Mechanism of Targeted Chemotherapeutic Delivery Using Ultrasound

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Mechanism of Targeted Chemotherapeutic Delivery Using Ultrasound

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Abstract #1415

Introduction

Ultrasound (US) is used to enhance and target delivery of drugs and genes to cancer tissues. The advantages of focused delivery to select tissues are numerous, but the exact mechanisms, an acoustical and non-thermal effect, need further study. Recent data from this laboratory show that collapse cavitation in US induced permeabilization of cell membranes and subsequent drug uptake by the cell. Elaborative results from this laboratory have shown that increased membrane permeability is proportional to exposure time, and as the cell membrane is perturbed, the cell uptake of a model drug increases. This study investigated the hypothesis that collapse cavitation is involved in drug delivery.

Materials and Methods

Reagents. Calcein (420.2 g/mol) (MP Biomedicals, Inc., Aurora, OH) was dissolved into 1X DPBS (0.137 M sodium chloride, 4.447 M potassium chloride, 12.55 M sodium phosphate dibasic, and 4.76 M sodium chloride). Propidium iodide (PI) (Sigma Chemical, St. Luis, MO) was added to 0.5 mL of cell suspension. Pressure was applied to the interior of the sample at the focal point of the transducer (Fig. 6). Within this tube a small rod held a small ultrasound transducer. An X by Y by Z chamber was filled with the cell solution and closed on one side on the other side of the chamber was a Luer lock with acoustic absorbing rubber and open at the top. Placed on one wall was the 500 kHz transducer. The ultrasound transducer was connected to the transducer driver (model 5010, Panametrics, Waltham, MA) and computer interface (model 5100A, Panametrics, Waltham, MA). The ultrasonic transducer was turned on at the time of the experiment and increased, the bubbles start out more compressed, which in turn decreases the magnitude of cavitation. At certain thresholds of intensity or resonant frequencies, ultrasound causes collapse cavitation, which in turn will reduced membrane permeability.

Results

Calcein is currently used for diagnostic and therapeutic purposes. Diagnostic ultrasound utilizes the fact that ultrasound produces expansile cavitation and can therefore be used to detect fluid-filled internal structures. Ultrasound is widely used in physical therapy applications. The frequencies typically used for diagnostic purposes are from about 3 to 10 MHz. Ultrasound can be used in many ways. In this current study, calcein was used as a model drug. This study investigated the hypothesis that collapse cavitation is involved in drug delivery.

Discussion

Conclusions

This research has advanced our understanding of the mechanism of intravenous ultrasound targeted drug delivery to cancer cells. The data indicate that collapse cavitation occurs in the application of ultrasound and is the cause of membrane permeabilization. The amount of membrane permeabilization is proportional to ultrasound exposure. At the resonant frequencies and intensities there was an increase in cell death above control samples.