

Ultrasound Modulation and Imaging in In Vitro Models

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Abstract: Recent advances in in vitro biological models, including organoids and engineered tissue constructs, have created new opportunities for investigating cellular responses and disease mechanisms in physiologically relevant environments. However, effective methods for noninvasive stimulation and quantitative readout of these systems remain limited. In this presentation, we introduce emerging approaches that integrate ultrasound-based modulation with advanced imaging and sensing techniques to interrogate biological processes in in vitro models.

First, we demonstrate that controlled ultrasound stimulation can modulate extracellular vesicle secretion from brain organoids. By coupling ultrasound-induced exosome release with surface-enhanced Raman spectroscopy (SERS), we establish a sensitive platform for molecular profiling of secreted vesicles. Using this approach, we show the potential to distinguish APOE genotypes through exosome-derived molecular signatures, suggesting a new strategy for noninvasive phenotyping of neurodegenerative disease models.

Second, we present label-free imaging of neuromelanin in brain organoids using photoacoustic microscopy. The strong optical absorption of neuromelanin enables high-contrast visualization and quantitative analysis of neuromelanin distribution in three-dimensional neural tissues. This technique provides a non-destructive imaging method for studying dopaminergic neuron development and degeneration in Parkinson's disease-related models.

Finally, we discuss the potential of photoacoustic imaging for drug response evaluation in organoid systems, providing a label-free approach to monitor structural and biochemical changes in three-dimensional in vitro models.

Together, these studies highlight the emerging role of ultrasound-based stimulation combined with multimodal imaging and sensing for probing biological activity in advanced in vitro models. These approaches may enable new platforms for disease modeling, biomarker discovery, and therapeutic evaluation.