Assessment of Soluble Cancer Biomarkers for Focused Ultrasound Therapy

Addressing critical barriers in noninvasive delivery and monitoring of anticancer agents in tumors

Inventors at Georgia Tech are advancing innovations and methods to longitudinally assess focused ultrasound (FUS)-targeted drug delivery and monitor the response to therapy. Key to this innovation is a hybrid Droplet Digital PCR™ targeted next-generation sequencing assay combined with novel closed-loop image guidance methods. These technologies together enable quantitative assessment of the secretion of cancer soluble biomarkers, such as circulating tumor DNA (ctDNA), in body fluids. Molecular reporters tag the ctDNA secreted by cancel cells in the blood, which can help medical professionals assess the efficacy of FUS-based therapeutic approaches and adjust them as needed in order to optimize treatments.

Summary Bullets

- **Simple**: Avoids reliance on magnetic resonance imaging (MRI)-based methods of monitoring and optimizing FUS therapy
- **Safe**: Relies on a small amount of fluid collected before/after FUS-targeted drug delivery
- **Robust**: Enables a range of new therapeutic interventions for cancerous tumors as well as both delivery and monitoring/optimizing of those therapies

Solution Advantages

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Potential Commercial Applications

- Monitoring and optimization of FUS-based therapy for treating disease such as cancer
- FUS-based delivery of anticancer agents to solid tumors

Background and More Information

Effective delivery of therapeutics for tumors, particularly of the brain, remains a major medical challenge. With the permeability of the blood brain barrier (BBB) decreasing 100-fold when the size of the drug is increased from 300 Da to 450 Da, BBB becomes one of the rate-limiting factors in the translation of blood-borne therapeutics into clinically effective therapy. Recent preclinical investigations have shown that FUS-based therapy enhanced by microbubbles can improve the permeability of the BBB to small and large molecular-weight anticancer agents as well as nanomedicine, thereby enhancing drug penetration and uptake.

Longitudinal assessment and quantification of FUS-meditated changes in BBB permeability and therapy is crucial for identifying appropriate treatment windows. While contrast MRI can assess changes in BBB permeability, safety is a significant concern due to the need for repeated dosing, especially for longitudinal measurements. By recognizing that the transport across the BBB is bidirectional, Georgia Tech investigators have provided evidence that detection of soluble molecules, such as ctDNA secreted by cancer cells in the blood, can provide a simple and effective method to assess FUS-mediated changes in BBB filtration.

Droplet Digital PCR is a trademark of Bio-Rad Laboratories, Inc. in certain jurisdictions.

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IP Status

: 63/024,544

Publications

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