Ultrasound-responsive Nanoparticles for Neurotherapeutic Delivery

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Neurodegenerative diseases cause incurable neuronal damage and often result in fatality. A major challenge in treating neurodegenerative diseases is the inability to deliver drugs to the brain due to the blood-brain barrier (BBB). To circumvent this problem, ultrasound-responsive nanoparticles were designed and tested as a potential solution for localized drug delivery to the brain. Liposomes, used as drug delivery vehicles, were conjugated to microbubbles (μBs) and treated with focused ultrasound (FUS). FUS causes μBs to cavitate and liposomes to burst, temporarily disrupting the BBB and allowing drugs to enter the brain. Liposome-conjugated μBs were prepared and tested for neurotherapeutic viability. Both μBs and liposomes were prepared using synthetic lipids with functionalized PEG linkages for self-conjugation. Liposomes were evaluated by encapsulating fluorescent dye and/or MRI contrast agent. Viability was analyzed using fluorescence microscopy, MRI, mathematical analysis, FUS, and particle sizing. Fluorescence microscopy demonstrated successful conjugation of liposomes onto μBs. MRI demonstrated that liposomes readily released encapsulated content when treated with FUS and heat; there was a 338% increase in R1 values between treated and untreated samples. However, mathematical analysis indicated that content release was only 24% efficient. Particle sizing over three weeks showed stable liposomes with a standard deviation of ±10 nm from initial diameters. This indicates secure shelf life and viability in medical applications. Future work includes increasing delivery efficiency of drug-encapsulated liposomes and in vivo experiments. This study is a step towards the use of liposome-conjugated μBs as a targeted, noninvasive drug delivery method to the brain.