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Poster Presentations - Radiation-Induced Cytokines and Normal Tissue Effects

Abstract 4341: A novel sonodynamic therapy using hydroxyl radical generated from ultrasound activated TiO_2 for human epithelial carcinoma cells

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<Background and Objective> Radical oxygen species, which are produced by the action of some chemotherapy drugs, radiation and some types of anticancer agent, are known to mediate cytotoxic activity by modifying the cellular homeostatic redox balance. Photodynamic therapy uses photosensitizers activated by light to induce cell death via formation of free radicals and is actually used in clinical setting. However the limited tissue penetrability of light has been a crucial problem because most of cancers often develop in deep tissue. The generation of hydroxyl radical was investigated during ultrasonic (US) irradiation and in the presence of titanium dioxide (TiO2) (Shimizu, et al. Ultrason. Sonochem. 2008). In this study, the effect of US combined with TiO2 particles on human epithelial carcinoma cell (A431) was investigated in vitro and in vivo. <Methods> TiO2 nanoparticles used were uniform in size of about 200 nm in diameter. A431 ($1.0x10^6$) were irradiated with US in the various density of TiO2 particles (0 to 10mg/ml). Cell viability was measured immediately after US irradiation (1 MHz, 2.0 W/cm2 for 30, 60, 120 and 300 sec) by using trypan blue exclusion assay. The effect of the combination of TiO2 particle injection (0.1, 1.0 and 10mg, day5) and US exposure (1 MHz, 2.0 W/cm2, 5 min duration, day 5, 7, 9, 11, 13) on subcutaneously implanted A431 solid tumors in female BALB c nu/nu mice were investigated by measuring tumor volume. <Results> The cell viability was significantly decreased after US irradiation in the presence of high dose of TiO2. In vivo results also showed significant inhibition of tumor growth in groups treated with high dose of TiO2 particles and US. The efficacies of US could not be demonstrated combined with low dose of TiO2 particles.<Conclusion> Our results demonstrate the potent toxicity of TiO_2 combined with US irradiation against tumor in vitro and also the growth inhibition of tumors in a mouse xenograft model. Moreover the cytotoxic efficacy of TiO_2 was dependent on the amount of TiO_2 particles attaching to cancer cells. These results suggest that the effective and low toxic method for accumulation of TiO2 in the tumor (injection, arterial injection, DDS, etc.) should be necessary for clinical use.

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