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Ultrasound Enhances the Efficacy of Chlorin e6-Mediated Photodynamic Therapy in MDA-MB-231 Cells

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Abstract

Sono-photodynamic therapy (SPDT) is a new modality for cancer treatment. Some studies have reported enhanced tumor cytotoxicity when sonodynamic therapy (SDT) is combined with photodynamic therapy (PDT). In this study, we investigated the cytotoxic effect of SPDT-activated chlorin e6 (Ce6) on MDA-MB-231 cells. Ce6 was found to localize mainly in mitochondria, with maximal uptake within 4 h. Cell survival was estimated by MTT (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltertrazolium bromide tetrazolium) assay 24 h after irradiation; the combined therapy enhanced cytotoxicity to a greater extent. Apoptosis was analyzed using annexin V-PE/7-ADD (*7*-aminoactinomycin D) staining as well as DAPI (4', 6-diamidino-2-phenylindole) staining, and the results indicated that the cells with apoptotic characteristics were significantly increased in groups given combined therapy. Rhodamine-123 staining and cytochrome c release revealed more serious damage of mitochondria after combined treatment. The generation of reactive oxygen species detected by flow cytometry was greatly increased in cells treated with the combination therapy, and the loss in cell viability could be effectively rescued with the reactive oxygen species inhibitor *N*-acetylcysteine. Moreover, enhancement of cell membrane permeability after ultrasound treatment was evaluated using FD-500, and it was found that the much higher uptake of Ce6 might be involved in PDT therapy with pre-treatment ultrasound. These results suggest that ultrasound enhances the cytotoxicity of Ce6-mediated PDT, possibly because of the increased intracellular Ce6 level and ROS formation by ultrasound pre-treatment.