Liquid-liquid phase separation in the tales of intrinsically disordered proteins

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Tons of biomolecules react in a cell simultaneously, but how does one biomolecule "know" where and when to react? The prevailing intrinsically disordered proteins (IDPs; >30% in eukaryotic cells) or proteins with intrinsically disordered regions (IDRs; >50% in eukaryotic cells), which do not adopt a defined three-dimension structure, may play a role in the spatiotemporal control of biochemical reactions. Recent studies have demonstrated that some IDPs undergo liquid-liquid phase separation (LLPS) to respond to environmental changes (e.g. temperature, pH) to determine the timing of a reaction ("when"). The increased local concentration within phase-separated droplets also controls the location ("where") to react. The physicochemical properties of these ID regions probably govern the location and timing for a molecule to react. In this talk, I will use TDP-43 [1,3,4], galectin-3 [2,5], and Musashi protein families [6] as examples to demonstrate how the physicochemical properties of IDRs can relate to their cellular functions and diseases.

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