The Effect of Ultrasound on Osmolysis of Metastatic Carcinomas

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Unlike most normal cells, aggressive carcinomas overexpress voltage-gated sodium channels (VGSC). Studies demonstrate a positive correlation between cancer cell aggressiveness and VGSC overexpression. Simultaneous blockage of Na+/K+-ATPase (sodium pump) and electrical activation of VGSC causes osmolysis in cancer cells. However, electrical stimulation follows narrow paths through tissue, decreasing effectiveness. Non-electrical stimuli such as ultrasound can also activate VGSC but with greater consistency. The goal of this study is to develop a new cancer treatment using simultaneous blockage of Na+/K+-ATPase and activation of VGSC by ultrasound to lyse cancer cells. Cancer cells were incubated with 100 nM ouabain and 4 uM veratridine for thirty minutes, followed by twenty minutes of continuous ultrasound stimulation (55 kHz, ~0.20 W/cm2). Cell viability was measured using a trypan blue assay and cell counts. Five cell lines were tested. Full treatment with ouabain, veratridine, and ultrasound resulted in the greatest amount of cell death compared to partial treatments. This is likely because full treatment produces the greatest intracellular sodium concentration. Amounts of cell death also directly correlated with the degree of VGSC overexpression, indicating this treatment would be most effective against aggressive cancers. However, MCF-10a cells (normal epithelial breast) showed significant cell death in response to ultrasound stimulation regardless of drug administration. This could be due to high vulnerability of this cell line to stimulation parameters in this study. The results of this study demonstrate that simultaneous Na+/K+-ATPase blockage and ultrasonic VGSC activation can be a promising new cancer treatment.