surgical resection. Because of a low, five-year survival rate after radical surgery, multi-modal adjuvant treatment must be used to prevent recurrence of systemic spread. The effectiveness of the exptl. cancer chemotherapy of mitomycin C (MMC), cisplatin (DDP), doxorubicin (DXR) and 5-fluorouracil (5-FU) was evaluated in three human pancreatic cancer xenografts serially transplanted in nude mice. When the effects of these agents were evaluated by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H tetrazolium bromide (MTT) assay, only MMC and DDP were effective on PAN-3-JCK, a poorly differentiated adenocarcinoma. When PAN-12-JCK, a moderately differentiated adenocarcinoma, was used an in vitro assessment of combined chemotherapy of MMC and DDP, a synergistic combination effect was obsd. Three xenografts were transplanted s.c. into nude mice and the max. tolerated doses of these agents were administered i.p. or i.v. (DXR). MMC showed pos. antitumor activity on PAN-3-JCK and PAN-12-JCK, and 5-FU was effective on PAN-12-JCK. These results reflect the low sensitivity of clin. pancreatic cancer to conventionally available antitumor agents, and suggest the possible synergistic combination antitumor activity of MMC and DDP.

Answer 17:

Bibliographic Information

Mitomycin C and cisplatin increase survival in a human pancreatic cancer metastatic model. Tomikawa, Moriaki; Kubota, Tetsuro; Matsuzaki, Shinjiro Wilson; Takahasi, Shin; Kitajima, Masaki; Moosa, A. R.; Hoffman, Robert M. Department of Surgery, School of Medicine, Keio University, Tokyo, Japan. *Anticancer Research* (1997), 17(5A), 3623-3625. Publisher: Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 128:162635 AN 1998:49732 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Pancreatic cancer is one of the most intractable of all human cancers. We have previously developed a patient-like model of human pancreatic cancer by surgical orthotopic implantation (SOI). After SOI of the human tumor xenograft PAN-12-JCK into the tail of the nude mouse pancreas, mitomycin C (MMC) and cisplatin (DDP) were administered i.p. at a dose of 4 and 6 mg/kg, resp., on day-7. The mice were obsd. for 95 days. There was a statistically significant increase in disease-free and overall survival rates in the MMC - and MMC + DDP-treated groups. Local tumor growth was eliminated only in the group treated with MMC + DDP. Hepatic metastasis and peritoneal disseminations were completely inhibited by MMC but not DDP. This study demonstrates the usefulness of the SOI model of pancreatic cancer to study the differential efficacy of agents affecting primary tumor growth metastasis and survival, thus presenting an opportunity for the discovery of new agents for this highly resistant cancer.

Answer 18:

Bibliographic Information

Potentiation of antitumor activity of mitomycin C by estradiol: Studies of human breast carcinoma xenografts serially transplanted into nude mice. Oka, Shoichi; Kubota, Tetsuro; Takeuchi, Tooru; Kitajima, Masaki. School Medicine, Keio University, Tokyo, Japan. *Journal of Surgical Oncology* (1996), 61(4), 256-261. Publisher: Wiley-Liss, CODEN: JSONAU ISSN: 0022-4790. Journal written in English. CAN 125:1678 AN 1996:308211 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effect of exptl. cancer chemotherapy with mitomycin C (MMC) was studied using three estrogen-receptor (ER)-pos. (MCF-7, R-27, and Br-10) and one ER-neg. (MX-1) human breast carcinoma xenograft serially transplanted into nude mice, and the effect of estradiol (E2) priming on the antitumor activity of MMC was investigated. I.m. injection of E2 at 1 mg/kg changed the ER state and increased the growth fraction detected by flow cytometry, although the growth rate of ER-pos. tumors was not effective by E2 priming. MMC suppressed the growth of the four xenografts in a dose-dependent manner. When 1 mg/kg E2 was administered 1 h before MMC treatment, which was given i.p. at a dose of 3 mg/kg, the antitumor activity of MMC was increased in comparison with MMC alone in ER-pos. strains, although the effect of MMC on MX-1 was not changed by E2-priming. Priming with E2 at this dose increases the growth fractions of ER-pos. breast carcinoma cells, which are sensitive to MMC, resulting in increased antitumor activity of MMC. This E2-primed MMC chemotherapy may be of value in the treatment of ER-pos. human breast cancer.

Answer 19:

Bibliographic Information

Targeting treatment of human HCC xenografts implanted in nude mice using bifunctional antibody HC-1 combined with mitomycin C. Wei, Chao; Tang, Zhaoyou; Liu, Kangda. Liver Cancer Inst., Shanghai Med. Univ., Shanghai, Peop. Rep. China. *Zhonghua Yixue Zazhi* (1994), 74(11), 676-9. Publisher: Zhonghua Yixue Zazhi, CODEN: CHHTAT ISSN: 0376-2491. Journal written in Chinese. CAN 122:255728 AN 1995:497624 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Bifunctional antibody (BFA) HC-1 possessing one binding site for mitomycin C (MMC) and a companion site directed against human hepatocellular carcinoma (HCC) cell membrane was constructed by chem. conjugation of two Fab' fragments of McAb MMC-1 and McAb HCMP-1. BFA could be specifically attached to tumor xenograft of nude mice bearing human HCC and thus simultaneously capture mitomycin C. The attachment of these complexes was detected by radioimmunoimaging in nude mice bearing human HCC using ¹³¹I labeled BFA HC-1. Clear imaging of the tumor was obtained in 6 days after i.p. injection. On the 8th day after the injection, tumor/liver (T/L) ratio was 8.04. When the BFA HC-1 was used to be combined with MMC for the targeting treatment of human HCC implanted in nude mice, the highly significant suppression of tumor growth and achieved. After two months of treatment, xenografts of 40% (4/10) mice disappeared and 60% (6/10) of the mice survived. Those mice treated only with MMC became more and more sick even if the grafted tumors shrank, and all of them died with 2 mo after therapy. The controls were treated with nonspecific IgG. Tumors grew very fast, and most of the controls died in 1 mo after the first injection. The results suggest that BFA HC-1 could conc. MMC on the human HCC cells, and it is a kind of suitable carrier for the targeting treatment of human HCC.

Answer 20:

Bibliographic Information

Enhancement of the antineoplastic effect of mitomycin C by dietary fat. Shao, Yu.; Pardini, Lani; Pardini, Ronald S. Department of Biochemistry, Univ. of Nevada, Reno, NV, USA. *Cancer Research* (1994), 54(24), 6452-7. Publisher: American Association for Cancer Research, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 122:45912 AN 1995:272615 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

In the present study, the authors investigated the effects of high dietary fat on the growth of MX-1 heterotransplanted in athymic mice and its response to mitomycin C (MC) treatment. The authors found that high fat intake (25% corn oil, wt./wt.) significantly increased tumor growth, but at the same time it also increased the tumor response to MC treatment compared to the control low fat diet (5% corn oil, wt./wt.). In the tumors from mice fed either low (5% wt./wt.) or high (25% wt./wt.) fat, MC treatment induced oxidative challenge, indicated by significantly increased tumor total superoxide dismutase, catalase, glutathione peroxidase, and glutathione S-transferase peroxidase activities, as well as increased tumor lipid peroxidn. Glutathione reductase activity was inhibited by MC treatment. Some of the enzymes which are known to activate MC, such as cytochrome b5 reductase and DT-diaphorase, were also induced in the tumor by high dietary fat intake. The enzyme activities in hepatic tissues were also altered by dietary fat and MC treatment but to a lesser

extent. The authors conclude that high dietary fat intake could enhance the chemotherapeutic effect of MC by increasing MC-activating enzyme activities. The obsd. increase in lipid peroxidn. after MC treatment in MX-1 human mammary carcinoma implanted in the nude mice could result from the obsd. inhibited glutathione reductase activity. It is tempting to speculate that this might be another antineoplastic mechanism for MC in addn. to its known role as a bioreductive alkylating agent. Alternatively, glutathione reductase may be a target for bioreductive alkylation.

Answer 21:

Bibliographic Information

Antitumor activity of SPM VIII, a derivative of the nucleoside antibiotic spicamycin, against human tumor xenografts.

Kamishohara, Masaru; Kawai, Hiroyuki; Odagawa, Atsuo; Isoe, Toshiyuki; Mochizuki, Junichiro; Uchida, Takeshi; Hayakawa, Yoichi; Seto, Haruo; Tsuruo, Takashi; Otake, Noboru. Pharmaceut. Res. Lab., Kirin Brewery Co., Ltd., Gunma, Japan. Journal of Antibiotics (1994), 47(11), 1305-11. Publisher: Japan Antibiotics Research Association, CODEN: JANTAJ ISSN: 0021-8820. Journal written in English. CAN 122:45884 AN 1995:228853 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of spicamycin analog SPM VIII against human stomach, breast, lung, colon and esophageal cancers was compared to that of mitomycin C (MMC) in the human tumor-nude mice xenograft model. Comparative studies of SPM VIII given i.v. at 6 mg/kg/day daily for 5 days and MMC given i.v. at 6.7 mg/kg on day 1 revealed that the antitumor spectrum of SPM VIII showed a different pattern from that of MMC and that SPM VIII caused tumor mass redns. in more tumors than did MMC in colon cancers (4/12 vs. 1/11). In addn. to this study, a comparative study of SPM VIII given i.v. at 12 mg/kg/day 8 times at 3- or 4-day intervals and 5'-deoxy-5-fluorouridine (5'-DFUR) given po at 185 mg/kg/day 5 days per wk for 4 wk showed that SPM VIII had the highest effect on SC-9 human stomach cancer and COL-1 human colon cancer among the 3 compds., resulting in a significant redn. of tumor mass. Although other pharmacol. studies are in progress, these results suggest that SPM VIII might be a novel antitumor compd. effective for human cancers including cancer of the digestive organs.

Answer 22:

Bibliographic Information

Combination chemotherapy of BOF-A2, a new 5-FU derivative, with various anticancer agents against human cancer xenografts in nude mice.

Fujita, Fumiko; Fujita, Masako; Fujita, Masahide; Sakamoto, Yasuo. Experimental Cancer Chemotherapy Research Laboratory Co., Ltd., Inoue Hospital, Japan. Gan to Kagaku Ryoho (1994), 21(10), 1619-25. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 121:271509 AN 1994:671509 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

To select a suitable combination chemotherapy with BOF-A2 from the view of both antitumor effect and decrease of side effect, the authors studied a combination of BOF-A2 with CPT-11, CDDP, mitomycin C (MMC) or interferon- α (IFN- α) against colon, stomach and renal cancer, resp., by using xenografted nude mice. The combination therapy of BOF-A2 with CDDP was effective against stomach cancer (H-111) from the cellular change and decreased side effect. The combination therapy of BOF-A2 with MMC showed additive effect against stomach cancer (H-111) from IR and cellular changes. The combination effect of BOF-A2 with IFN- α was additive and synergistic against renal cancer (H-12). The combination therapy with CPT-11 was effective e (IR \geq 58%) from antitumor effect, additive from IR and synergistic from cellular change against lung cancer (H-74) and colon cancer (H-110), to which conventional drugs were generally insensitive and spontaneously tolerant. BOF-A2 was expected to be a promising new anticancer agent in the future clin. trial.

Answer 23:

Bibliographic Information

Synergistic antitumor activity of combination chemotherapy with mitomycin C and cisplatin against human gastric cancer xenografts in nude mice. Saikawa, Yoshiro; Kubota, Tetsuro; Kuo, Tsong-Hong; Furukawa, Toshiharu; Kase, Suguru; Tanino, Hirokazu; Isobe, Yo; Watanabe, Masahiko; Ishibiki, Kyuya; et al. School of Medicine, Keio University, Japan. *Journal of Surgical Oncology* (1994), 56(4), 242-5. CODEN: JSONAU ISSN: 0022-4790. Journal written in English. CAN 121:245426 AN 1994:645426 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A new combined cancer chemotherapy regimen of mitomycin C (MMC) and cisplatin (DDP) showed synergistic antitumor activity against human gastric cancer xenografts St-40 and SC-1-NU in BALB/c nu/nu mice. The drugs were administered i.p. at doses of 2 or 4 mg/kg for MMC and 3 or 6 mg/kg for DDP, resp. To clarify the schedule-dependent antitumor activity of MMC and DDP against St-40 and SC-1-NU, different sequential therapies were conducted. Simultaneous administration of these agents showed the highest antitumor activity against SC1-NU among the three regimens used, whereas the sequence of MMC followed by DDP showed higher antitumor activity than the reverse sequence against St-40. The intratumoral concn. of platinum was significantly increased in St-40 treated with the sequence MMC to DDP, in comparison with the sequence DDP to MMC. The max. tolerated dose (MTD) of this combination was 4 mg MMC plus 6 mg DDP per kg in all the combinations, and these MTDs were 2/3 of the corresponding values for their single use. Since this combination increased the antitumor activity of each single agent without any increase in their toxicity, it would appear to be useful clin.

Answer 24:

Bibliographic Information

Antitumor activity of LY 188011, a new deoxycytidine analog, against human cancers xenografted into nude mice. Fujita, Masahide; Fujita, Fumiko; Inaba, Hiizu; Taguchi, Tetsuo. Research Institute Microbial Diseases, Osaka University, Japan. *Gan to Kagaku Ryoho* (1994), 21(4), 517-23. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 121:221179 AN 1994:621179 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

LY 188011 (gemcitabine) was evaluated for its antitumor effect in 15 human tumors xenografted in nude mice (7 gastric, 2 colorectal, 2 breast, 2 lung and 2 liver cancer lines); in the latter 4 cases, the results were compared with those obtained with mitomycin C. LY 188011 reduced the vol. of tumor xenografts in 7 lines, including drug-resistant colorectal and lung cancer lines. The antitumor effect of LY 188011 was further confirmed by pathol. observation. Moreover, LY 188011 was more potent in 2 lung cancer models than mitomycin C, and it induced fewer side effects. LY 188011 seemed to be an excellent candidate for clin. trials for the treatment of cancer.

Answer 25:

Bibliographic Information

Modulation of tumor hypoxia by conventional chemotherapeutic agents. Durand, Ralph E.; LePard, Nancy E. Medical Biophysics Dept., B.C. Cancer Research Centre, Vancouver, BC, Can. *International Journal of Radiation Oncology, Biology, Physics* (1994), 29(3), 481-6. CODEN: IOBPD3 ISSN: 0360-3016. Journal written in English. CAN 121:195401 AN 1994:595401 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

We have evaluated the capacity of a no. of common cancer chemotherapeutic drugs to modulate the oxygenation of human tumor

xenografts growing in murine hosts. Considerable effort has been expended on developing methods to radiosensitize hypoxic cells, or to selectively kill them with appropriate chems. Another approach, suggested by our ongoing studies with spheroids in vitro, is to modify tumor oxygenation by physiol. means. The feasibility of this approach is illustrated in this article using human tumor xenografts in mice treated with doxorubicin or mitomycin C plus radiation. The therapeutic potential of the combination treatments has been assessed using fluorescence-activated cell sorting techniques to isolate and differentially study hypoxic vs. aerobic cell subpopulations from the xenografts. Addnl., drug-induced changes in blood flow have been quantified at the macroscopic level with laser Doppler flowmetry, and at the microregional level with image anal. techniques. At doses which produced only modest amts. of tumor cell killing, doxorubicin and mitomycin C markedly altered tumor blood flow in all tumor types examd., and with all assays used. Common anti-cancer agents may find new use as blood flow modifiers for combined modality treatments, in addn. to their conventional use as "pure" cytotoxins.

Answer 26:

Bibliographic Information

Predictability of clinical response to anticancer agents in human cancer xenografts. Tsukamoto, Fumine. Med. Sch., Osaka Univ., Suita, Japan. Osaka Daigaku Igaku Zasshi (1994), 46(4), 251-61. CODEN: ODIZAK ISSN: 0369-710X. Journal written in Japanese. CAN 121:124753 AN 1994:524753 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Nude mouse transplanted human tumors retained original sensitivity to antitumor drugs, and was useful in secondary screening for the sensitivity to tumor chemotherapy. Fresh tumor tissues were transplanted and maintained in nude mice in 77 cases (tried: 247 cases), and sensitivity of the transplanted tumors to chemotherapy was compared between human therapy and in nude mice using regimen used clin. in 17 cases with 21 expts. (stomach, breast, colon, pancreas, esophagus, melanoma). Tested drugs were adriamycin, cisplatin, cyclophosphamide, cytarabine, dacarbazine, doxifluoridine, epirubicin, 5-fluorouracil, M-83 (a mitomycin C deriv.), mitomycin C, tegafur, and UFT. Chemotherapy in nude mice was effective in 6 expts., which coincided with clin. results in 5 cases. The ineffective 15 cases in nude mice coincided with the clin. results in all cases.

Answer 27:

Bibliographic Information

Similarity of serum - tumor pharmacokinetics of antitumor agents in man and nude mice. Kubota, Tetsuro; Inoue, So; Furukawa, Toshihuru; Ishibiki, Kyuya; Kitajima, Masaki; Kawamura, Eiji; Hoffman, Robert M. Sch. Med., Keio Univ., Tokyo, Japan. Anticancer Research (1993), 13(5A), 1481-4. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 120:315103 AN 1994:315103 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A pharmacokinetic comparison was made between nude mice and human gastric cancer patients. This comparison is important in order to optimize the human tumor xenograft - nude mouse system as a screening panel for potential antitumor agents. In this report, mitomycin C (MMC), doxorubicin (DXR), 5-fluorouracil (5-FU) and cisplatin (DDP) were administered to nude mice bearing human tumor s.c. xenografts in max. tolerated doses and to patients with gastric cancer at conventional doses. The concns. of antitumor agents in serum and tumor were detected by bioassay for MMC and 5-FU, by high performance liq. chromatog. for DXR, and by at. absorption method for DDP. Peak drug concns. in the serum (C_{max}) of mice and humans correlated well with statistical significance ($R = 0.999$, $P < 0.0001$). When C_{max} and drug concns. in the tumor (T) of mice and human were compared with each other to evaluate the uptake of drugs into the tumor from the serum and calcd. as T/C_{max} , similar results were obsd. for the same agent with statistical significance ($r = 0.990$, $p < 0.02$). These results indicate that the human tumor xenograft - nude mouse system and humans are essentially similar pharmacodynamically, which further validates the use of this system to evaluate potential antitumor agents.

Answer 28:

Bibliographic Information

Relevance of DT-diaphorase activity to mitomycin C (MMC) efficacy on human cancer cells: differences in in vitro and in vivo systems. Nishiyama, Masahiko; Saeki, Shuji; Aogi, Kenjiro; Hirabayashi, Naoki; Toge, Tetsuya. Res. Inst. Nucl. Med. Biol., Hiroshima Univ., Hiroshima, Japan. International Journal of Cancer (1993), 53(6), 1013-16. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 119:40426 AN 1993:440426 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Using 4 human cancer cell lines, 4 tumors xenografted into nude mice, and 11 fresh tumor specimens removed at surgery, the authors investigated the relevance of NAD(P)H:quinone oxidoreductase (DT-diaphorase, DTD) activity (nmoles/min-mg protein) to mitomycin C (MMC)-induced cytotoxicity. In culture cell lines, KB cells had significantly higher levels of DTD activity (8260) than PH101 (1934), SH101 (1805) or K562 (1796), and the highest sensitivity to MMC. In contrast, the higher the DTD activity of xenografts, the greater their resistance to MMC, while the inhibition rate of relative tumor growth for MMC, as evaluated by the NCI protocol, was highest in SH-6, high in CH-5, lower in CH-4 and lowest in EH-6. The investigation using 11 fresh tumor specimens also showed an inverse relationship between IC50 values after a 30-min MMC treatment, as evaluated by ATP assay and DTD activities. Moreover, a non-toxic DTD inhibitor, dicoumarol (DIC), or FAD, suppressed the efficacy of MMC in culture cells, but enhanced it in xenografts. Thus, the authors suggest that DTD may play an important role in MMC-induced cytotoxicity but MMC metab. by DTD in solid tumors may differ from that in culture cells.

Answer 29:

Bibliographic Information

Elevated DT-diaphorase activity and messenger RNA content in human non-small cell lung carcinoma: relationship to the response of lung tumor xenografts to mitomycin C. Malkinson, Alvin M.; Siegel, David; Forrest, Gerald L.; Gazdar, Adi F.; Oie, Herbert K.; Chan, Daniel C.; Bunn, Paul A.; Mabry, Mack; Dykes, Donald J.; et al. Mol. Toxicol. Environ. Health Sci. Program, Univ. Colorado, Boulder, CO, USA. Cancer Research (1992), 52(17), 4752-7. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 117:163489 AN 1992:563489 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The enzyme DT-diaphorase [DTD; NAD(P)H:quinone oxidoreductase, EC 1.6.99.2], is an obligate two electron reductase which catalyzes redn. of a broad range of substrates, including quinones. We report here variations in DTD concns. among different classes of lung tumors known also to vary in their responsiveness to cytotoxic agents. Small cell lung carcinomas (SCLCs) and cell lines derived from them have the low DTD activities and mRNA content characteristic of formal human lung, whereas nonsmall cell lung carcinomas (NSCLCs) have greatly elevated levels. DTD activity was increased up to 80-fold in NSCLC tumors relative to normal lung and 20-35-fold in NSCLC relative to SCLC cell lines. Increased DTD activity appeared to be a function of the NSCLC phenotype rather than a result of derivation from a cell type rich in DTD, since all histol. classes of NSCLC showed this phenotype. In addn., where transfection of SCLC cell lines with the v-Ha-ras protooncogene caused a transition to a NSCLC phenotype, DTD activity was also elevated. Neuroendocrine-pos. cells (SCLC, carcinoids, and a few NSCLC lines) typically had far lower DTD activities than did cell lines which lacked neuroendocrine markers (most NSCLC cells and mesotheliomas). High DTD activity may be exploited in the design of drugs which undergo bioreductive activation by this enzyme. Consistent with this, xenografts derived from NSCLC cell lines with high DTD that were grown in athymic nude mice were more susceptible to the antitumor quinone, mitomycin C, than were xenografts derived from SCLC cells contg. low DTD. These data provide a mechanistic basis for the rational design of more effective bioreductive antitumor agents for use against NSCLC.

Answer 30:

Bibliographic Information

A new type of antitumor substances, polyoxomolybdates. Fujita, Haruhisa; Fujita, Tomonobu; Sakurai, Toshiharu; Seto, Yoshiko. Sch. Med., Keio Univ., Tokyo, Japan. *Chemotherapy (Tokyo)* (1992), 40(2), 173-8. CODEN: NKRZAZ ISSN: 0009-3165. Journal written in English. CAN 117:375 AN 1992:400375 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The growth suppressions of [NH₃CHMe₂]₆[Mo₇O₂₄].3H₂O (PM-8) against Co-4, human colon cancer, xenografted under the renal capsule in cd-1 mice were equal or superior to that of 5-fluorouracil, mitomycin C, 1-(4-amino-2-methylpyrimidine-5-yl)methyl-3-(2-chloroethyl)-3-nitrosourea HCl, adriamycin, and cis-Pt diammine dichloride. Potent antitumor activity of PM-8 was also established against MX-1, human breast cancer, and OAT, human lung cancer, xenografted in athymic nude mice. Antitumor activities of other polyoxomolybdates are also described.

Answer 31:

Bibliographic Information

The influence of stromal cells on the MTT assay. (II). Study on the nude mouse system. Suto, Akihiko. Sch. Med., Keio Univ., Tokyo, Japan. *Japanese Journal of Surgery* (1991), 21(3), 308-11. CODEN: JJSGAY ISSN: 0047-1909. Journal written in English. CAN 115:197590 AN 1991:597590 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A fresh surgical specimen from colon carcinoma was tested by the 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide assay (MTT assay) and transplanted into nude mice. After 5 transfers in male BALB/c nude mice, the xenograft was then tested again by the MTT assay. The in vivo chemosensitivity pattern of the xenograft was essentially identical to that of the in vitro fresh surgical specimen, whereas the sensitivity of the xenograft was increased. To exclude the stromal cells from the nude mouse, anti-BALB/c serum was added to the primarily cultured colon carcinoma xenograft, and its chemosensitivity to mitomycin C (MMC) assessed. Although the sensitivity of the serum-treated group to MMC was slightly higher than that of the untreated group, the dose-response curves of the tumor cells of MMC were similar to each other. Thus, the chemosensitivity pattern of tumor cells seemed to be stable with or without normal cells, although the sensitivity itself was reduced by the presence of normal cells.

Answer 32:

Bibliographic Information

In vivo inhibitory effect of anticancer agents on human pancreatic cancer xenografts transplanted in nude mice. Imai, Shiro; Nio, Yoshinori; Shiraishi, Takahiro; Manabe, Tadao; Tobe, Takayoshi. Fac. Med., Kyoto Univ., Kyoto, Japan. *Anticancer Research* (1991), 11(2), 657-64. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 115:174179 AN 1991:574179 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Pancreatic cancer is one of the neoplasms resistant to chemotherapy. In the present study human pancreatic cancer xenografts (3 adenocarcinomas and 1 cystadenocarcinoma) were s.c. transplanted in nude mice and after the tumors grew to 100-300 mm³, the mice were i.p. administered with mitomycin C (MMC), adriamycin (ADR), 5-fluorouracil (5-FU), carboquone (CQ), cisplatin (CDDP), nimustine chloride (ACNU) or DWA2114R at 1/3 LD₅₀ on days 0, 4, and 8. The tumor sizes on day 12 were compared with those on day 0. MMC and CQ significantly inhibited the tumor growth of 3 lines, and ACNU, CDDP and ADR inhibited the growth of 1 line. Further, 5-FU, futrafur, carmofur, UFT, and L-phenylalanine mustard (L-PAM) were orally administered to mice into which 1 adenocarcinoma line had been transplanted. While none of fluoropyrimidines inhibited tumor growth, L-PAM at 4 mg/kg significantly inhibited growth, although it was accompanied by severe body wt. loss. In the present study several agents significantly inhibited tumor growth, but none of them could induce the regression of the tumor when used singly. These results suggest that CQ, ACNU,

CDDP and L-PAM may be applied to the chemotherapy of pancreatic cancer. However, the effect of a single agent is restricted and the development of new combination treatments is urgently required.

Answer 33:

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 34:

Bibliographic Information

Studies on chemotherapy for adenocarcinoma of the uterine cervix using xenografts transplanted in nude mice. Yamagishi, Masaji. Fac. Med., Toyama Med. Pharm. Univ., Toyama, Japan. Nippon Sanka Fujinka Gakkai Zasshi (1991), 43(2), 165-72. CODEN: NISFAY ISSN: 0300-9165. Journal written in Japanese. CAN 115:341 AN 1991:400341 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Adenocarcinoma of the human uterine cervix was successively transplanted into nude mice and the effects of chemotherapy on adenocarcinoma of uterine cervix were investigated in this transplanted tumor. First, it was confirmed that both the original tumor and the transplanted tumor were apparently histol. the same as adenocarcinoma of the uterine cervix (endocervical type). And the transplanted tumor was shown to have the features of adenocarcinoma by an electron microscope. The doubling time of the transplanted tumor was 9.2 days. For the chemotherapy study, first the therapeutic effects of 11 kinds of agents were screened by single-agent chemotherapy applied to the transplanted tumor. From the results of this series, 6 regimens for multi-agent chemotherapy were tried on the transplanted tumor. The effects of the chemotherapy were evaluated following Battelle Columbus Labs. Protocol and histopathol. The relative regression rates for the tumors treated with mitomycin C (MMC) + cyclophosphamide (CPM) and MMC + CPM + methotrexate (MTX) were 72.99 and 80.9% ($T_n/T_o = 0.84$), resp. The results suggest that the combinations of MMC + CPM or MMC + CPM + MTX are regimens that are possibly effective on the adenocarcinoma of human uterine cervix and are worth be trying clin.

Answer 35:

Bibliographic Information

Comparative study of antitumor agents in serum and tumor between nude mouse and human. Inoue, So. Sch. Med., Keio Univ., Tokyo, Japan. Keio Igaku (1991), 68(1), 57-65. CODEN: KEIGAS ISSN: 0368-5179. Journal written in Japanese. CAN 115:188 AN 1991:400188 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The pharmacokinetic comparison between nude mouse and human beings is important to using the human tumor xenograft-nude mouse system as a screening panel for newly developed antitumor agents. Mitomycin C, adriamycin, 5-fluorouracil, cisplatin, and the platinum-related compds. (carboplatin and DWA2114R) were administered to nude mice bearing human tumor xenografts in max. tolerated doses and to patients with cancer in conventionally available doses in clinics. The concns. of antitumor agents in serum and tumor were detected by bioassay, HPLC, and the at. absorption method. The max. serum concn. (Cmax) in $\mu\text{g}/\text{mL}$ and concn. in tumor (T) in $\mu\text{g}/\text{g}$ in nude mouse and human were compared to each other and the shift of drugs from serum to tumor was calcd. as T/Cmax. Although the different doses of the agents were administered in nude mice and humans, the T/Cmax ratios were similar to each other.

Answer 36:

Bibliographic Information

Response of A431 experimental human solid xenograft to mitomycin C in combination with human epidermal growth factor in mice. Amagase, Harunobu; Tamura, Koichi; Hashimoto, Ken; Fuwa, Tohru; Murakami, Teruo; Yata, Noboru. Inst. Med. Res., Wakunaga Pharm. Co., Ltd., Hiroshima, Japan. Journal of Pharmacobio-Dynamics (1990), 13(4), 263-8. CODEN: JOPHDQ ISSN: 0386-846X. Journal written in English. CAN 113:34444 AN 1990:434444 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The authors previously demonstrated that the antitumor efficacy of various antitumor agents such as 5-fluorouracil and cisplatin against exptl. solid tumors was enhanced by pre- or simultaneous administration of human epidermal growth factor (hEGF). In the present study, the combined therapy by hEGF and mitomycin C (MMC) as an antitumor agent was studied in A431 solid tumor-bearing mice to det. the dosage schedule of hEGF. When MMC alone was injected i.p. (2 mg/kg) every 7th day to the tumor-bearing mice, tumor wts. increased to 2138 mg from 282 mg during 22 d. Tumor wt. in every day treatment of hEGF alone for 21 d increased to the same extent in the treatment by MMC alone. On the other hand, the increase of the solid tumor wt. in the every day treatment and in the every 7th day treatment of hEGF, in combination with the every 7th day administration of MMC, were as follows: from 282 mg to 1522 mg (71.2% of MMC alone) and from 280 mg to 1245 mg (58.2% of MMC alone), resp., demonstrating a greater antitumor potency of MMC in combination with the every 7th day treatment with hEGF. Both combined therapies did not affect the toxicity of MMC as evaluated by the decrease in nontumorous body wt. Single s.c. administration of hEGF to A431 tumor-bearing mice caused the decrease of the binding capacity of hEGF to A431 tumor cells by 80% 24 h after the administration. However, the decreased binding capacity recovered to the untreated control level 4 d after the administration of hEGF. In conclusion, the every 7th day treatment with hEGF was superior to the every day treatment in its ability to increase the susceptibility of A431 solid tumor to MMC.

Answer 37:

Bibliographic Information

Enhancement of antitumor activity of mitomycin C against human breast carcinoma xenografts by the pretreatment of KM2210. Yamamoto, Takaaki; Kubota, Tetsuro; Oka, Shoichi; Josui, Kazuya; Fujita, Shin; Arisawa, Yoshito; Suto, Akihiko; Inoue, So; Kuzuoka, Masahiko; et al. Sch. Med., Keio Univ., Japan. Gan to Kagaku Ryoho (1990), 17(1), 109-14. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 112:229381 AN 1990:229381 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Three human breast carcinoma xenografts, MCF-7, R-27 and T-61 serially transplanted into nude mice were treated with mitomycin C (MMC) alone, KM2210 alone and KM2210 followed by MMC. One hundred or 300 mg of KM2210 per kg were administered orally daily from Day 1 to 4 and MMC at the dose of 3 mg/kg was given i.p. on Day 5. The antitumor activity of MMC on these xenografts was enhanced by the pretreatment of KM2210, suggesting the new combination chemo- and endocrine therapy on hormone dependent human breast carcinomas.

Answer 38:

Bibliographic Information

Evaluation of predictability of in vitro SDI assay in comparison with in vivo nude mouse assay. Fujita, Masahide; Tanigawa, Keiko; Fujita, Fumiko; Sakamoto, Yasuo; Shimozuma, Kojiro; Kusuyama, Takatsugu; Inaba, Hiizu; Taguchi, Tetsuo. Res. Inst. Microb. Dis., Osaka Univ., Osaka, Japan. Gan to Kagaku Ryoho (1989), 16(10), 3435-41. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 112:69560 AN 1990:69560 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Twenty lines of human gastro-intestinal and breast cancer xenografts, in which chemosensitivity spectra by the in vivo nude mouse assay had been clarified, were subjected to the in vitro SDI (succinate dehydrogenase inhibition) assay using MTT dye to assess the accuracy of this drug sensitivity test against 4 drugs, i.e., mitomycin C (MMC), adriamycin (ADM), 5-fluorouracil (5-FU), and cisplatin (CDDP). After 3 days incubation, the suspension of tumor cells showed a marked decrease of SD activity even when no anticancer drug was added to the assay medium. Among these 4 drugs evaluated, MMC exhibited a statistically significant correlation between chemosensitivity values of the in vitro SDI assay and those of the nude mouse assay. However, the other 3 drugs demonstrated no correlation between the values of these two methods. Since the primary cultured fibroblasts revealed, in general, lower sensitivity to these drugs, contamination of fibroblast may decrease the SDI values when materials from solid tumors with rich stroma such as a type of stomach cancer were subjected. It is considered that the prediction of chemosensitivity to every drugs will be impossible by an in vitro SDI assay.

Answer 39:

Bibliographic Information

Comparative study on the anticancer activities of KW2149 and mitomycin C against human tumor xenografts using subrenal capsule assay. Takagami, Shinichi; Nishiyama, Masahiko; Kim, Ryungsa; Kirihara, Yoshimasa; Jinushi, Kazuto; Saeki, Kazuotshi; Saeki, Toshiaki; Nosoh, Yoshihiro; Niimoto, Minoru; Hattori, Takao. Res. Inst. Nucl. Med. Biol., Hiroshima Univ., Hiroshima, Japan. Gan to Kagaku Ryoho (1989), 16(6), 2189-93. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 111:146378 AN 1989:546378 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The anticancer activity of KW2149 (I), a new deriv. of mitomycin C (MMC), against 5 human tumor xenografts derived from digestive organs was compared in a 4-day subrenal capsule assay (SRCA) in normal immunocompetent mice. KW 2149 and MMC were administered i.p. for 3 days after implantation, and the anticancer activity and the wt. loss of mice were evaluated. The total doses were 1/2, 1/3, and 1/4 of the LD50 value of each agent. The anticancer activities of the 2 drugs were almost the same with no difference in 3 xenografts. The anticancer activity of KW 2149 correlated more with the administered doses than did that of MMC. The toxicity of KW 2149 and MMC were similar as detd. by wt. loss.

Answer 40:

Bibliographic Information

The drug sensitivity of human gastric cancer implanted into the subcutis and stomach wall of nude mice. Yamashita, Takumi. Pathol. Sect. Res. Lab., Nippon Kayaku Co., Ltd., Japan. Nippon Gan Chiryō Gakkaishi (1989), 24(3), 611-16. CODEN: NGCJAK ISSN: 0021-4671. Journal written in Japanese. CAN 111:70493 AN 1989:470493 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This study was designed to establish a model able to predict the clin. efficacy of anticancer agents against cancers of specific organs. Seven-wk old, male nude mice were implanted with 1×10^6 cells of human gastric cancer G/F into either their subcutis or the stomach wall. Fourteen days after the implantation, the mice were injected daily once for 10 days with peplomycin or mitomycin C. Peplomycin was effective on the s.c. tumors with an inhibition rate of 26 and 64% at 1.5 and 6.0 mg/kg, resp. Peplomycin was ineffective on the tumors in the stomach wall. Mitomycin C was ineffective on the s.c. tumors, but effective on the tumors in the stomach wall and the inhibition rate was 52 and 63% at 0.13 and 0.5 mg/kg, resp. Peplomycin and mitomycin C levels in the s.c. tumors were 2-7 times and .apprx.3 times higher than those in the stomach wall, resp. Thus, drug distribution could not explain the differences in drug sensitivity. The sensitivity of the tumor in the stomach wall to peplomycin and mitomycin C was consistent with the clin. efficacy of these drugs against human gastric cancers. Thus, models where the tumors are implanted into the source organ are useful for predicting clin. efficacy in exptl. cancer chemotherapy.

Answer 41:

Bibliographic Information

Changes in two-dimensional gel electrophoretic patterns of cellular protein spots in tumors after administration of mitomycin C. Takahashi, Tetsuya. Sch. Med., Keio Univ., Tokyo, Japan. Nippon Geka Gakkai Zasshi (1988), 89(4), 494-507. CODEN: NGGZAK ISSN: 0301-4894. Journal written in Japanese. CAN 109:163090 AN 1988:563090 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Treatment of the human stomach carcinoma (Exp 4) xenografted into nude mice with mitomycin C (MMC) caused histol. pleomorphism. No histol. changes were evident in another stomach (H-111) or 2 colon carcinomas (SW 403, SW 480). The most remarkable protein spot decreases after MMC were evident in Exp 4, with moderate changes in SW 403 and SW 480, in correlation with the sensitivities to MMC. Tumors which regrew after MMC had similar protein spot patterns and histol. features as control tumors.

Answer 42:

Bibliographic Information

Enhancement of hyperthermochemotherapy for human gastric cancer in nude mice by thermosensitization with nitroimidazoles. Fujimoto, S.; Ohta, M.; Shrestha, R. D.; Kokubun, M.; Miyoshi, T.; Mori, T.; Arimizu, N.; Okui, K. Sch. Med., Chiba Univ., Chiba, Japan. British Journal of Cancer (1988), 58(1), 42-5. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 109:142139 AN 1988:542139 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Hyperthermia therapy for human gastric cancer xenotransplanted into the hindlegs of nude mice was performed to det. whether misonidazole (MISO) or metronidazole (MTR), derivs. of nitroimidazole, would intensify the antitumor effects of hyperthermia alone, or combined with mitomycin C (MMC). MISO, MTR, and MMC were given i.p. at 500, 500, and 2.0 mg/kg, resp., and MISO or MTR was administered 45 min before MMC. Hyperthermia was applied twice at 48-h intervals, by means of a water bath at 43.5° for 23 min. Tumor tripling times following heat alone, MTR plus heat, and MISO plus heat were .apprx.6.7, 8.0, and 7.9 days, resp., compared with 4.6 days for the control, but tumor regression occurred in the heat plus MISO group only. Tumor tripling times for MMC plus heat,

MMC plus MTR plus heat, and MMC plus MISO plus heat were 9.6, 11.6, and 17.1 days, resp., compared to 4.6 days for the control and 6.7 days for heat alone. Thus, the antitumor activity of MMC plus MISO plus heat is an additive phenomenon.

Answer 43:

Bibliographic Information

Combined effects of UFT with other anticancer agents using in vivo chemosensitivity tests. Nishiyama, Masahiko; Niimi, Ken; Takagami, Shinichi; Hirabayashi, Naoki; Yamaguchi, Masahiro; Saeki, Toshiaki; Yoshinaka, Ken; Dian-Chang, Wang; Niimoto, Minoru; Hattori, Takao. Res. Inst. Nucl. Med. Biol., Hiroshima Univ., Hiroshima, Japan. Japanese Journal of Surgery (1988), 18(1), 93-7. CODEN: JJSGAY ISSN: 0047-1909. Journal written in English. CAN 109:389 AN 1988:400389 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The combined and tumor activity of UFT (tegafur-uracil mixt. 1:4 molar ratio) and other anticancer agents (mitomycin C, 5-fluorouracil, adriamycin, methotrexate, and cis-diamminedichloroplatinum) were studied against 3 human tumor xenografts in a nude mouse exptl. system and in a subrenal capsule assay. The effectiveness of the combination of UFT and mitomycin C was shown in both assays against all tumor xenografts tested.

Answer 44:

Bibliographic Information

Augmentation of activity of cis-diamminedichloroplatinum(II) and mitomycin C by interferon in human malignant mesothelioma xenografts in nude mice. Sklarin, Nancy T.; Chahinian, A. Philippe; Feuer, Eric J.; Lahman, Liz A.; Szrajner, L.; Holland, James F. Mt. Sinai Sch. Med., City Univ. New York, New York, NY, USA. Cancer Research (1988), 48(1), 64-7. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 108:48895 AN 1988:48895 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Two human mesothelioma xenograft lines, BG and ES, serially passaged in athymic mice, were studied to det. the efficacy of α -interferon in this type of tumor. Treatment began after progressive tumor growth was established. Recombinant human α -interferon-2a (Roferon-A) was given s.c. at a site distant from the tumor, at a dose of 2×10^5 IU 5 days per wk for 5 wk. Mild inhibitory activity was noted in both lines with interferon alone. cis-Diamminedichloroplatinum(II) (CDDP) (4 mg/kg) weekly \times 5 was effective in line BG, while mitomycin C (1.5 mg/kg) weekly \times 3 was effective in line ES. CDDP was not as effective in line ES. The moderate activity of CDDP in line BG and of mitomycin C in line ES was markedly increased by the addn. of α -interferon. The combination of mitomycin C and α -interferon was as effective as mitomycin C and CDDP. No addnl. toxicity was noted by the addn. of α -interferon. The combination of recombinant human α -interferon-2a and active chemotherapeutic agents is effective in mesothelioma xenografts.

Answer 45:

Bibliographic Information

Antitumor efficacy of polyamine antimetabolites and mitomycin C under polyamine-free diet. Fujimoto, Shigeru; Shrestha, Ram Dhoj; Ohta, Masayasu; Igarashi, Kazuei; Kokubun, Masashi; Okui, Katsuji; Fujita, Masahide; Taguchi, Tetsuo. Sch. Med., Chiba Univ., Osaka, Japan. Gan to Kagaku Ryoho (1987), 14(10), 2930-5. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 108:31479 AN 1988:31479 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Treatment of nude mice xenografted with human gastric cancer was carried out by polyamine antimetabolites combined with mitomycin C (MMC) and polyamine-free diet. Polyamine antimetabolites, α -difluoromethylornithine (DFMO) and ethylglyoxal-bis-guanylhydrazine (EGBG), were given i.p. in a daily dose of 1000 mg/kg and 20 mg/kg, resp., for 6 consecutive days. MMC (2.0 mg/kg) was administered every other day. The polyamine-free diet was given from 4 days before start of the treatment through the end of the study. Although the tumor growth rate of the control group given polyamine-free diet was similar to that given normal diet, in the mice treated with EGBG, or DFMO plus MMC, the antitumor effect in the polyamine-free diet group was superior to the normal diet group. In comparison with tumor growth suppression due to EGBG plus DFMO or MMC only, the polyamine-free diet group showed a better result than the normal diet group to some extent. In mice treated with EGBG or DFMO plus MMC, tumor tissue spermine levels in the polyamine-free diet group were depressed, compared to the normal diet group. Furthermore, marked suppression of DNA biosynthesis was obsd. in mice given EGBG or DFMO plus MMC together with the polyamine-free diet. Apparently, combined treatments of polyamine antimetabolites and MMC revealed a marked enhancement of antitumor effects, under conditions of polyamine depletion, which may be responsible for the alteration in DNA structure.

Answer 46:

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 47:

Bibliographic Information

Fundamental and clinical investigations on the reinforcement of the effects of combination cancer chemotherapy by flow cytometric analysis of DNA histograms. New attempts at reinforcement of antitumor effects using FCM. Sato, Yasumitsu. Sch. Med., Akita Univ., Japan. Akita Igaku (1986), 13(4), 561-86. CODEN: AKIGDV ISSN: 0386-6106. Journal written in Japanese. CAN 107:168379 AN 1987:568379 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effects of cis-diamminedichloroplatinum (CDDP), peplomycin (PEP), mitomycin C (MMC), adriamycin (ADM), etoposide (VP-16), 5-fluorouracil (5-FU), and vindesine (VDS) upon the viability and cell cycle progression of cultured human esophageal cancer cells (TE-2, AE-2), human esophageal (AEN-2), or gastric (TK) tumor xenografts growing in nude mice were measured and compared using flow cytometry (FCM) in order to improve the methods of selecting the individual agents and establish the most effective regimen for combination cancer chemotherapy. Anal. of the influence of chemotherapeutic agents on cell cycle kinetics using FCM appeared to be very important in the development of an effective cancer chemotherapy. Recruitment and partial synchronization were esp. useful in reinforcing the antitumor effects of combination chemotherapy on solid cancers.

Answer 48:

Bibliographic Information

Combination chemotherapy of human gastrointestinal and breast cancer xenografts in nude mice with 5'-deoxy-5-fluorouridine and mitomycin C. Fujita, Fumiko; Fujita, Masahide; Shimozuma, Kojiro; Taguchi, Tetsuo. Res. Inst. Microb. Dis., Osaka Univ., Osaka, Japan. Nippon Gan Chiryō Gakkaishi (1986), 21(7), 1386-96. CODEN: NGCJAK ISSN: 0021-4671. Journal written in Japanese. CAN 107:126609 AN 1987:526609 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effects of exptl. combination chemotherapy with 5'-deoxy-5-fluorouridine (5'-DFUR) and mitomycin C (MMC) against 13 human gastrointestinal and breast cancer xenografts in BALB/c nude mice were evaluated in comparison with each of the single agent chemotherapy. With single agent therapy, remarkable suppression with I.R (inhibition rate) $\geq 80\%$ was obtained in 5 lines in each drug. In contrast, combined therapy achieved I.R ($\geq 80\%$ in every line except one (92%). Besides, tumor shrinkage was obsd. in 7 lines in combination chemotherapy compared to 3 each in single agent therapies. Consequently, synergistic effects were seen in 8 (62%) of 13 lines examd. Side effects in combination therapy were equiv. to or slightly less than the corresponding single agent therapy.

Answer 49:

Bibliographic Information

Effects of alternating chemotherapy with 2 non-cross-resistant drug combinations on human alimentary and breast cancer xenografts in nude mice. Fujita, Fumiko; Fujita, Masahide; Yamauchi, Teruo; Sakamoto, Yasuo; Shimozuma, Kojiro; Inaba, Hiizu; Taguchi, Tetsuo. Res. Inst. Microb. Dis., Osaka Univ., Osaka, Japan. Gan to Kagaku Ryoho (1987), 14(5, Pt. 1), 1297-304. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 107:126598 AN 1987:526598 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effectiveness of alternating chemotherapy with the combination regimens I [mitomycin C (MMC) and 5'-deoxy-5-fluorouridine (5'-DFUR)] and II [cisplatin(CDDP), 5'-DFUR, and vindesine(VDS)] was evaluated using 3 lines of cancer xenografts (breast, colon, and pancreas) in nude mice with special emphasis on relapse-free survival. Results showed that cyclic delivery of two non-cross-resistant drug combinations with optimal treatment doses and timing prevented toxic effects and induced long-term survival without relapse.

Answer 50:

Bibliographic Information

Effect of combination of UFT and MMC (UFT-M therapy) on human colonic cancer xenotransplanted in nude mice. Takahashi, Yutaka; Kikuchi, Reiko; Ueno, Masashi; Mai, Masayoshi. Cancer Res. Inst., Kanazawa Univ., Japan. Gan to Kagaku Ryoho (1987), 14(5, Pt. 1), 1345-7. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 107:89434 AN 1987:489434 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

UFT in combination with MMC (mitomycin C) had better antitumor action with less side effect (decreases in body wt, etc.) than did UFT or MMC alone in nude mice xenotransplanted with human colon cancer. The results are discussed with regard to the usefulness of this combination in the treatment of digestive tract cancer.

Answer 51:

Bibliographic Information

Chemo-sensitive differences of primary, metastatic and recurrent tumors of human colorectal cancer. Yamada, Kazutaka; Takao, Sonshin; Maenohara, Shigeo; Saihara, Tetushi; Yoshinaga, Atsunori; Haruyama, Katsuro; Mitsuda, Kazunobu; Makizumi, Kanro; Ishizawa, Takashi; Shimazu, Hisaaki. Sch. Med., Kagoshima Univ., Kagoshima, Japan. Nippon Shokakibyo Gakkai Zasshi (1986), 83(11), 2318-24. CODEN: NIPAA4 ISSN: 0369-4259. Journal written in Japanese. CAN 106:207311 AN 1987:207311 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Tumor lines xenografts in nude mice used in this study include COK-1 and COK-7. COK-1 (PT, LN and RE) has been established from the primary (PT) lymph node metastatic (LN) and local recurrent (RE) tumors of human colon cancer, and COK-7 (PT and LiM) has been established from the primary (PT) and liver metastatic (LiM) tumors of human rectal cancer. These tumor lines were used for the study of chemotherapeutic responses to such anti-cancer drugs as 5-fluorouracil [51-21-8], cyclophosphamide [50-18-0], cisplatin [15663-27-1], and mitomycin C (MMC) [50-07-7]. Chemotherapeutic responses to these drugs in each tumor line were as follows: COK-1 (PT) responded to only MMC, while COK-1 (RE) responded to both MMC and cisplatin. However, COK-1 (LN) did not respond to any drug studied. In case of COK-7 (PT) it did not respond to drug as well, though COK-7 (LiM) showed a response to MMC. These results indicate that each tumor line of COK-1 and COK-7 has chemosensitive differences in primary, metastatic, and recurrent tumor lines.

Answer 52:

Bibliographic Information

Efficacy of anticancer agents in vitro and in vivo using cultured human endometrial carcinoma cells. Study of therapeutic index. Yasui, Yoshie. Sch. Med., Nagoya City Univ., Nagoya, Japan. Nippon Sanka Fujinka Gakkai Zasshi (1987), 39(2), 303-6. CODEN: NISFAY ISSN: 0300-9165. Journal written in English. CAN 106:188338 AN 1987:188338 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Employing the new cell line, NUE-1, which was derived from cells of ascites in a woman with endometrial carcinoma, the sensitivity test for anticancer agents was carried out in culture and xenografts in nude mice. Anticancer activity in vitro was evaluated by counting surviving cells, and the therapeutic index was expressed by LD50 for mice/MLD90 (90% mean LD) in vitro. NUE-1 cells were inoculated s.c. in BALB/c nude mice, and then tumors serially transplanted were used as materials. Anticancer agents (adriamycin (ADM) [23214-92-8], cisplatinum [15663-27-1], chromomycin A3 [7059-24-7], carbazilquinone [24279-91-2], and mitomycin C [50-07-7]) at 1/3 LD50 dosage for mice were administered i.p. on a schedule of 3 doses for every 4 days. The results were as follows: (a) the therapeutic index of ADM was highest at 5-19 times the others; (b) in vivo, ADM demonstrated chemotherapeutic effectiveness, whereas the others had no significant effect; and (c) there was a close correlation between the therapeutic index and in vivo anticancer effect using nude mice.

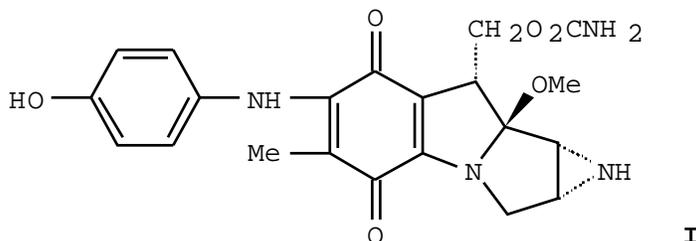
Answer 53:

Bibliographic Information

Effect of 7-N-(p-hydroxyphenyl)mitomycin C against human tumor xenografts serially transplanted into nude mice. Asanuma, Fumiki; Kubota, T.; Tsuyuki, K.; Nakada, M.; Kubouchi, K.; Kurihara, H.; Koh, J.; Ishibiki, K.; Abe, O. Sch. Med., Keio Univ., Tokyo, Japan. Editor(s): Spitzzy, K. H.; Karrer, K. Proc. Int. Congr. Chemother., 13th (1983), 17 261/39-261/45. Publisher: Verlag H. Egermann, Vienna, Austria CODEN: 53XPA8 Conference written in English. CAN 105:145749 AN 1986:545749 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effect of 7-N-(p-hydroxyphenyl)mitomycin (I), (I), a deriv. of mitomycin C (MMC), against human tumor xenografts serially transplanted into nude mice was evaluated with ref. to its pharmacokinetics; human tumor strains, MX-1 (breast carcinoma), Co-3 (colon carcinoma), and Co-4 (colon carcinoma) were examd. Tumor regressions were obsd. in MX-1 and Co-4, whereas the growth of Co-3, a resistant strain to MMC, was retarded and the T/C value was 32.7%. Concn. of M-83 in blood and serum was similar to each other in mice bearing the 3 tumors, and $t_{1/2\beta}$ was 32.6 min by radioassay and approx. 10 min by bioassay. As for drug concn. in the tumor, peak values by radioassay in MX-1 and Co-4 were higher than that in Co-3. It was also obsd. that this drug was the most inactivated by tumor homogenates of Co-3 in vitro. I appears to have an anti-tumor spectrum which is different from MMC; the inactivation of I in the tumor may be related to its anti-tumor effect.



Answer 54:

Bibliographic Information

Experimental and clinical studies on sensitivity test of anticancer agents by ³H-thymidine autoradiography using human malignant tumor transplanted in nude mice. Nishimawari, Kazuharu. Res. Inst. Nuclear Med. Biol., Hiroshima Univ., Hiroshima, Japan. Nippon Geka Gakkai Zasshi (1986), 87(2), 141-53. CODEN: NGGZAK ISSN: 0301-4894. Journal written in Japanese. CAN 105:107845 AN 1986:507845 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The ³H-labeled thymidine [50-89-5] uptake of human xenografts transplanted in nude mice and treated with various anticancer agents was studied by autoradiog. and compared with the histol. changes on the same specimen. Human malignant tumors were transplanted into nude mice and treated with i.p. administration of Mitomycin C (MMC) [50-07-7] 5-Fluorouracil (5-FU) [51-21-8] and Cyclophosphamide (CPM) [50-18-0]. The rate of pos. sensitivity was 65.5% in MMC, 34.9% in 5-FU and 51.8% in CPM by autoradiog. evaluation, while by histol. evaluation 18.9, 14.6, and 16.9%, resp. Apparently, the autoradiog. evaluation of the tumor sensitivity to anticancer agents is more sensitive than the histol. evaluation. As to MMC and CPM, significant correlations were demonstrated between the results of this method and those of the exptl. chemotherapy in accordance with the Battelle Columbus Labs. Protocol using human malignant tumors serially transplanted into nude mice.

Answer 55:

Bibliographic Information

Xenografts in pharmacologically immunosuppressed mice as a model to test the chemotherapeutic sensitivity of human tumors. Floersheim, G. L.; Bieri, A.; Chiodetti, Nicole. Zent. Lehre Forsch., Kantonssp., Basel, Switz. International Journal of Cancer (1986), 37(1), 109-14. CODEN: IJCNAAW 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 56:

Bibliographic Information

Experimental chemotherapy of human carcinomas serially transplanted into nude mice. Kubota, Tetsuro; Asanuma, F.; Tsuyuki, K.; Kurihara, H.; Inada, T.; Ishibiki, K.; Abe, O. Dep. Surg., Keio Univ., Tokyo, Japan. Editor(s): Spitzky, K. H.; Karrer, K. Proc. Int. Congr. Chemother., 13th (1983), 18 291/55-291/59. Publisher: Verlag H. Egermann, Vienna, Austria CODEN: 53XPA8 Conference written in English. CAN 104:14592 AN 1986:14592 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

In nude mice transplanted with human carcinomas, most gastrointestinal carcinomas were suppressed by mitomycin C [50-07-7] and were insensitive to cyclophosphamide (CPA) [50-18-0], whereas 2 breast carcinomas and 1 hemangiosarcoma were markedly suppressed by CPA, suggesting that the chemosensitivities of these tumors were different. No differences were found in chemosensitivity between the gastric and colon carcinomas. No correlations were obsd. between the histol. differentiations of the carcinomas and the chemosensitivity to mitomycin C, adriamycin [23214-92-8], aclarubicin [57576-44-0], and CPA. However, the growth-rate of the tumors correlated with the chemosensitivity to mitomycin C and aclarubicin, i.e., the rapid-growing tumors were more sensitive than the slow-growing tumors to the drugs.

Answer 57:

Bibliographic Information

Antitumor effects of two polyamine antimetabolites combined with mitomycin C on human stomach cancer cells xenotransplanted into nude mice. Fujimoto, Shigeru; Igarashi, Kazuei; Shrestha, Ram Dhoj; Miyazaki, Masaru; Okui, Katsuji. Sch. Med., Chiba Univ., Chiba, Japan. International Journal of Cancer (1985), 35(6), 821-5. CODEN: IJCNW ISSN: 0020-7136. Journal written in English. CAN 103:134621 AN 1985:534621 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor effects of α -difluoromethylornithine (DFMO) [70052-12-9], methylglyoxal bis(guanylhydrazone) (MGBG) [459-86-9], and mitomycin C (MHC) [50-07-7], administered sep. or in various combinations, on human stomach cancer cells xenotransplanted into nude mice were studied. DFMO (1000 mg/kg in 2 divided doses) and MGBG (50 mg/kg) were given i.p. for 7 consecutive days from the time when the tumor weighed about 100 mg. MMC (2 mg/kg) was given i.p. every other day from the same time. Animals treated with either DFMO or MGBG alone displayed tumor growth comparable to that seen in untreated controls. In mice treated with DFMO combined with MGBG, with or without MMC, or in mice treated only with MMC, tumor growth was lower than in untreated mice. In the group which received only combined DFMO-MGBG, there was a rapid regrowth of the tumor after termination of therapy. Tumor putrescine [110-60-1] levels decreased within 4 days following the administration of DFMO; however, spermidine [124-20-9] levels did not decline with either DFMO or MGBG treatment even after 7 days. When combined DFMO-MGBG was given, there was a decline in spermidine levels 7 days after the initiation of treatment. In contrast, when MMC was administered alone, putrescine and spermidine levels in the tumor did not differ from those in control mice. Spermine [71-44-3] decreased markedly in tumor with the combined

administration of DFMO-MGBG as well as with combined DFMO-MGBG-MMC, but decreased only slightly when MMC alone or MMC combined with either DFMO or MGBG was administered. By the 7th treatment day, DNA biosynthesis in the tumor had dropped markedly in all groups except those receiving DFMO or MGBG alone.

Answer 58:

Bibliographic Information

Assessment of the combined effects of mitomycin C with α -interferon or γ -interferon by the clonogenic assay technique.

Hirabayashi, Naoki; Nishiyama, Masahiko; Yamaguchi, Masahiro; Yoshinaka, Ken; Nosoh, Yoshihiro; Toge, Tetuya; Niimoto, Minoru; Hattori, Takao; Ohkita, Takeshi. Res. Inst. Nucl. Med. Biol., Hiroshima Univ., Hiroshima, Japan. Gan to Kagaku Ryoho (1985), 12(5), 1056-62. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 103:115783 AN 1985:515783 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Combination chemotherapy of human tumor xenografts in nude mice with mitomycin C [50-07-7] and α -interferon indicated synergism from the 2 agents in 4 (3 gastric and 1 colon) of 5 tumors; although mitomycin C and γ -interferon were synergistically active against 2 gastric tumors, antagonism was obsd. in 1 gastric and 1 colon line.

Answer 59:

Bibliographic Information

Characterization of human AFP [human alpha-fetoprotein] producing stomach cancer xenotransplanted in nude mice and the effect of a conjugate of MMC [mitomycin C] with antibody to human AFP on this tumor.

Takahashi, Yutaka. Cancer Res. Inst., Kanazawa Univ., Kanazawa, Japan. Nippon Shokakibyō Gakkai Zasshi (1985), 82(1), 18-27. CODEN: NIPAA4 ISSN: 0369-4259. Journal written in Japanese. CAN 103:32030 AN 1985:432030 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Three human α -fetoprotein (AFP)-producing stomach tumors were serially transplanted in BALB/c nu/nu nude mice; the transplanted tumors retained not only their morphol. but also the function of the original tumors. Serum AFP level in the mice ranged from 10,690 ng/mL to 38,540 ng/mL, and increased progressively. A pos. correlation was obsd. between serum AFP level and tumor wt. Further, all 3 tumors produced both AFP and the normal serum proteins albumin, α 1-anti-trypsin, and transferrin. Mitomycin C conjugated to AFP antibodies inhibited the growth of these tumors in mice; the effect of the antibody-conjugated drug was 10 times greater than that free mitomycin C.

Answer 60:

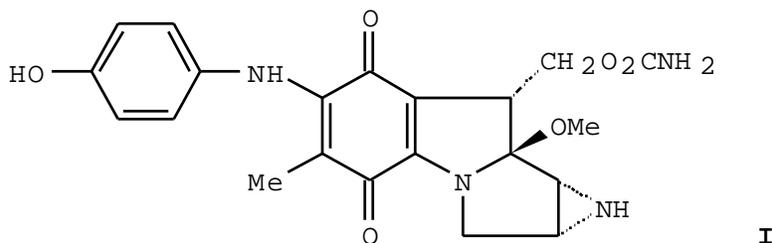
Bibliographic Information

Antitumor activity and pharmacokinetics of 7-N-(p-hydroxyphenyl)mitomycin C in human tumor xenografts transplanted into nude mice.

Asanuma, Fumiki. Sch. Med., Keio Univ., Tokyo, Japan. Journal of Antibiotics (1985), 38(3), 401-10. CODEN: JANTAJ ISSN: 0021-8820. Journal written in English. CAN 102:214719 AN 1985:214719 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effects of 7-N-(p-hydroxyphenyl)mitomycin C (M-83)(I) [70343-57-6] against human tumor xenografts serially transplanted into male BALB/c nude mice were evaluated. M-83 showed pos. antitumor effect against 6 out of 8 tumor strains. The antitumor spectrum of this agent was similar to that of mitomycin C except for 2 strains. Peak serum concns. of M-83, as detected by bioassay, were obsd. at 1 min and again at 5 min; elimination half-life $T_{1/2\beta}$ was 10.9 min and the area under curve AUC060 was 112.4 $\mu\text{g}\cdot\text{min}/\text{mL}$ when 15 mg/kg of the agent was administered. In the tumor, the peak concn. and AUC060 detected by radioassay correlated well with the value of drug efficacy TRW/CRW. AUC060 detected by bioassay in the tumor tissue was 18.6 $\mu\text{g}\cdot\text{min}/\text{g}$ which is approx. 10% of the AUC obtained by radioassay indicating some inactivation of the agent by the tumor cells.



Answer 61:

Bibliographic Information

Anticancer drug sensitivity tests using nude mice. Noso, Yoshihiro; Yoshinaka, Ken; Nishimawari, Kazaharu; Hirono, Masashi; Tani, Tadanori; Niimoto, Minoru; Hattori, Takao. Hiroshima Univ., Hiroshima, Japan. *Gan no Rinsho* (1984), 30(9), 1181-5. CODEN: GANRAE ISSN: 0021-4949. Journal written in Japanese. CAN 102:17009 AN 1985:17009 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Both isotope assay and histol. methods were found useful for the screening of neoplasm inhibitors in nude mice bearing human tumors. The results of the sensitivity study were well correlated with the clin. findings with the testing drugs. The survival rate of patients who received the drugs was higher than that of controls. The drugs used for testing were mitomycin C [50-07-7], 5-fluorouracil [51-21-8], and cyclophosphamide [50-18-0].

Answer 62:

Bibliographic Information

Screening test of antitumor agents by human tumor cell lines in nude mice in ascitic form. Kitahara, Takeshi; Minato, Keisuke; Shimoyama, Masanori. Natl. Cancer Cent. Hosp., Japan. *Gan no Rinsho* (1984), 30(9), 1158-67. CODEN: GANRAE ISSN: 0021-4949. Journal written in Japanese. CAN 102:17008 AN 1985:17008 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Human breast cancer and leukemic cells implanted in nude mice appeared to be useful models for the screening of neoplasm inhibitors. The sensitivities of implanted tissues to drugs were similar to those found in patients. Studies on the suitable route of administration in these mice provide the best administration routes for humans.

Answer 63:

Bibliographic Information

Chemosensitivity to mitomycin C and cell kinetics of human tumor xenografts serially transplanted into nude mice.

Nakada, Munehiko. Sch. Med., KEIO Univ., Tokyo, Japan. Nippon Geka Gakkai Zasshi (1984), 85(7), 694-704. CODEN: NNGZAK ISSN: 0301-4894. Journal written in Japanese. CAN 102:234 AN 1985:234 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Mitomycin C [50-07-7] suppressed the growth of the well differentiated stomach and colon human adenocarcinomas, St-40 and Co-4, resp., xenografted into nude mice; however, poorly differentiated variants of the tumors, St-4 and Co-3, resp., were less sensitive to the effects of mitomycin C. In vitro, the growth of St-4, St-40, and Co-4 cells was inhibited by mitomycin C. St-4 cells showed a low growth fraction in vivo and increased [³H]thymidine incorporation in vitro, suggesting recruitment of G0 cells to the growth fraction in vitro. Thus, the chemosensitivity of the 4 cells lines to mitomycin C appears to be related to the growth fraction both in vivo and in vitro.

Answer 64:

Bibliographic Information**Effect of a conjugate of mitomycin C and antibody to human alpha-fetoprotein on the human alpha-fetoprotein producing tumor xeno-transplanted into nude mouse.**

Takahashi, Yutaka; Mai, Masayoshi; Akimoto, Ryuichi; Tsukada, Yutaka; Hara, Takeshi; Sudo, Katsuko. Inst. Cancer Res., Kanazawa Univ., Kanazawa, Japan. Igaku no Ayumi (1984), 130(12), 811-12. CODEN: IGAYAY ISSN: 0367-7826. Journal written in Japanese. CAN 101:222239 AN 1984:622239 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Mitomycin C conjugated with antibodies to rat α -fetoprotein (raised in horses) suppressed the growth of α -fetoprotein-secreting human gastric tumor cells xenografted in nude mice; neither the drug nor the antibody prepn. was effective alone. The mitomycin C-antibody conjugate was not effective in suppressing the growth of non-(α -fetoprotein)-secreting tumor cells.

Answer 65:

Bibliographic Information**Increased cytotoxic effects of various anticancer drugs by α -interferon (HLBI) on human tumor xenografts in nude mice.**

Nosoh, Yoshihiro; Yoshinaka, Ken; Yamaguchi, Masahiro; Tani, Tadanori; Toge, Tetsuya; Niimoto, Minoru; Hattori, Takao. Res. Inst. Nucl. Med. Biol., Hiroshima Univ., Hiroshima, Japan. Gan to Kagaku Ryoho (1984), 11(8), 1623-8. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 101:163319 AN 1984:563319 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effect of 7 anticancer agents in combination with interferon on gastric cancer and malignant melanoma of human transplanted s.c. in nude mice was studied. Of the 7 drugs, mitomycin C [50-07-7] and adriamycin [23214-92-8] showed the greatest inhibition of tumor growth in combination with interferon.

Answer 66:

Bibliographic Information

Childhood rhabdomyosarcoma xenografts: responses to DNA-interacting agents and agents used in current clinical therapy. Houghton, Janet A.; Cook, Ruby L.; Lutz, Pamela J.; Houghton, Peter J. Div. Biochem. Clin. Pharmacol., St. Jude Child. Res. Hosp., Memphis, TN, USA. *European Journal of Cancer & Clinical Oncology* (1984), 20(7), 955-60. CODEN: EJCODS ISSN: 0277-5379. Journal written in English. CAN 101:163109 AN 1984:563109 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A lab. model of childhood rhabdomyosarcoma (RMS) has been used to evaluate cytotoxic agents used in current clin. protocols, and DNA-reacting agents that have had either limited or no evaluation in this histiotype. Seven lines of RMS each derived from a different patient were grown as xenografts in immune-deprived mice, six of these being from specimens derived from previously untreated patients. Of the conventional agents, vincristine [57-22-7] was the most effective. Of the other agents evaluated [L-phenylalanine mustard (L-PAM) [148-82-3], cis-dichlorodiammineplatinum (cis-DDP) [15663-27-1], mitomycin C [50-07-7] and 5-(3,3-dimethyl-1-triazeno)-imidazole-4-carboxamide (DTIC) [4342-03-4]], L-PAM caused complete regressions in six of seven lines, including those resistant to cyclophosphamide [50-18-0]. DTIC had marked activity in five tumors, and mitomycin C in three lines. Cyclophosphamide was active in five tumors, although efficacy was less marked in two lines in comparison to DTIC and mitomycin C.

Answer 67:

Bibliographic Information

Chemosensitivity of human gastrointestinal and breast cancer xenografts in nude mice and predictability to clinical response of anticancer agents. Fujita, M.; Fujita, F.; Taguchi, T. Dep. Oncol. Surg., Osaka Univ., Osaka, Japan. Editor(s): Sordat, Bernard. *Immune-Defic. Anim., Int. Workshop Immune-Defic. Anim. Exp. Res.*, 4th (1984), Meeting Date 1982, 311-15. Publisher: Karger, Basel, Switz CODEN: 51ONAB Conference written in English. CAN 101:103450 AN 1984:503450 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effectiveness of 13 drugs against 14 lines of human gastrointestinal and breast cancers xenografted in nude mice was studied. Despite identical origins of organ and similarities in histol. types, degrees of differentiation, and growth rate, each line of cancer demonstrated different spectra of sensitivity to various agents. The effectiveness of various chemotherapeutic agents against human gastric cancer xenografts in nude mice was compared with the clin. effects of these drugs in clin. trials and phase II studies. The results indicated that the nude mouse-human cancer system would be useful in preclin. secondary screening.

Answer 68:

Bibliographic Information

Comparative data from experimental chemotherapy of human tumor xenografts in nude mice, and the clinical responses of the patient-donors. Taguchi, Tetsuo; Fujita, Masahide. Univ. Osaka, Osaka, Japan. *Eksperimental'naya i Klinicheskaya Farmakoterapiya* (1983), 12 77-83. CODEN: EKFMA7 ISSN: 0367-0589. Journal written in Russian. CAN 100:167828 AN 1984:167828 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A high degree of correlation was found between the effects of ftorafur [17902-23-7] in combination with MFC (mitomycin C [50-07-7], 5-fluorouracil [51-21-8], and cytosine arabinoside [147-94-4]) on the growth of tumor xenografts of 3 different human tumors in nude mice and the effects of the same chemotherapy on the patient-donors of the cell lines.

Answer 69:

Bibliographic Information

New combined antitumor therapy with polyamine biosynthesis inhibitors and mitomycin C. Fujimoto, Shigeru; Shrestha, Ram Dhoj; Miyazaki, Masaru; Ohyama, Yoshiaki; Endo, Fumio; Shimura, Takanori; Takahashi, Osamu; Sugasawa, Hirotake; Okui, Katsuji; et al. Sch. Med., Chiba Univ., Chiba, Japan. Gan to Kagaku Ryoho (1983), 10(11), 2347-52. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 100:29377 AN 1984:29377 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The combination of polyamine biosynthesis inhibitors, α -difluoromethylornithine (DFMO) [70052-12-9] and methylglyoxal-bisguanyldrazone (MGBG) [459-86-9], and mitomycin C (MMC) [50-07-7] given i.p. to nude mice xenotransplanted with human gastric cancer resulted in the inhibition of tumor growth and a marked decline of spermine levels in the tumor tissues. 23451 45231.

Answer 70:

Bibliographic Information

Response of a human colon adenocarcinoma (DLD-1) to x-irradiation and mitomycin C in vivo. Spremulli, Ellen N.; Leith, John T.; Bliven, Sarah F.; Campbell, Debora E.; Dexter, Daniel L.; Glicksman, Arvin S.; Calabresi, Paul. Dep. Med., Roger Williams Gen. Hosp., Providence, RI, USA. International Journal of Radiation Oncology, Biology, Physics (1983), 9(8), 1209-12. CODEN: IOBPD3 ISSN: 0360-3016. Journal written in English. CAN 99:101621 AN 1983:501621 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Mice hosting a heterogeneous human colon xenograft tumor produced by s.c. injection of the DLD-1 tumor cell line were treated either with x-irradn. alone, with mitomycin C alone (4 mg/kg), or with x-irradn. given 2 h after i.p. injection of mitomycin C (4 mg/kg). Radiation alone produced a dose-dependent delay in the time needed for tumors to regrow to twice their size at the time of irradiation, and in the mice receiving mitomycin C plus x-irradn., an addnl. growth delay equiv. to that produced by 3-3.5 Gy of x-rays was seen at all x-ray dose levels. As the DLD-1 tumor xenografts do not appear to possess a significant hypoxic fraction, the 2 agents appear to be acting in a simple additive cytotoxic manner by the killing of oxic tumor cells.

Answer 71:

Bibliographic Information

Effect of anti-vascular endothelial growth factor antibody on the progression of human gastric cancer orthotopic xenotransplanted into nude mice. Tao H; Lin Y; Yin H; Yao M Department of Surgery, Ruijin Hospital, Shanghai Second Medical University, Shanghai 200025 Zhonghua wai ke za zhi [Chinese journal of surgery] (1999), 37(4), 248-50. Journal code: 0153611. ISSN:0529-5815. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Chinese. PubMed ID 11829834 AN 2003292738 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

OBJECTIVE: To study the inhibiting effect of anti-vascular endothelial growth factor (VEGF) on the growth and metastasis of gastric cancer. METHODS: The anti-tumor and anti-metastasis effect of anti-VEGF antibody, mitomycin C (MMC) were investigated by means of an orthotopic xenotransplanted model of human gastric cancer SGC-7901 in nude mice

which had been randomly divided into 4 groups: control group receiving PBS, group receiving 50 microg/mice anti-VEGF antibody, group receiving 2 mg/kg MMC, and group receiving 50 microg/mice anti-VEGF antibody combined with 2 mg/kg MMC. Anti-VEGF antibody was given i.p. twice a week and MMC was administered i.p. once a week for 8 weeks from day 7 after transplantation. All animals were sacrificed at the end of 10 weeks. The tumor was weighted and the intra-tumoral microvessel density (MVD) was recorded, and the liver was histologically examined in order to discover micrometastasis. RESULTS: Both anti-VEGF antibody and MMC showed a significant inhibitory effect on the growth of primary tumors; in the combination treatment group the inhibitory effect was more significant than single agent. Liver metastasis developed in 19 of 28 mice (67.9%) of the controls and in 6 of 11 mice (54.5%) receiving MMC. In contrast, liver metastasis occurred in 2 of 10 mice (20%) receiving anti-VEGF antibody and none receiving combination treatment. In addition, the MVD was less significant in the anti-VEGF antibody group and combination treatment group than other groups. CONCLUSIONS: Anti-VEGF may provide a new approach to the treatment of gastric cancer by inhibiting tumor angiogenesis, and combination of anti-VEGF antibody with MMC could be more effective.

Answer 72:

Bibliographic Information

Phase II study: treatment of non-Hodgkin's lymphoma with an oral antitumor derivative of bis(2,6-dioxopiperazine). Ohno R; Yamada K; Hirano M; Shirakawa S; Tanaka M; Oguri T; Kodera Y; Mitomo Y; Ikeda Y; Yokomaku S; + Department of Medicine, Nagoya University School of Medicine, Branch Hospital, Japan Journal of the National Cancer Institute (1992), 84(6), 435-8. Journal code: 7503089. ISSN:0027-8874. (CLINICAL TRIAL); Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 1538420 AN 92167304 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

BACKGROUND: Although razoxane (ICRF-159), a derivative of bis(2,6-dioxopiperazine), has shown significant antitumor activity in several murine tumors, inadequate bioavailability has limited its clinical efficacy. Sobuzoxane (MST-16), another derivative of bis(2,6-dioxopiperazine), has shown activity against a broad spectrum of murine tumors and human tumor xenografts in nude mice and a lack of cross-resistance to vincristine, doxorubicin, cyclophosphamide, fluorouracil, etoposide, and mitomycin C. These findings suggest that MST-16 has a mode of cytotoxic activity different from that of other antitumor agents. **PURPOSE:** The present late phase II study was conducted to evaluate the clinical efficacy and toxicity of MST-16 in non-Hodgkin's lymphoma (NHL). **METHODS:** As part of a multi-institutional cooperative study, we conducted a study of MST-16 in 27 patients with NHL who were assessable for drug efficacy and toxicity. MST-16, a bis(2,6-dioxopiperazine) analogue and an inhibitor of topoisomerase II, was administered orally at a dose of 1600 mg/m² a day for 5-7 days at intervals of 2-3 weeks. **RESULTS:** Response consisted of one complete remission and seven partial remissions in 27 assessable patients. Response was achieved at a median of 13 days (range, 9-62 days) after initiation of therapy and lasted a median of 46 days (range, 29-155 days). Major toxic effects were leukopenia in 70% of the patients, thrombocytopenia in 44%, and gastrointestinal disorders in 37%. **CONCLUSIONS:** MST-16 was shown to be effective in NHL and deserves further clinical trial, since the drug shows little cross-resistance to available antitumor drugs. **IMPLICATIONS:** Phase II clinical studies of MST-16 in treatment of breast cancer, gastric cancer, and adult T-cell leukemia and lymphoma are also being conducted in Japan. Future trials of combination chemotherapy using MST-16 with other antitumor drugs are warranted in view of the additive effects observed in studies of MOLT-3 cells and studies of L1210 leukemia in mice.

Answer 73:

Bibliographic Information

Antitumor activity of 7-N-(2-((2-(gamma-L-glutamylamino) ethyl) dithio) ethyl) mitomycin C (KW2149) against human tumor xenografts serially transplanted into nude mice. Kubota T; Inada T; Inoue S; Kuzuoka M; Arisawa Y; Suto A; Kodaira S; Ishibiki K; Abe O Department of Surgery, School of Medicine, Keio University, Tokyo Japanese journal of clinical oncology (1989), 19(3), 216-21. Journal code: 0313225. ISSN:0368-2811. Journal; Article;

(JOURNAL ARTICLE) written in English. PubMed ID 2554025 AN 90041446 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The antitumor activity and toxicity of 7-N-(2-((2-(gamma-L-glutamylamino) ethyl) dithio) ethyl) mitomycin C (KW2149) were evaluated using a human tumor xenograft--nude mouse system, and compared with those of the maternal compound, mitomycin C. The maximum tolerated dose of KW2149 was estimated to be 15 mg/kg by bolus intraperitoneal or intravenous injection, at which a remarkable reduction of spleen weight was observed, suggesting bone marrow suppression by this agent. A bolus injection of KW2149 seemed to be more effective than a divided injection schedule, when a total of 15 mg KW2149/kg was administered to mice bearing breast (MX-1) and colon (Co-4) carcinomas. The antitumor activity of KW2149 was dose-dependent, and the difference in antitumor effect according to route of administration was minimal. The antitumor spectrum of KW2149 was essentially identical to that of mitomycin C administered intraperitoneally as a bolus at a dose of 6 mg/kg.

Answer 74:

Bibliographic Information

Combined therapy of xenografts of human pancreatic carcinomas with rTNF-alpha and mitomycin C. Klapdor R; Franke N; Bahlo M I. Medical Department, University of Hamburg, FRG Onkologie (1989), 12(3), 143-7. Journal code: 7808556. ISSN:0378-584X. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 2503798 AN 89344847 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Based on previously published experimental studies in nude mice indicating that rTNF-alpha as well as mitomycin C are able to induce significant growth inhibition of xenotransplants of gastrointestinal and pancreatic carcinomas we have investigated the antitumor effects of rTNF-alpha (0.8 mg/kg daily for 21 days) and mitomycin C (2.4 mg/kg once weekly, day 1, 7, 14) as single drugs and in combination (0.8 + 2.4) in nude mice bearing xenografts of 4 human pancreatic carcinomas and 1 colorectal cancer. Serum CA 19-9 was measured additionally to tumor growth rate. The results demonstrate that combined treatment is more effective compared to rTNF-alpha and mitomycin C alone. Combined therapy resulted in a significant inhibition of tumor growth in 3 of 5 xenografts and in decrease of tumor volume to less than 50% of the initial values in 2 of 5 tumors. The results support the concept that combinations of cytokines with cytostatics might be of value for treatment of gastrointestinal and pancreatic cancer in vivo.

Answer 75:

Bibliographic Information

Anticancer activities of a new mitomycin derivative KW 2149, against human tumors xenografted into nude mice. Nishiyama M; Kim R; Saeki T; Takagami S; Kirihara Y; Jinushi K; Toge T; Niimoto M; Hattori T Dept. of Surgery, Hiroshima University Gan to kagaku ryoho. Cancer & chemotherapy (1988), 15(11), 3133-7. Journal code: 7810034. ISSN:0385-0684. (COMPARATIVE STUDY); (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 3142368 AN 89049206 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Anticancer activity of KW 2149, a new derivative of mitomycin C (MMC), was investigated using 4 human tumors xenografted into nude mice. The basic methodology was essentially the same with NCI's therapeutic protocol. For the

comparative study, KW 2149 or MMC was administered intraperitoneally at a schedule of q4d X 3. Daily doses were determined as a 1/3, 1/4 and 1/5 of LD50 value of each anticancer agent (7.5 mg/kg, 5.6 mg/kg and 4.5 mg/kg for KW 2149, and 2.7 mg/kg, 2.1 mg/kg and 1.7 mg/kg for MMC). Anticancer activity of KW 2149 seemed to be dependent on the doses. Comparing with MMC, KW 2149 produced higher response rates at the doses of 1/3 and 1/4 of LD50 and was less toxic judging from the decrease of the body weight. This study may indicate an utility of KW 2149, as a new anticancer agents, or suggest the difference of anticancer activities between these two agents.

Answer 76:

Bibliographic Information

Contradictory antitumor efficacies produced by the combination of DNA attacking drugs and polyamine antimetabolites. Shrestha R D; Fujimoto S; Okui K First Department of Surgery, School of Medicine, Chiba University, Japan The Japanese journal of surgery (1987), 17(4), 263-8. Journal code: 1302176. ISSN:0047-1909. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 3119905 AN 88063609 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The antitumor effects of two polyamine antimetabolites, alpha-difluoromethylornithine (DFMO) and methylglyoxal-bis-guanylhydrazone (MGBG), when combined with cis-diamminedichloroplatinum (CDDP) or mitomycin C (MMC), were studied using human gastric cancer cells xenotransplanted into nude mice. DFMO 1000 mg/kg and MGBG 50 mg/kg were given intraperitoneally for 6 successive days, while CDDP 3 mg/kg or MMC 2 mg/kg was given every second day. Although DFMO and MGBG plus MMC did suppress the tumor growth, the combination with CDDP led to no suppression, and rapid growth occurred after the cessation of therapy. The inhibition of tumoral DNA biosynthesis and a decline in polyamine levels, were also not observed. The polyamine antimetabolites when used with CDDP did not produce the desired antitumor efficacy, even though the platinum concentration in the tumor tissue was high. On the contrary, however, DFMO and MGBG when combined with MMC did suppress tumor growth, inhibited DNA biosynthesis, and tissue polyamine levels were low. These results suggest that though CDDP and MMC belong to a similar category of DNA attacking, bifunctional alkylating agents, the findings of these two drugs are contradictory. Here, the mechanism of action no doubt plays a contributory role.

Answer 77:

Bibliographic Information

Combination cancer chemotherapy of human gastric and colon carcinomas in nude mice--sequential cancer chemotherapy involving mitomycin C and tegafur. Kubota T; Ishibiki K; Abe O Gan to kagaku ryoho. Cancer & chemotherapy (1986), 13(4 Pt 1), 938-44. Journal code: 7810034. ISSN:0385-0684. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 3083789 AN 86185585 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Three human tumor xenografts serially transplanted into nude mice were used for an experimental combination cancer chemotherapy consisting of mitomycin C (MMC) and tegafur (FT-207). The strains used for the experiments were two gastric (St-4 and St-15) and one colon (Co-3) carcinomas. The minimal effective doses of MMC were administered i. p. 24h after the s. c. tumor inoculations followed by 60 mg/kg of FT-207 in the three different modalities i. p. These were (A) daily administration of FT-207, (B) FT-207 only, 24h after MMC treatment and (C) FT-207 only, 5 days after MMC treatment. The antitumor effect assessed by the tumor weight at the end of the experiment was found to be (A) divided by (B) greater than (C), whereas the total administration doses of FT-207 were (A) greater than (B) = (C). As this result suggested the significance of FT-207 given 24h after MMC, flow cytometric analysis of St-15 tumor was conducted 24

and 48 h after the MMC treatment. It was observed that the incidence of 2n cells was depressed and the amount of 4n cells increased by MMC, indicating the recruitment of tumor cells into the proliferating phase. Because these recruited cells were thought to be sensitive to FT-207, it was supposed that the antitumor effect was elevated when FT-207 was given 24h after MMC. This semi-synchronized combination cancer chemotherapy involving MMC and FT-207 might therefore be useful for clinical application.

Answer 78:

Bibliographic Information

In vitro chemosensitivity tests on human tumor xenografts by clonogenic assay: the combined use of mitomycin C with alpha-interferon or gamma-interferon. Hirabayashi N; Yoshinaka K; Nosoh Y; Toge T; Niimoto M; Hattori T; Ohkita T The Japanese journal of surgery (1985), 15(4), 279-84. Journal code: 1302176. ISSN:0047-1909. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 3932733 AN 86038194 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Using the human tumor clonogenic assay technique, the effects of Mitomycin C plus either alpha-interferon or gamma-interferon were studied against five human tumor xenografts serially transplanted into nude mice (three gastric and two colon cancers). When the survival fraction found with the drug combination was smaller than the multiplication of survival fractions with either drug alone, the combined effect was defined as synergism. Similarly, antagonistic effect was defined when the survival fraction of drug combination was larger than the larger one observed in either interferon or Mitomycin C alone. Four out of five human tumor xenografts (three gastric and one colon cancers) showed synergistic effects in combination of alpha-interferon with Mitomycin C. Though two gastric cancer xenografts exhibited synergistic effects in combination of gamma-interferon with Mitomycin C, antagonistic effects, which was not found in combination of alpha-interferon with Mitomycin C, were observed in one gastric cancer and one colon cancer xenografts.

Answer 79:

Bibliographic Information

Experimental hyperthermo-chemotherapy for human gastric carcinoma transplanted in the nude mice.

Fujimoto S; Shrestha R D; Miyazaki M; Endoh F; Shimura T; Sugasawa H; Takahashi O; Kawata S; Ohta M; Kurihara M; + Gan to kagaku ryoho. Cancer & chemotherapy (1984), 11(12 Pt 2), 2724-8. Journal code: 7810034. ISSN:0385-0684. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 6439123 AN 85071185 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Human gastric carcinomas serially xenotransplanted into BALB/c nu/nu mice were treated by hyperthermo-chemotherapy with mitomycin C (MMC). The antitumor efficacy was assessed by both single and double treatments of 25-minute hyperthermia (43.5 degrees C) and/or 2.0 mg/kg of MMC (ip). Tumor weight was estimated using Battelle's Columbus Laboratories protocol. To assess DNA biosynthesis in the tumor cells, the xenotransplanted tumors were excised at prescribed times after these treatments 60 minutes after 3H-thymidine injection (ip), and were examined microscopically. In the group treated twice by hyperthermo-chemotherapy marked growth inhibition and microscopic damage of the tumors were observed, while such features were not recorded in groups treated twice by hyperthermia only and chemotherapy only, nor in groups given single hyperthermo-chemotherapy, or hyperthermia and chemotherapy. In the single-treated groups, DNA biosynthesis was remarkably inhibited by hyperthermo-chemotherapy over 24 hours. The present results suggest that repeated treatments of hyperthermo-chemotherapy with MMC may be effective in the treatment of human gastrointestinal cancer.

Answer 80:

Bibliographic Information

Cell cycle perturbations in heterotransplanted squamous-cell carcinoma of the head and neck after mitomycin C and cisplatin treatment. Wennerberg J; Alm P; Björklund A; Killander D; Langström E; Trope C International journal of cancer. Journal international du cancer (1984), 33(2), 213-22. Journal code: 0042124. ISSN:0020-7136. (COMPARATIVE STUDY); Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 6420350 AN 84110646 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Cell kinetic studies are of interest for clarifying the concepts of chemotherapeutic strategy in the multimodality therapy of advanced squamous-cell carcinoma of the head and neck. A poorly-differentiated squamous-cell carcinoma of the head and neck heterotransplanted to nude mice was used for analyses of chemotherapeutically induced cell cycle perturbations. The heterotransplanted tumour, in its 15th or later passages in nude mice, was treated with either Mitomycin C or cisplatin. After determination of dose-response relationships and toxicity, treated tumours were biopsied at different times and cell cycle distribution pattern, 3HTdR incorporation into DNA, histology and tumour volume were recorded. Mitomycin C and cisplatin gave the same pattern of cell cycle perturbations, although the changes induced by cisplatin were more profound. There was an initial increase of the fraction of cells in the S phase, concomitant with a reduction of the fraction of cells in G₀ + G₁ phase. When these perturbations were normalized a transient increase of the fraction of cells in G₂ + M phase was observed. However, while cisplatin caused an initial transient depression of DNA synthesis, the Mitomycin-C-treated tumours exhibited a short-lasting increase of DNA-synthesis. The maxima of the induced changes in cell cycle phase distribution and DNA-synthesis lasted for only 24-48 h, which may be of importance for scheduling combinations of drugs. Though both drugs induced profound changes in tumour volume growth and cell kinetics, there was no change in the histopathological picture of the treated tumours. Routine histopathological examination is thus not likely to be of value evaluating the effect of chemotherapy.

Answer 81:

Bibliographic Information

Occurrence of drug resistance in human tumor implanted in nude mice. Inaba M; Nagashima K; Sakurai Y Gann = Gan (1982), 73(4), 633-6. Journal code: 8214471. ISSN:0016-450X. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 6818091 AN 83106270 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

A line of human breast tumor xenograft in nude mouse, MX-1, acquired resistance to vincristine or mitomycin C during multiple treatments; both drugs were effective against the parent line of this tumor. If the treatment was started when the tumor was smaller than 500 mm³ in size, MX-1 was responsive to the initial treatment with vincristine (0.8 mg/kg) or mitomycin C (3.4 mg/kg), and some animals survived with complete regression of the tumor. However, some of the recurrent tumors were able to tolerate multiple treatments with either of these agents, and finally acquired apparent resistance to the agent. On the other hand, when tumors larger than 5,000 mm³ were treated with vincristine, the occurrence of resistance was observed with much higher frequency than when small tumors were treated. Resistant tumors thus obtained exhibited significant refractoriness to each agent when they were reimplanted in new mice and treated in the same manner. This suggests that the occurrence of resistance can be ascribed to changes not in metabolic functions of the host animal but in the tumor cell populations.