Phase separation and biomolecular condensates in biology and disease

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Condensates formed by liquid-liquid phase separation can create functionally distinct membraneless compartments consisting of proteins and RNAs, which have major roles in cellular organization and physiology. RNP granules are a specific type of condensates that assemble by phase separation of RNA-binding proteins (RBPs) and RNA. Recent data also suggest that aberrant phase transitions of RBPs into RNA/protein aggregates may be closely tied or even causative to the pathogenesis associated with diseases such as amyotrophic lateral sclerosis.

In this talk, I will discuss how the concept of biomolecular condensates has expanded our view of biology and disease. I will introduce in vitro reconstitution systems based on condensation that now allow us to rebuild complex structures such as RNP granules in the test tube. Using these reconstitution systems, we have gained important insights into the molecular rules of RNP condensates, such as the molecular grammar and conformational changes underlying condensate assembly, the driving forces and amino acids that govern aberrant phase transitions, and molecular mechanisms of condensate regulation and control. I will further discuss how the concept of phase separation has allowed us to identify novel functions of RNP condensates, and I will demonstrate how phase separation can be used by cells to sense and respond to changes in the environment and regulate fundamental cellular processes such as protein synthesis.