Name(s)
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Project Number
S0614

Project Title
Developing Phase Change Nanoparticles for Focused Ultrasound Induced Targeted Neuromodulatory Drug Release

Abstract

Objectives/Goals
The current, commonly-used technique of systemic drug delivery for modulating brain function lacks specificity, decreases efficiency, and threatens patient safety. An urgent need exists for a new approach towards noninvasive, targeted drug delivery to the brain. To address this need, this study embraces two unique elements: 1. Drug encapsulation in phase-change nanoparticles, and 2. Drug release via focused ultrasound (FUS).

Methods/Materials
Stage 1: The anesthetics propofol and dexmedetomidine were each encapsulated in phase-change nanoparticles with a biodegradable PEG-PLGA amphiphilic block copolymer matrix. Perfluoropentane (PFP), emulsified through sonication, formed the liquid core of the nanoparticles.
Stage 2: Nanoparticle properties of size, polydispersity, and drug loading were quantified.
Stage 3: In vitro drug release via FUS was performed in a water bath. The released drug was captured in a layer of solvent above the aggregate of nanoparticles, and this layer was then extracted for drug release measurement.

Results
The hydrodynamic diameters of both propofol-loaded nanoparticles and dexmedetomidine-loaded nanoparticles were less than 500 nm, essentially eliminating the risk of embolism in capillaries; the polydispersity indices were less than 0.1, lending constancy to the pharmacokinetics and biodistribution of the nanoparticles. The nanoparticles were effective in encapsulating propofol, but encapsulation of dexmedetomidine was more challenging, potentially due to precipitation of dexmedetomidine out of the micelle. The maximum drug release in vitro occurred at 1.7797 MPa (42.26% for propofol and 54.34% for dexmedetomidine).

Conclusions/Discussion
The results of this study indicate that phase-change nanoparticles can successfully encapsulate neuromodulatory drugs and respond effectively to focused ultrasound. This novel approach to neuromodulation establishes a platform for developing phase-change nanoparticles for all small-molecule lipophilic neuromodulatory drugs, and thus for any molecule that passively crosses the blood-brain barrier (BBB). FUS-induced drug release from phase-change nanoparticles improves safety (no BBB opening, clinically-approved particle components) and specificity (local drug release, high spatial and temporal resolution), with ideal attributes for clinical translation and important applications for treating cancer and neurodegenerative diseases.

Summary Statement
My project establishes a novel platform for developing phase-change nanoparticles for all small-molecule lipophilic neuromodulatory drugs for focused-ultrasound induced targeted drug delivery to the brain.

Help Received
I acknowledge my family and teacher for their constant support, and Dr. Raag Airan and Qian Zhong from Stanford University for guidance and for giving me the opportunity to develop my project in their lab.