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Journal club

CELL ORGANIZATION BY LIQUID PHASE SEPARATION

Cells contain tens of thousands of different molecular components, the activities of which need to be coordinated in time and space to sustain cell function. This coordination is achieved by compartmentalization of molecular components into diverse lipid membrane-bound cell organelles that perform distinct functions. Moreover, cells contain various non-membrane-bound compartments, such as the nucleolus and cytoplasmic stress granules. How non-membrane-bound compartments are assembled and organized has remained mysterious — until a study by the Hyman laboratory introduced a simple physical explanation.

Brangwynne *et al.* investigated how one type of non-membrane-bound compartment — the P granules — accumulates in the posterior half of the *Caenorhabditis elegans* one-cell embryo to specify the germ cell lineage. Earlier work had suggested that their asymmetrical distribution might result from directional migration of P granules, but, using particle tracking, Brangwynne *et al.* showed that this was not the case. Instead, they revealed that P granules dissolved in the anterior regions of the embryo, whereas they increased in volume in the posterior regions. Hence, the authors hypothesized that P granules assemble by condensation of soluble components in the posterior regions of the embryo.

They then used a variety of assays to characterize the physical properties of P granules. Application of shear force induced dripping of smaller drops from P granules, which, upon subsequent contact, coalesced again to larger spherical units. Furthermore, photobleaching experiments showed that P granule components were highly mobile and that, at a slower rate, P granule components were exchanged with the surrounding cytoplasm. Together, these are characteristic features of liquid droplets, suggesting that P granules form by a demixing phase transition in the fluid cytoplasm. Genetic perturbation experiments further suggested that the asymmetrical distribution of P granules might arise from a gradient of polarity factors controlling the dew point.

Overall, Brangwynne *et al.* provided key insights into the mechanism of germ cell lineage specification, yet the implications of this study reach far beyond. The introduction of the liquid phase separation theory to cell biology has inspired researchers to probe physical properties of various other non-membrane-bound compartments, many of which turned out to be liquid-like. Hence, biomolecular condensates emerge as a new principle of cellular organization with broad implications in various biological processes.

Daniel W. Gerlich
Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA), Vienna Biocenter (VBC), 1030 Vienna, Austria.
daniel.gerlich@imba.oeaw.ac.at

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