Genetic Level Programming of Molecular Assembly of Intrinsically Disordered Proteins

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A number of dynamic, protein-rich intracellular structures containing phase separated, unstructured proteins comprising low-complexity amino acid sequences have recently been shown to serve a variety of important cellular functions, including signaling, compartmentalization and stabilization. The understanding of these structures, and the ability to synthesize models of them, has been limited. In this talk, we present simple methods for programming diverse assemblies comprised of a series of elastin-like polypeptides, model intrinsically disordered proteins possessing sequences of low-complexity. By encoding the stimulus-induced aqueous phase behavior of proteins at the amino acid sequence level, we demonstrate the reversible formation of a variety of protein-rich structures, ranging from uniform nano-, meso-, and micro-scale puncta (small, distinct particulates) to multilayered, orthogonally-phase-separated, multicomponent microgranules. We further show how such nanoscale assemblies (i) can be stabilized by controlled biomineralization, (ii) can be used for simple bioassays for diagnostic or drug discovery applications, or (iii) can be used as building blocks for the hierarchical formation of micellar hydrogels with surprising mechanical properties and potential use in controlled delivery of nanoparticles for drug delivery applications.