In Vivo Transfection of Melanoma Cells by Lithotripter Shock Waves[1]

Shiping Bao, Brian, D. Thrall, Richard A. Gies, and Douglas L. Miller[2]

United States Transuranium and Uranium Registries, Washington State University, Richland, Washington 99352 [S. B.], and Battelle Pacific Northwest National Laboratory, P O Box 999, Richland, Washington 99352

The potential for gene transfection during shock wave tumor therapy was evaluated by searching for shock wave-induced DNA transfer in mouse tumor cells. B16 mouse melanoma cells were cultured by standard methods and implanted s.c. in female C57BL/6 mice 10-14 days before treatment. A luciferase reporter vector was used as the DNA plasmid for intratumoral injection at 0.2 mg/ml tumor. Air at 10% of tumor volume was injected after the DNA in some tumors to enhance acoustic cavitation activity. The shock wave generation system was similar to a Dornier HM-3 lithotripter with pressure amplitudes of 24.4 MPa peak positive and 5.2 MPa peak negative. Luciferase production in isolated tumor cells was measured with a luminometer 1day after treatment to assess gene transfer and expression. Exposure to 800 shock waves, followed by immediate isolation and culture of tumor cells for 1day, yielded 1.1 (0.43 SE) pg/10^6 cells for plasmid injection only and 7.5 (2.5 SE) pg/10^6 cells for plasmid plus air injection. Significantly increases luciferase production, relative to shams, occurred for 200-, 400-, 800-, and 1200-shock wave treatments with plasmid and air injection. Gene transfer therefore can be induced during lithotripter shock wave treatment *in vivo*, particularly with enhanced acoustic cavitation, which supports the concept that gene and shock wave therapy might be advantageously merged.

USTUR-0083-97