

Chem 218: Student Exit Seminar

Lipid and Acoustic Strategies for Chemical Patterning and Gene Delivery



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ABSTRACT: Supported lipid membranes are versatile biomimetic coatings for the chemical functionalization of inorganic surfaces. Developing simple and effective fabrication strategies to form supported lipid membranes with micropatterned geometries is a long-standing challenge. We demonstrate how the combination of chemical lift-off lithography (CLL) and easily prepared lipid bicelle nanostructures can yield micropatterned, supported lipid membranes on gold surfaces with high pattern resolution, conformal character, and biofunctionality. We further showed that bicelles can be used as a passivation strategy to reduce fouling in microfluidics designed for intracellular delivery. Of note, constricted microfluidic geometries that deform cells to a fraction of their diameter have emerged as a promising technology that facilitates high-performance gene editing. Unfortunately, these technologies are inherently limited by device lifetime due to the accumulation of cellular debris and eventual clogging. As these microfluidic technologies transition from conceptual prototypes to functional tools, there is a need to develop next-generation platforms with high-throughput and long lifespan. Towards this goal, we report the design and application of lipid-coated microfluidic and acoustofluidic platforms that are able to deliver plasmid rapidly and safely to model and human primary cell types. Our lipid-coated microfluidic system demonstrated a dramatic reduction in fouling, with blocking efficiency towards nonspecific protein adsorption and cell adhesion as compared to bare polydimethylsiloxane and glass microfluidic devices. We explored the application of our lipid layer by coating constricted microfluidic channels designed for the intracellular delivery of biomolecular cargo. We observed significant reductions in the accumulation of cell debris and delivery of large dextran molecules and plasmid while retaining high viability. In parallel, we developed an acoustofluidic method to deliver plasmids to immortalized and primary human cell types, based on the permeabilization of cell membranes with acoustic waves and shearing against the walls of glass microcapillaries. This acoustofluidic-mediated approach achieves fast and efficient intracellular delivery of an enhanced green fluorescent protein-expressing plasmid to cells at a scalable throughput of 200,000 cells/min in a single channel. Analyses of intracellular delivery and nuclear membrane rupture revealed mechanisms underlying acoustofluidic delivery and successful gene expression. Collectively, our studies show that these technologies are promising platforms for gene delivery and useful tools for investigating membrane repair.

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12:00 p.m.