Developing Biomimetic Platforms Containing Biomembranes: Enabling Study of Membrane Proteins in Action

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Membrane proteins (MPs) reside within the cellular membrane and play a key role in modulating a wide range of physiological processes, from neuronal signaling to immune and hormonal response. Their malfunctioning has been implicated in various diseases ranging from cancer and cardiovascular disease to immunological and neuropsychiatric disorders, which makes them the most important pharmaceutical target. Studying MPs in vitro is very challenging due to the difficulties associated with stabilizing the hydrophobic domains of these proteins outside the native lipid environment while maintaining their functional activity. Additionally, this class of proteins have proven to be intractable for crystallization. Biomembrane-mimicking systems are emerging as a promising approach for the biochemical/biophysical characterization of MPs. I will discuss our progress in creating biomimetic platforms comprising functionally active MPs reconstituted in a detergent/lipid environment. We utilize intermolecular interactions and tailored syntheses to create biomimetic nanostructures to: stabilize MPs, interface MPs with the outside world, and serve as a biosensor recognition element. Furthermore, we have developed experimental and computational methods based on neutron scattering techniques for elucidating the structural information of MPs in biologically active configurations. These model systems and methods enable us to generate crucial knowledge about the structure-function relationship of MPs for rational design of therapeutics, in addition to advancing biosensors and high-throughput drug screening platforms.