Polymer-coated lipid microbubbles for safe, efficient, highly localized gene delivery

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Technology description

Summary

Gene therapy, the process of introducing genomic material into host cells for therapeutic benefit, has been used to treat numerous genetic conditions and cancer. However, current gene delivery methods have suffered from low efficacy and technical limitation, decreasing their clinical impact. The most common and effective gene delivery method is based on viral particles, which have limited cargo capacity, high-production costs, are difficult to manufacture, and carry a risk of inflammation and mutagenesis, resulting in grave safety concerns. This technology utilizes lipid microbubbles optimized with a polymer coating to target genes directly to a site of interest without the use of virus particles. The technology provides a safe, efficient, and highly localized method of gene delivery that can be adapted for other cargo, such as biological materials, synthetic compounds, and contrast dyes. As such, the technology provides a robust and precise delivery system that can be used to both diagnose and treat multiple diseases, giving it a wide range of clinical applications.

Polymer-coated microbubbles for increased DNA binding capacity, effective gene transfection, and safe, economical gene delivery

This technology increases gene transfection by chemically engineering lipid microbubbles with high bioavailability and DNA loading capacity. Microbubbles have previously been used to enhance ultrasound contrast imaging and open the blood-brain barrier, as they break when hit with an ultrasonic pulse. While attempts have been made to conjugate microbubbles with plasmid DNA using electrostatic interactions in the past, gene expression and DNA capacity has been low, limiting their utility. Instead, this technology coats the surface of lipid microbubbles with polyethylenimine (PEI), a polymer that is known to increase gene transfection efficiency and DNA loading capacity, using thiolation. Additionally, inert polyethyleneglycol (PEG) is used to improve biocompatibility and mitigate PEI cytotoxicity. The PEI-PEG microbubbles are injected intravenously and when ultrasound is applied to a site of interest, only those bubbles at the site burst and release their DNA payloads. With the

polymer coating, transfection efficiency is expected to be higher and safer than other gene delivery methods, making microbubbles more cost effective in comparison to virus particles.

A prototype of this technology has been shown to bind up to four times as much DNA as cationic microbubbles, and successfully targets DNA constructs to tumors in mouse models.

Publications

Sirsi SR, Borden MA. "Advances in ultrasound mediated gene therapy using microbubble contrast agents." Theranostics. 2012 Feb (12):1208-22.

Application area

Cargo carrier for targeted gene therapy

Oxygen delivery to hypoxic tissues

Carrier for drug delivery across blood-brain barrier

Ultrasound contrast agent for clinical diagnostics

Advantages

Microbubbles are a versatile, safe cargo delivery method
Cheaper production costs in respect to viral vectors
Simpler production scheme
Can carry genes, drugs, gases, and chemical contrast dyes
Can cross blood-brain barrier
Can be targeted using ultrasound
Can be used in both research and clinical settings

Institution

Columbia University

Inventors

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