Ultrasound Induced Gene Transfection and its Implication in Cancer Gene Therapy

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Ultrasound has been used for cancer hyperthermia therapy and recently been reported to facilitate gene Transfection in vitro. To understand the mechanism for this gene Transfection and to explore the potential application in cancer gene therapy, the influence of different ultrasonic exposure and cell conditions on Transfection efficiency were tested. Cultured Chinese hamster ovary cells at stationary or logarithmic phase were exposed to 2.25 MHZ ultrasound in the presence of 10% Albunex and 20 ug/ml luciferase reporter vector pGL_2. Sterile polyethylene exposure chambers filled with 4.5 ml of the cell suspension in medium with or without serum were rotated at 60 rpm during the one-minute exposure. After exposure, cells were cultured for two days for the analysis of luciferase gene expression and cell proliferation.

Cell proliferation decreased with the increasing exposure pressure amplitudes. At the exposures of 0, 0.28, 0.40, 0.56, and 0.80 MPa, 0.017, 12, 100, 130, and 130 pg (in serum-free medium), and 0.0065, 33, 260, 300 and 330 pg (in medium with 10% serum) of luciferase per 10^6 cells were obtained, respectively, for the cells at logarithmic phase. No significant difference was found when cells were exposed at either stationary or logarithmic phase. Exposure at 0.8 MPa of cell suspensions without Albunex and without chamber rotation, which minimizes ultrasonic cavitation, yielded cell proliferation and luciferase activity essentially equal to shams.

These results suggest that ultrasonic cavitation, which produces sonoporation of plasma membrane, is responsible for the observed gene Transfection. The advantages of Transfection by sonoporation include that the efficiency is no significantly influenced by the stage of cell growth and the Transfection can be done in the complete medium with serum. These advantages, along with the ability to focus ultrasound in most areas of the body could provide a novel approach in many medical applications such as cancer gene therapy.

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