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Editorial: Ribonucleoprotein formation and regulation

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Editorial on the Research Topic
Ribonucleoprotein formation and regulation

Messenger RNA (mRNA) does not exist naked in the cell. Rather, mRNAs are bound to proteins that facilitate their processing from pre-mRNA, transport to the cytoplasm, and translation into proteins. Other types of RNA, such as ribosomal RNA (rRNA) and small nuclear RNA (snRNA) are likewise associated with proteins. Formation of these RNA-protein complexes, termed ribonucleoproteins (RNPs), is complicated and in many cases requires assembly chaperones that are not part of the final complex. RNPs are involved in many critical cellular functions including pre-mRNA splicing and mRNA translation. Despite the tremendous knowledge gained about RNP biogenesis, including the identification of cellular locales where RNPs accumulate (e.g., nucleoli, Cajal bodies and stress granules), a clear understanding of the various cellular machineries required for the formation of RNPs, and how they may differ in various cell types or disease states, is lacking.

This Research Topic on Ribonucleoprotein Formation and Regulation sought to increase our understanding of any area related to RNP biogenesis, function, regeneration and regulation and includes two original research articles (Matera et al., Lett et al.) one review (Adjibade and Mazroui), and one mini-review (Yang et al.).

Adjibade and colleagues provide a comprehensive review of stress granules (Adjibade and Mazroui), which are cytoplasmic complexes of mRNA and proteins (mRNPs) that form when translation initiation is stalled. In particular, their article explores current knowledge of conditions that induce stress granules (SGs) and the impact of translation initiation factors on the formation of these compartments. The review also examines the role RNA binding proteins (RBPs) in the formation of SGs or RNA condensation. For example, the phase separation properties of the RBP TDP-43, which induces RNA condensation, is discussed. Additional topics in this review include the role of RNA in SG formation and the influence of RNA modifications on the regulation of mRNA accumulation in SGs. Finally, this review explores new technologies to examine mechanisms of SG-mediated translational repression, including the creation of reporter systems that can assess whether translation might take place in SGs.

Yang and colleagues provide an update on recent findings of USP36, a nucleolar-enriched deubiquitylase (Yang et al.). USP36 contributes to various aspects of ribosome biogenesis. Interestingly, this protein is also reported to possess SUMO (small ubiquitin like modifier) ligase activity, promoting SUMOylation of several proteins involved in formation of ribosomes, including those that form small nucleolar RNPs (snoRNPs) that modify rRNA, such as Nop58 and DKC1. The role that USP36's DUB and SUMO activity may play in various disease states, including oncogenic pathways, is discussed. Additionally, Yang and colleagues posit that a better mechanistic characterization of USP36 using inhibitors of

its DUB activity, SUMO activity, or both DUB/SUMO activity would provide significant insight into how the regulation of ribosomal biogenesis integrates into other cellular regulatory pathways such as the cell cycle and oncogenic transformation.

Lett and colleagues present original data showing that coilin, a major component of Cajal bodies (CBs), also has SUMO ligase-like activity (Lett et al.). CBs are domains found in the nucleus that contribute to the formation of many different RNP types such as snRNPs and telomerase. Reduction of coilin, in cell types with or without many CBs, decreases global protein SUMOylation. Examination of the microRNA (miRNA) biogenesis machinery demonstrates that DGCR8, a component of the microprocessor that is involved in miRNA formation, has altered phosphorylation and SUMOylation upon depletion of coilin. Additional experiments show that the SUMOylation of the PML body protein Sp100 is reduced upon coilin reduction, as is the expression of SMN. Taken together with other data showing that coilin interacts with components of the SUMOylation machinery, these findings support the idea that coilin promotes protein SUMOylation, possibly via interactions mediated by the large region of intrinsic disorder located within coilin.

Matera and colleagues provide original data revealing that the SMN (survival motor neuron) complex interacts with a wide variety of components of the proteostasis network (Matera et al.). SMN is mutated in patients with spinal muscular atrophy (SMA) and the SMN complex acts as an assembly chaperone for snRNP biogenesis. By examining the proteomic network of the SMN complex, Matera et al. demonstrate that the heat shock cognate protein Hsc70-4, and other members of the heat shock HspA family members show increased association with the misfolded/mutant forms of SMN. Notably, the mRNA encoding Hsc70-4 is targeted by a mutant form of TDP-43 that causes Amyotrophic Lateral Sclerosis (ALS) in mouse and fly models (Coyne et al., 2017). And the mouse ortholog of Hsc70-4 was shown to be a powerful suppressor of the SMA phenotype in mice (Kim et al., 2023). Hence, data presented in this article provide evidence that chaperone-related dysfunction is important for the etiology of both ALS and SMA.

Collectively, the work presented in these articles demonstrates new insights into RNP formation and regulation and provides discussion about further questions that have arisen as a result of these new insights.

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References

Coyne, A. N., Lorenzini, I., Chou, C. C., Torvund, M., Rogers, R. S., Starr, A., et al. (2017). Post-transcriptional inhibition of hsc70-4/HSPA8 expression leads to synaptic vesicle cycling defects in multiple models of ALS. *Cell. Rep.* 21, 110–125. doi:10.1016/j.celrep.2017.09.028

Kim, J. K., Jha, N. N., Awano, T., Caine, C., Gollapalli, K., Welby, E., et al. (2023). A spinal muscular atrophy modifier implicates the SMN protein in SNARE complex assembly at neuromuscular synapses. *Neuron* 111, 1423–1439.e4. doi:10.1016/j.neuron.2023.02.004