Abstract

Living cells are composed of a complex mixture of macromolecules. To regulate their activity, cells partition these molecules into specialized compartments called organelles. Typically, lipid membranes form a selective barrier between an organelle and the cytoplasm, allowing each compartment to maintain a distinct biochemical composition that is tailored to its function. However, recent progress has revealed numerous compartments that are not enclosed by membranes. Instead, these compartments consist of local concentrations of proteins and nucleic acids that rapidly exchange with the surrounding cytoplasm or nucleoplasm.

Our lab focuses on the nucleolus, a large membraneless organelle responsible for ribosome biogenesis. By genetically manipulating the size of C. elegans embryos, we identified a concentration threshold below which nucleolar components remain dissolved in the nucleoplasm and above which they condense to form the nucleolus. Moreover, the size of the nucleolus scales with the size of the cell. Finally, despite nonequilibrium activity in the cell, the kinetics of nucleolar assembly are consistent with thermodynamic models of first-order phase transitions. These results indicate that the nucleolus assembles by liquid-liquid phase separation of the nucleoplasm. Given the ubiquity of membraneless organelles across the tree of life, phase separation is now recognized as a general mechanism for compartmentalization of cells.