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Role of PAR and RNA in biomolecular condensate formation

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Condensates are intracellular compartments that accumulate certain biomolecules without the help of membranes. These molecular assemblies may emerge as a result of sub-stoichiometric mechanisms (binding, bridging), liquid-liquid phase separation (LLPS) or their superposition [1]. Understanding how a specific structure is formed is necessary for correct predictions of how it will behave. Nucleic acids (DNA, RNA, and poly(ADP-ribose) [PAR]) are key scaffold molecules that function during the architectural organization and dynamic restructuring of condensates. PAR is produced in the cells of higher eukaryotes and has features of structure and synthesis that distinguish it from canonical nucleic acids [2]. Similarities and differences between PAR and RNA can determine their interplay during the formation and functioning of condensates with complex architecture. In our review work we analyze the basic principles of how the properties of constituent nucleic acids (length, sequence, structure, and rigidity) influence condensate organization. We discuss the role of RNA in the formation of condensates with different morphologies and varying RNA-protein composition. We also examine in detail the majority of known PAR-containing condensates (the nucleolus, DNA repair foci, transcription hubs, the spindle, RNP granules and extracellular mineral particles) to understand the function of PAR in their assembly. We conclude that both being polymeric scaffolds, PAR and RNA can enter into multiple specific and nonspecific interactions. For nonspecific electrostatic contacts, these anionic polynucleotides are interchangeable. However, PAR may function as a more rapidly synthesized and less site-dependent RNA analog initiating RNA-dependent systems at early stages of their activity. It is possible that similarities between PAR and RNA can be used in systems with phase re-entrant behavior [3]. In particular, based on our data, we hypothesize that PAR synthesis itself may have the features of re-LLPS process. Despite its low-complexity, PAR can be recognized through a variety of protein domains [4]. Therefore, PAR and RNA can bind with different partner proteins, ensuring the immiscibility of liquid phases and the formation of multilayer condensates. Due to reversibility of PAR synthesis and degradation, this polymer is more advantageous for the assembly of transient compartments, while RNA can contribute to organization of less dynamic condensates.

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