

Answer 1:

### Bibliographic Information

#### **Combination therapy with antiangiogenic treatment and photodynamic therapy for the nude mouse bearing U87**

**glioblastoma.** Jiang, Feng; Zhang, Xuepeng; Kalkanis, Steven N.; Zhang, ZhengGang; Yang, Hongyan; Katakowski, Mark; Hong, Xin; Zheng, Xuguang; Zhu, Zhenping; Chopp, Michael. Department of Neurology, Henry Ford Hospital, Detroit, MI, USA. Photochemistry and Photobiology (2007), Volume Date 2008, 84(1), 128-137. Publisher: Blackwell Publishing, Inc., CODEN: PHCBAP ISSN: 0031-8655. Journal written in English. CAN 148:162394 AN 2008:128672 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

### Abstract

The objective of this study was to evaluate the effects of combination therapy with photodynamic therapy (PDT) and a novel antiangiogenic regimen using monoclonal antibodies against both vascular endothelial growth factor receptors (VEGFR)-1 (MF1) and VEGFR-2 (DC101) on intracranial glioblastoma xenografts in nude mice. Nude mice bearing intracerebral U87 glioblastoma were treated with PDT and the antiangiogenic regimen (MF1 and DC101) either alone or in combination, while those left untreated served as tumor controls. Tumor vol. and animal survival time were analyzed to evaluate the outcome of different treatment modalities. In addn., the immunohistochem. expression of VEGF in the brain adjacent to the tumor, von Willebrand factor (vWF), apoptotic, and proliferative markers in the tumor area were examd. PDT or MF1 + DC101 alone significantly reduced the tumor vol. and prolonged the survival time of glioma-implanted animals. Combined therapy markedly reduced tumor vol. and increased survival time with significantly better outcomes than both monotherapies. Both vWF and VEGF levels significantly increased after PDT while they both significantly decreased after antiangiogenic treatment, compared with no treatment. PDT plus antiangiogenic treatment led to significant decreases in both vWF and VEGF expression, compared with PDT alone. Either PDT or antiangiogenic treatment alone significantly increased tumor cell apoptosis compared with no treatment, while combination therapy resulted in further augmentation of apoptosis. Antiangiogenic treatment with or without PDT significantly decreased tumor cell proliferation, compared with either no treatment or PDT alone. In summary, we demonstrate both significant inhibition of tumor growth and extended survival of mice treated by the combination therapy with PDT and antiangiogenic agents, compared with each single treatment, suggesting that the combination therapy may be a promising strategy to improve clin. outcomes in glioblastoma.

Answer 2:

### Bibliographic Information

#### **Photodynamic therapy for experimental tumors using ATX-S10(Na), a hydrophilic chlorin photosensitizer, and diode laser.**

Mori, Masahiko; Sakata, Isao; Hirano, Toru; Obana, Akira; Nakajima, Susumu; Hikida, Muneo; Kumagai, Toshio. Medical Research Laboratories, Wyeth Lederle Japan, Ltd., Shiki, Japan. Japanese Journal of Cancer Research (2000), 91(7), 753-759. Publisher: Japanese Cancer Association, CODEN: JJCREP ISSN: 0910-5050. Journal written in English. CAN 133:263278 AN 2000:618468 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

### Abstract

ATX-S10(Na), a hydrophilic chlorin photosensitizer having an absorption max. at 670 nm, is a candidate second-generation photosensitizer for use in photodynamic therapy (PDT) for cancer treatment. The effectiveness of PDT using ATX-S10(Na) and a diode laser for exptl. tumors was evaluated in vitro and in vivo. In-vitro PDT using ATX-S10(Na) and the diode laser showed drug concn., laser dose- and drug exposure time-dependent cytotoxicity to various human and mouse tumor cell lines. In Meth-A sarcoma-implanted mice, optimal PDT conditions were found where tumors were completely eliminated without any toxicity. Against human tumor xenografts in nude mice, the combined use of 5 mg/kg ATX-S10(Na) and 200 J/cm<sup>2</sup> laser irradiation 3 h after ATX-S10(Na) administration showed excellent anti-tumor activity, and its efficacy was almost the same as that of PDT using 20 mg/kg porfimer sodium and a 100 J/cm<sup>2</sup> excimer dye laser 48 h after porfimer sodium injection. Microscopic observation of tumor tissues revealed that PDT using ATX-S10(Na) and the diode laser induced congestion, thrombus and degeneration of endothelial cells in tumor vessels, indicating that a vascular shutdown effect plays an important role in the anti-tumor activity of PDT using ATX-S10(Na) and the diode laser.

Answer 3:

#### Bibliographic Information

**Killing effects of hemoporphyrin derivative-laser on tumors in exptl. animals.** Sun, Zhengfeng; Jiang, Jiawei; Dai, Yanping; Zhang, Hua; Wu, Qingzheng. Section of Laser, Ruijin Hospital, Shanghai 2nd Medical University, Shanghai, Peop. Rep. China. *Shanghai Yixue* (1998), 21(5), 294-295. Publisher: Zhonghua Yixuehui Shanghai Fenhui, CODEN: SIHSD8 ISSN: 0253-9934. Journal written in Chinese. CAN 129:257027 AN 1998:459103 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

#### Abstract

S.c. xenografted S180 sarcoma in Kunming mice grown to diams. of 0.5-0.8 cm after 7-12 days were used to test the killing effect of various hemoporphyrin derivs.: PSD-001, PSD-007, light hemoporphyrin, and photofrin II at doses of 10, 20, and 100 mg/kg in combination with different laser device: the A ion laser with  $\lambda$  of 647 nm, the O ion laser with  $\lambda$  of 630, and the Ag vapor laser with  $\lambda$  of 627 transmitted by light fibers 24 or 48 h after the administration of the drugs. The photosensitive dynamics of various combinations were different, which was related to the drug dosage, the laser power d., and time duration of laser irradiation. The comparative data were reported and evaluated.

Answer 4:

#### Bibliographic Information

**Effects of photodynamic therapy on xenografts of human mesothelioma and rat mammary carcinoma in nude mice.** Gibson, S. L.; Foster, T. H.; Feins, R. H.; Raubertas, R. F.; Fallon, M. A.; Hilf, R. Sch. Med. Dent., Univ. Rochester, Rochester, NY, USA. *British Journal of Cancer* (1994), 69(3), 473-81. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 121:103205 AN 1994:503205 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

#### Abstract

The authors have examined the effectiveness of photodynamic therapy against R3230AC rat mammary adenocarcinoma and human mesothelioma as xenografts in the same host. The results demonstrate that the xenografted human tumor is significantly more responsive to photodynamic treatment than the rodent mammary tumor. Studies also showed that the mesothelioma xenograft was fluence rate- and fluence-dependent while the rat tumor exposed to the same conditions demonstrated neither of these dependencies. This disparity in response was not attributable to a difference in either whole-tumor uptake or subcellular distribution of the porphyrin photosensitizer. Anal. of the effects of visible irradiation on cytochrome c oxidase activity, measured in mitochondria prepared from tumors borne on hosts injected with photosensitizer, demonstrated that photoradiation-induced enzyme inhibition was significantly greater in mesothelioma than in R3230AC mammary tumor preps. However, in parallel studies conducted in vitro, when photosensitizer and light were delivered to previously unperturbed mitochondria, rates of enzyme inhibition were not significantly different. Both tumors were established in long-term cell culture. While the uptake of porphyrin photosensitizer was equiv. in both cell lines, the R3230AC cells displayed a significantly greater photosensitivity than the mesothelioma cells. The data presented here demonstrate that the mechanisms that govern response to photodynamic therapy are complex, but in the case of these two xenografted tumors host response to therapy is not likely to play a significant role.

Answer 5:

#### Bibliographic Information

**Photodynamic therapy of human squamous cell carcinoma in vitro and in xenografts in nude mice.** Megerian, Cliff A.; Zaidi, Syed I.A.; Sprecher, Robert C.; Setrakian, Sebouh; Stepnick, David W.; Oleinick, Nancy L.; Mukhtar, Hasan. Dep. Otolaryngol., Univ. Hospital Cleveland, Cleveland, OH, USA. *Laryngoscope* (1993), 103(9), 967-975. CODEN: LARYA8 ISSN: 0023-852X. Journal written in English. CAN 120:100771 AN 1994:100771 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

**Abstract**

Photodynamic therapy (PDT) of cancer is an exptl. tumor therapy which is based on the combined use of a systemically administered photosensitizer to a tumor-bearing host and local illumination of the lesion by a high-intensity visible light source, typically a tunable argon dye laser. Human squamous cell carcinoma (HSCC) is the most frequently encountered malignancy of the head and neck. In this study, responses of HSCC cells to PDT were examd. in in vitro and in vivo systems. In in vitro studies, the HSCC cells showed a pos. photodynamic response with Photofrin-II (Pf-II), chloroaluminum phthalocyanine tetrasulfonate (AIPcTS), and a newly synthesized silicon phthalocyanine (SiPc IV). Single cell suspension of HSCC injected s.c. on the back of athymic nude mice resulted in a well-circumscribed tumor mass. The animals required a low tumor dose for the successful establishment of a tumor. The tumor was minimally immunogenic and showed neither macroscopic signs of early metastasis to lung, kidney, liver, or spleen nor evidence of surrounding erythema, fluctuation, or tenderness until the late stages of necrosis. I.p. administration of AIPcTS or SiPc IV to tumor-bearing mice resulted in rapid uptake of the photosensitizers in liver, skin, and tumor tissue. At 24 h following the i.p. administration of AIPcTS or SiPc IV to tumor-bearing animals, the tumor to normal skin ratio of the photosensitizer was 1.6 or 1.5, resp. Administration of Pf-II (5 mg/kg) to tumor-bearing animals followed 24 h later by irradiation of the tumor (135 J/cm<sup>2</sup>, 630 nm light from an argon pumped-dye laser) resulted in >80% ablation in tumor vol. 24 h post-PDT. These characteristics make this tumor model system suitable for PDT studies of human tumor cells in vitro as well as in vivo.

Answer 6:

**Bibliographic Information**

**Photoimmunodiagnosis with antibody-fluorescein conjugates: In vitro and in vivo preclinical studies.** Pelegrin, A.; Folli, S.; Wagnieres, G.; Braichotte, D.; Buchegger, F.; Chatelain, A.; Van den Bergh, H.; Mach, J. P. Inst. Biochem., Univ. Lausanne, Epalinges, Switz. *Journal of Cellular Pharmacology* (1992), 3(1), 141-5. CODEN: JOCPEK ISSN: 0939-1096. Journal written in English. CAN 118:142614 AN 1993:142614 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

**Abstract**

The use of dyes has been helpful for the photodiagnosis of small cancers accessible to endoscopic examn. An important limiting factor of this technol. is that the presently used fluorescent dye mixt. has a relatively poor capacity to accumulate preferentially in malignant tissue and a low quantum yield of fluorescence. To improve these parameters, fluorescein was coupled to an anti-carcinoembryonic antigen (CEA) MAb and the biodistribution of several conjugates was studied in nude mice bearing a human colon carcinoma xenograft. In vitro, such conjugates with fluorescein to MAb molar ratios ranging 4-19, trace labeled with <sup>125</sup>I, showed >82% binding to insolubilized CEA. However, since the aim of this work was the evaluation of MAb-dye conjugates designed for in vivo tumor localization, all newly prepd. MAb-fluorescein conjugates were tested in the exptl. model of nude mice bearing CEA expressing human colon carcinoma xenografts. Under these exptl. in vivo conditions, the conjugate contg. 10 fluorescein mols. per MAb mol. gave an excellent tumor localization (up to 30% of the injected dose per g tumor at 24 h), whereas a conjugate with 19 fluorescein mols. per MAb mol. gave almost no in vivo localization in the tumor, probably due to a very short half-life. Tumor-to-liver, -kidney, and -muscle ratios of 20, 30, and 72, resp., were obtained at 48 h after injection of the conjugate contg. 10 fluorescein mols. per MAb mol. In the spectrofluorometric anal., a high fluorescence intensity was obsd. in the tumor after injection of the anti-CEA MAb conjugate. To compare these results with a conventionally used dye, mice bearing the same xenografts received a purified form of hematoporphyrin, Photofrin II. The intensity of the fluorescence signal of the tumor after an injection of 0.44 µg fluorescein coupled to 20 µg of MAb was 8-fold higher than that obtained after injection of 60 µg of Photofrin II.

These results illustrate the possibility of improving the specificity of in vivo tumor localization of dyes for laser-induced fluorescence photodetection and phototherapy by coupling them to MAb directed against tumor markers.

Answer 7:

**Bibliographic Information**

**The effect of glucose administration on the uptake of Photofrin II in a human tumor xenograft.** Peng, Q.; Moan, J.; Cheng, L. S. Dep. Biophys., Inst. Cancer Res., Oslo, Norway. *Cancer Letters* (Shannon, Ireland) (1991), 58(1-2), 29-35. CODEN:

CALEDQ ISSN: 0304-3835. Journal written in English. CAN 115:67635 AN 1991:467635 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

**Abstract**

Athymic BALB/c nude mice bearing a human melanoma cell line LOX were given the photosensitizing drug Photofrin II (10 mg/kg) i.p. Mice were also given i.p. glucose, galactose, or glucose plus nordihydroguaiaretic acid (NDGA, an inhibitor of glycolysis). Multiple injections of glucose (3 g/kg) given at -1, 0, +1, and +3 h relative to the injection of Photofrin II at time 0 increased the uptake of Photofrin II in the tumor 4 h after the Photofrin II injection, while the uptake in the other tissue remained unchanged. Galactose had no effect on the uptake of Photofrin II in the tissues studied (tumor, muscle, skin, and liver). NDGA abolished the effect of glucose.