Recent discoveries have elucidated the crucial role for liquid-liquid phase separation phenomena in cellular biology. I will briefly introduce recent discoveries in three-dimensional phase partitioning of the cytoplasm and nucleoplasm, followed by our recent observations on phase separation in mammalian plasma membranes. The plasma membrane is the physical and functional interface between a cell and its environment, and is responsible for a myriad of parallel processing tasks that must be tightly regulated to avoid aberrant signaling. To achieve this functional complexity, mammalian cells produce hundreds of lipid species that are actively turned over and trafficked to produce spatial and temporal gradients between cellular compartments. Membrane physiology is also dependent on the physical phenotypes arising from the collective behaviors of lipids. A key example is the partitioning of membranes into functional lateral domains, e.g. membrane rafts. Although such domains have been implicated in many cellular processes, their properties, compositions, and precise functional roles remain elusive. I will present the results of two distinct projects that address:

1. Metabolic engineering of mammalian membranes. We explore the consequences of dietary lipid inputs on membrane composition, organization, and function in the context of directing mesenchymal stem cell differentiation.
2. Protein partitioning between coexisting membrane phases. Using experimental and computational approaches, we are defining the relationships between protein structure and their affinity for ordered membrane domains. From these insights, we explore the functional connections between ordered lipid phases and sub-cellular traffic.

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