Protein phase transition: from biology towards new protein materials

Many cellular organelles can form via phase separation of proteins and nucleic acids. Yet, the molecular mechanisms that govern the lifetime, the composition and the size of these membrane-less compartments remain largely elusive. Here, we analyze the microscopic processes underlying the phase separation of biological proteins, and we use these lessons to induce controlled self-assembly of soluble proteins in biotechnology. Specifically, we focus on the phase separation of the DEAD-box protein ATPase Dhh1, which is strongly associated with the formation of processing bodies (P-bodies) in yeast. We identify the role of ATP and RNA in triggering the nucleation and growth of the protein-rich droplets, as well as in maintaining the protein dense phase in the liquid state. These results reveal molecular mechanisms that cells have plausibly developed to accurately control the reversible assembly and the biophysical properties of P-bodies. Moreover, we demonstrate the possibility to mimic these mechanisms and induce similar behaviours in soluble proteins by conjugating low complexity domains to soluble globular regions. We show that these biologically derived molecular adhesives enable the self-assembly of these proteins into supramolecular architectures via a multistep process. This multistep pathway involves an initial liquid−liquid phase transition, which creates protein-rich droplets that mature into protein aggregates over time. These protein aggregates consist of permeable structures that maintain activity and release active soluble proteins. We further demonstrate that this feature, together with the dynamic state of the initial dense liquid phase, allows one to directly assemble different globular domains within the same architecture, thereby enabling the generation of both static multifunctional biomaterials and dynamic microscale bioreactors.

References

Faltova L., Küffner A. et al, “Multifunctional Protein Materials and Microreactors using Low Complexity Domains as Molecular Adhesives”, ACS Nano, 2018, 12, 9991-9999