Novel tools to examine intracellular phase transitions and RNP granules

Zoher Gueroui

Department of Chemistry
Ecole Normale Supérieure - Paris

Ribonucleoprotein (RNP) granules, which include germ, neuronal, and stress granules, are ubiquitous membrane-less organelles. They regulate RNA processing and thereby play a pivotal role in overall gene expression output, while their dysregulation and solidification into toxic and pathological aggregates have been associated with viral infection, cancer, and age-related diseases. For example, redistribution of RNA-binding proteins, most notably TDP-43, from the nucleus to cytoplasmic inclusions is a hallmark forms of amyotrophic lateral sclerosis (ALS). Yet, current approaches have failed to identify the critical parameters that are essential to control RNP granule formation, functions, or dysregulations.

By combining synthetic biology and biophysics, we have developed a novel methodology allowing the controlled formation in cells of artificial membrane-less granules that are made of synthetic RNA-protein scaffolds (ArtiGranule)[1]. Our artificial RNA-protein granules recapitulate the hallmarks of phase-separated liquid membrane-less organelles and can be used to dissect RNP granule biogenesis. Our approach also illustrates how liquid-liquid phase separation could be a key principle for organizing cellular biochemistry as well as be used for engineering novel objects and functionalities in living cells.

1. Garcia-Jove Navarro M, Kashida S, Chouaib R, Souquere S, Pierron G, Weil D, Gueroui Z. *submitted*, *bioRxiv.* doi: https://doi.org/10.1101/457986

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Phase transitions in cells