

The Faculty of Biotechnology and Food Engineering

Seminar

Dr. Dan Bracha

Lighting Up Intracellular Phase Space Using Phase-Separated Protein Droplets

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Abstract

Liquid-liquid phase separation (LLPS) of intrinsically disordered protein regions (IDRs) underlies the assembly of diverse membrane-less compartments, which play essential roles in organizing the cellular biomolecular content and regulating biochemical reactions. However, a quantitative understanding of the driving forces underlying intracellular phase behavior and the principles by which phase separation can be confined to specific cellular subregions is lacking. In this talk, I will present a novel biomimetic tool that uses light to drive the assembly and disassembly of phase-separated compartments at spatiotemporally definable cellular subregions. This platform has allowed us to map protein-specific intracellular phase diagrams for the first time, providing unprecedented access to the effective energy landscape that governs phase separation and its responsiveness to mutations and post-translational modifications. We find that local clustering of weakly self-associating IDRs to slowly diffusing scaffolds may give rise to phase separation even at low protein abundance that is insufficient for global phase separation. This approach has begun to yield rich quantitative insights into the largely unexplored link between intracellular liquids, gels, and the onset of pathological protein aggregation.

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