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Development of self-assembling peptide tags for studying intracellular protein supramolecules

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In living cells, protein assembling via non-covalent interactions forms functional supramolecular systems. The mimicry of protein supramolecules through artificial construction leads to understanding the essence of their structure formation and functional expression, and applying them to the construction of artificial functional systems.

Self-assembling peptides can be easily designed and functionalized, making them versatile materials in various biological applications. In the present study, self-assembling peptides were utilized as genetically encoded tags to assemble proteins in cells. Y15 peptide tag was employed to construct artificial clusters of the target proteins. Subsequently, protein-protein interactions between the target clusters and client proteins spontaneously recruited into the clusters were analyzed through fluorescence imaging and tandem mass spectrometry. Furthermore, a YK peptide tag that can induce the formation of phase-separated droplets was developed. Co-chaperone protein HOP was found to form liquid droplets with YK tagging. Moreover, Hsp70 and Hsp90 were found to play a crucial role in maintaining the fluidity of reconstructed HOP droplets.

Taken together, this study provides methodologies for studying the intracellular protein supramolecules through artificial construction and demonstrates the applicability of self-assembling peptides for intracellular environments.