

Answer 1:

Bibliographic Information

Pegylated and conventional interferon- α induce comparable transcriptional responses and inhibition of tumor growth in a human melanoma SCID mouse xenotransplantation model. Krepler, Clemens; Certa, Ulrich; Wacheck, Volker; Jansen, Burkhard; Wolff, Klaus; Pehamberger, Hubert. Department of Dermatology, Division of General Dermatology, Department of Clinical Pharmacology, Section of Experimental Oncology/Molecular Pharmacology, University of Vienna, Vienna, Austria. *Journal of Investigative Dermatology* (2004), 123(4), 664-669. Publisher: Blackwell Publishing, Inc., CODEN: JIDEAE ISSN: 0022-202X. Journal written in English. CAN 142:153857 AN 2004:826310 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Interferon-alpha (IFN- α) is widely used for the treatment of viral infections and primary cancers. In the present study, we investigated whether the anti-proliferative activity of IFN- α is capable of inhibiting melanoma tumor development in the absence of protective immune responses in a severe combined immunodeficiency (SCID) mouse model. Mice treated with either regular (100 μ g/ 3 times per wk) or pegylated (300 μ g/ once weekly) human IFN- α 2a showed a marked redn. in tumor wt. after 4 wk of treatment. Tumor wt. in pegylated and conventional IFN- α -treated animals was reduced by 61% and 67%, resp., as compared to saline control (both $p \leq 0,01$). A decrease of proliferation and an increase of apoptotic tumor cells were obsd. in IFN-treated tumors. DNA microarrays were applied to analyze transcriptional responses in tumors after 4 wk of treatment and a subset of about 90 genes was differentially expressed. Twenty-four novel and five known interferon-inducible genes were up- and 65 genes downregulated. A direct comparison of IFN- α and pegylated IFN- α did not reveal any significant differences in tumor growth inhibition, indicating that this novel and more stable class of IFN is functionally equiv. Despite the structural difference between pegylated and conventional IFN- α , both agents caused similar transcriptional responses in human melanoma xenotransplants.

Answer 2:

Bibliographic Information

The modulating effect of interferon alpha-2a on the antitumor activity of UFT against a human gastric carcinoma xenograft, SC-1-NU, in nude mice. Kubota, Tetsuro; Kurihara, Naoto; Kase, Suguru; Watanabe, Masahiko; Kumai, Koichiro; Kitajima, Masaki; Inada, Takao. School of Medicine, Keio University, Tokyo, Japan. *Surgery Today* (1996), 26(1), 12-14. Publisher: Springer, CODEN: SUTOE5 Journal written in English. CAN 124:306730 AN 1996:229275 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The modulating effect of recombinant human interferon alpha-2a (IFN) on the antitumor activity of UFT, a mixed compd. of tegafur and uracil at a molar ratio of 1:4, was investigated against SC-1-NU, a human gastric cancer xenograft serially transplanted in nude mice. IFN was administered s.c. at a dose of 60,000 IU/mouse daily for 14 days, and UFT was given at a dose of 15 mg/kg as tegafur daily, except on Sundays, for 3 wk. The agents were administered either alone or simultaneously. Synergistic antitumor activity on SC-1-NU was produced by the combination of IFN and UFT without any increment of side effects, and the combination therapy also increased intratumoral thymidylate synthetase (TS) inhibition and the amt. of 5-fluorouracil (5-FU) in the intratumoral RNA. Thus, IFN seems to modulate the antitumor activity of UFT against SC-1-NU through an inhibition of DNA synthesis and RNA distortion, and therefore this combination could be useful for clin. application.

Answer 3:

Bibliographic Information

Recombinant human interferon alpha-2a increases the antitumor activity of 5-fluorouracil on human colon carcinoma xenograft Co-4 without any change in 5-FU pharmacokinetics. Kase, Suguru; Kubota, Tetsuro; Watanabe, Masahiko; Furukawa,

Toshiharu; Tanino, Hirokazu; Kuo, Tsong-Hong; Saikawa, Yoshiro; Teramoto, Tatsuo; Kitajima, Masaki. School Medicine, Keio University, Tokyo, Japan. *Anticancer Research* (1995), 15(1), 153-6. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 123:81309 AN 1995:625455 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The authors investigated the modulating effect of recombinant human interferon α -2a (IFN- α) on the antitumor activity of 5-fluorouracil (5-FU) against a human colon carcinoma xenograft (Co-4) in nude mice with ref. to changes in the pharmacokinetic pattern of 5-FU. Mice bearing Co-4 received 5-FU i.p. at a dose of 90 mg/kg once with or without IFN- α , which was administered s.c. at a dose of 60,000 IU/mouse daily for 7 days before 5-FU treatment. When the area under the curve and peak plasma concn. of 5-FU with or without IFN- α were measured as pharmacokinetic parameters, the pharmacokinetics of 5-FU was not changed by IFN- α administration. Apparently, the modulating effect of IFN- α on 5-FU does not involve augmentation of 5-FU pharmacokinetic parameters.

Answer 4:

Bibliographic Information

Recombinant human interferon- α 2a increases hormone receptor level of a human breast carcinoma xenograft in nude mice and enhances the anti-proliferative activity of tamoxifen. Josui, Kazuya; Kubota, Tetsuro; Kitajima, Masaki. Sch. Med., Keio Univ., Tokyo, Japan. *Japanese Journal of Cancer Research* (1992), 83(12), 1347-53. CODEN: JJCREP ISSN: 0910-5050. Journal written in English. CAN 118:145698 AN 1993:145698 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effect of recombinant human interferon- α 2a (rhIFN- α 2a) on the hormone receptor level and antitumor activity of tamoxifen (TAM) was investigated in nude mice using ZR-75-1, an estrogen receptor (ER)-pos., and progesterone receptor (PgR)-neg. human breast carcinoma xenograft. ER levels (max. binding sites) of tumors treated with rhIFN- α 2a at a dose of 6×10^5 U/mouse/day for 1 or 3 wk were not different from the control, whereas those with rhIFN- α 2a at a dose of 6×10^4 U/mouse/day for 1 or 3 wk were higher than the control (3.9-4.4-fold) with a significant difference. The increase of ER by the rhIFN- α 2a was investigated using a sucrose d. gradient method. The peak was only seen at 8 S in both rhIFN- α 2a-treated tumor and control ER, and the sedimentation patterns were almost the same, suggesting that both ERs were essentially equiv. On the other hand, PgR of all the treated groups could be detected, while that of the control group was undetectable. The antitumor effect of the combination treatment of rhIFN- α 2a and TAM was compared with those of single treatments. While rhIFN- α 2a at a dose of 6×10^5 U/mouse/day and TAM did not show a combination effect, rhIFN- α 2a at a dose of 6×10^4 U/mouse/day and TAM showed a synergistic combination effect, and ER was decreased to the threshold of detection by the combination treatment. Thus, a low dose of rhIFN- α 2a increased the ER levels of ER-pos. human breast cancer in vivo as well as in vitro and enhanced the anti-proliferative effect of TAM, and the newly synthesized ER was essentially the same as the original ER.

Answer 5:

Bibliographic Information

Polyamines and human carcinoid: suppression of growth with combinations of α -difluoromethylornithine, somatostatin and interferon. Evers, B. M.; Townsend, C. M., Jr.; Tyring, S. K.; Hurlbut, S. C.; Uchida, T.; Thompson, J. C. Dep. Surg., Univ. Texas, Galveston, TX, USA. *Falk Symposium* (1992), 62(Polyamines Gastrointest. Tract), 335-45. CODEN: FASYDI ISSN: 0161-5580. Journal written in English. CAN 117:204692 AN 1992:604692 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The growth of a functioning human carcinoid cell line, xenografted into nude mice, was suppressed by α , α -difluoromethylornithine, alone or in various combinations with somatostatin or interferon- α -2a. Treatment with these agents did not produce the toxic side effects commonly associated with conventional chemotherapeutic regimens. The relation of these results to the inhibition of polyamine formation

by difluoromethylornithine is discussed.

Answer 6:

Bibliographic Information

Modulation by recombinant α -2A-interferon the activity and mechanism of action of 5-fluorouracil on xenografted human colon cancer in nude mice: preliminary report. Yoshida, Kazuhiko; Fujikawa, Toru; Tanabe, Akihiro; Sakurai, Kenji. Sch. Med., Jikei Univ., Tokyo, Japan. Nippon Geka Gakkai Zasshi (1992), 93(5), 559. CODEN: NGGZAK ISSN: 0301-4894. Journal written in Japanese. CAN 117:142964 AN 1992:542964 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The anticancer activity of 5-fluorouracil (5-FU) can be potentiated by recombinant α -2A interferon (γ INF α -2a). The effects of γ INF α -2a on intratumor levels of 5-FU, 5-fluorodeoxyuridylate (5-FdUMP), and thymidylate synthase were studied to elucidate the modulation mechanism of γ INF α -2a. The intratumor levels of 5-FU and 5-FdUMP in xenografted human colon cancer in nude mice were not changed by the combination of γ INF α -2a. However, the free and total thymidylate synthase (TS) in tumor tissue was significantly increased. The increase in total TS indicated an increase of 5-FdUMP binding to TS, and the increase in free TS may suggest the existence of 5-FU resistance.

Answer 7:

Bibliographic Information

Interferon alpha-2a shows antitumor activity in combination with 5-fluorouracil against human colon carcinoma xenografts: a study in reference to thymidylate synthetase activity inhibition. Kubota T; Inada T; Ogata Y Department of Surgery, School of Medicine, Keio University, Tokyo, Japan Surgery today (1992), 22(5), 481-3. Journal code: 9204360. ISSN:0941-1291. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 1421872 AN 93043976 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

To clarify the mode of antitumor activity shown by a combination of recombinant human interferon alpha-2a (IFN) and 5-fluorouracil (5-FU), experimental therapy was performed on human colon carcinoma (Co-4) xenografts serially transplanted into nude mice, using IFN and 5-FU, either alone or in combination. IFN alone showed dose-dependent antitumor activity and 5-FU also revealed a moderate antitumor effect. Although IFN, given as 600,000 units/mouse daily sc x 14, and 5-FU, given as 60 mg/kg q4d x 3 ip, showed additive antitumor activity against Co-4, the thymidylate synthetase (TS) inhibition rate was unchanged in the tumors treated with the IFN/5-FU combination in comparison with those treated with 5-FU alone. This suggests that the antitumor activity of IFN and 5-FU in combination does not involve augmentation of the TS inhibition by 5-FU.