# Deciphering the Molecular Grammar and function of RNA Condensate Assembly

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Gene expression is coordinated to cellular activity and adapted to stress. At the lowest scale, transcription control can regulate whether an mRNA is transcribed, but it has become evident that rapid, efficient and adaptable responses to cues is achieved by controlling gene expression at the post-transcriptional level. A fundamental problem in cell biology is how the transcriptome organizes within the densely packed cellular space to allow efficient spatiotemporal regulation of mRNA expression?

Evidence suggests that post-transcriptional regulation in developing *C. elegans* oocytes is achieved by RNA binding proteins (RBPs) that dynamically regulate maternal mRNAs. Recent data from our team further suggests that translationnally repressed mRNAs can be found in a single molecule soluble form that can self-assemble into homotopic clusters that can further coalesce into larger multiphase heterotypic assemblies. These membrane-less mRNA super-assemblies are liquid-like bodies in which mRNAs and proteins are, for most condensates, the major components. These biomolecular condensates can compartmentalize, concentrate and dynamically partition components, providing the cell with regulatory capabilities beyond canonical molecular regulatory mechanisms [1] .

However, the mechanism of assembly and precise function of those different condensates remains an open question. Here, I propose to (1) dissect the mRNA sequence that drive condensate assembly, and to (2) test the consequence of RNA condensation on RNA:protein interactions. Finally, (3) I will address whether RNA condensation is correlated to translation and decay interplay. Using high resolution imaging approaches of mRNA localization within C. elegans gonads, I uncovered that mRNA 3'UTR sequences are unexpectedly insufficient to insure mRNA segregation into homotypic clusters. In addition, I adapted the OOPS biochemical approach, whose preliminary results suggest that preventing mRNA aggregation into granule disrupts RNA:protein interaction stoichiometries on a proteome-wide scale. Regarding the last question, I took advantage of a single molecule sensitivity RNA imaging approach to demonstrate that repressed/condensed mRNAs are protected from decay as compared actively translated single mRNAs. My preliminary results support models in which (1) mRNA condensation controls RNA:protein interaction stoichiometries within the cell, (2) mRNA condensation is associated with the protection of mRNA from decay.

[1] Cardona AH, Ecsedi S, Khier M, Yi Z, Bahri A, Ouertani A, Valero F, Labrosse M, Rouquet S, Robert S, Loubat A, Adekunle D, Hubstenberger A. Self-demixing of mRNA copies buffers mRNA:mRNA and mRNA:regulator stoichiometries. Cell. 2023 Sep 28;186(20):4310-4324.e23. doi: 10.1016/j.cell.2023.08.018. Epub 2023 Sep 12. PMID: 37703874.