Multifunctional Protein Materials and Microreactors using Low Complexity Domains as Molecular Adhesives

Lenka Faltova[1], Andreas M. Küffner[1], Maria Hondele[2], Karsten Weis[2], Paolo Arosio[1]

[1] Department of Chemistry and Applied Biosciences, Institute for Chemical and Bioengineering, ETH Zürich, Switzerland.

[2] Department of Biology, Institute for Biochemistry, ETH Zürich, Switzerland.

Recent findings indicate that a class of disordered amino acid sequences promotes functional phase transition of biomolecules in nature. Such sequences consist of low complexity domains (LCDs) of a few amino acids. In this work, we exploit these sequences by conjugating them to soluble globular domains to develop molecular adhesives that enable sensitive, controlled self-assembly of these proteins into supramolecular architectures. In particular, we used the enzyme adenylate kinase and the green fluorescent protein as soluble domains, and we show that the addition of low complexity regions induces the formation of protein particles *via* a multi-step process. This multi-step 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 show that the LCDs dictate specific non-covalent intermolecular interactions and phase properties that are largely independent of the given globular domain. 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.

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