A 3-year founded PhD project is available at ENS, Paris, France.

(starting Oct-Dec 2024)

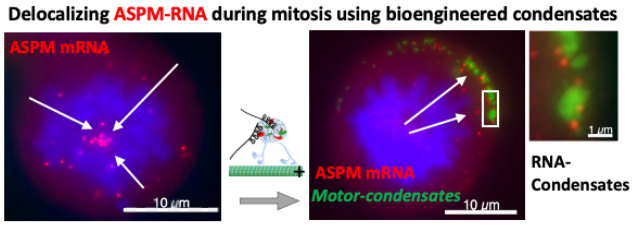
Interdisciplinary Approaches to Study Biomolecular Condensates and mRNA Local Translation

Our team is seeking a motivated PhD student to develop innovative tools in biology and biophysics using an interdisciplinary approach. Our laboratory, located in the heart of Paris, engages in interdisciplinary research, fostering a collaborative environment where biologists, physical chemists, and biophysicists work together. We benefit from a rich academic setting, close to renowned institutes such as ENS, Curie Institute, and Collège de France. This project includes significant collaborations with partners in France (IGH, IBENS) and Japan (IQB-CiRA, Kyoto University).

Context: Biomolecular condensates are crucial for RNA regulation and gene expression[1], influencing processes from embryo polarization to neural development. Dysfunctions in condensates are linked to diseases such as viral infections, cancer, and neurodegenerative disorders. Despite advances in understanding RNA condensate formation and localization, linking their functions remains challenging due to a lack of spatial manipulation tools. To address this, our team at ENS has developed bioengineered motor condensates to manipulate mRNA localization[2,3,4]. These tools will be applied to study human centrosomal mRNAs, recently discovered by E. Bertrand at IGH-Montpellier and H. Le Hir at IBENS-Paris[5,6]. The PhD objectives are: (i) Develop and use chemo- and optogenetic tools to perturb RNA condensates for local translation studies. (ii) Investigate how centrosome function depends on mRNA localization and local translation, in collaboration with IGH and IBENS teams.

Methods and workflow: The student will use advanced techniques in Molecular and Cell Biology, Protein and RNA Engineering, Quantitative Imaging (FRAP, Particle Tracking), Single Molecule FISH, Biophysics. Data and image analysis will utilize machine learning models.

Expected results: The PhD student will build on strong preliminary experiments. The project aims to: (i) Develop novel tools to manipulate mRNA localization and translation in cells. (ii) Establish causal links between mRNA localization, local translation, and cellular functions using centrosomal mRNAs as a model.



Observation of bioengineered condensates formed by phase separation in human cells. By engineering condensates functionalized with kinesins and dynein-like motors, we demonstrated the ability to target condensates and their associated RNA to either the cell periphery or the centrosomes.

Profile: Interested applicants should hold a master's degree in Quantitative Biology, Biophysics, Chemical Biology, or a related field and demonstrate a strong interest in interdisciplinary work.

Applications (curriculum vitae, statement of research interests, and contact information of at least 2 references) should be addressed to: zoher.gueroui@ens.fr

References

1. Liquid phase condensation in cell physiology and disease. Shin Y, Brangwynne CP. *Science*. 2017.
2. RNA at the surface of phase-separated condensates impacts their size and number Cochard A., Garcia-Jove Navarro M., Kashida S., Kress M., Weil D., and Gueroui Z *Biophysical Journal* 2022. https://doi.org/10.1016/j.bpj.2022.03.032
3. RNA is a critical element for the sizing and the composition of phase-separated RNA-protein condensates. Garcia-Jove Navarro M, Kashida K, Chouaib R, Souquere S, Pierron G, Weil D, and Gueroui Z. *Nature Communications.* 2019. https://www.nature.com/articles/s41467-019-11241-6.

4. Condensate functionalization with motors directs their nucleation in space and allows manipulating RNA localization. Cochard A, Safieddine A, Combe P, Benassy M-N, Weil D, Gueroui Z
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5. Safieddine, A. *et al.* A choreography of centrosomal mRNAs reveals a conserved localization mechanism involving active polysome transport. *Nat Commun* 12, 1352 (2021).
6. Kwon, O. S. *et al.* Exon junction complex dependent mRNA localization is linked to centrosome organization during ciliogenesis. *Nat Commun* 12, 1351 (2021).