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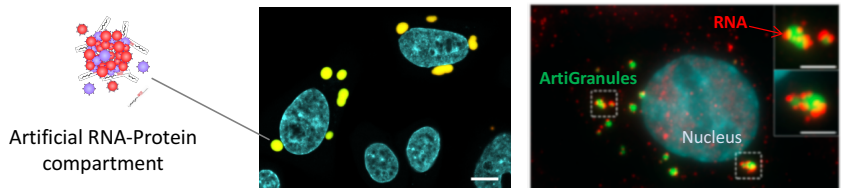
« MASTER PROPOSAL »

New tools to study intracellular phase separation and the biogenesis of RNA-protein compartments in physiological cells and diseases

1. Topics

Membrane-less organelles are ubiquitous functional sub-units of cells that are involved in many vital functions such as RNA regulation, shaping the general gene expression output[1,2]. Importantly, their dysfunction is linked to viral infection, cancer, and neurodegenerative diseases. For instance, the solidification of RNA-protein membrane-less organelles into toxic aggregates have been associated to pathological diseases such as amyotrophic lateral sclerosis (ALS)[1,2]. Beyond their molecular composition, these organelles are very complex regarding their biochemical and biophysical properties, which implies the development of novel tools for their study.

By combining chemical biology, biophysics and cell biology, our team has recently developed a novel methodology (ArtiGranule) to form artificial membrane-less organelles, within living cells, with tunable biochemical and biophysical properties (Garcia-Jove et al[3]). The engineered synthetic granules succeed in recapitulating the intracellular phase transition process that control the formation of RNA-protein granules. We also found that our approach can be extended to study membrane-less organelles in human cells including iPSC and neurons.



Observation of artificial RNA-protein granules, formed by phase separation in human cells[3].

2. Techniques/méthodes utilisées

Molecular and Cell Biology, Protein engineering, Confocal Microscopy, Quantitative Imaging (FRAP, Image analysis, Particle Tracking), Single Molecule FISH, Cytometry.
Biophysics, RNA-Protein engineering, Synthetic Biology.

3. Expected results / Résultats attendus

The outputs of the master project are multiple and original at the international level:
(1) Expanding our toolbox for inducing the assembly of artificial organelles with fine-tuned properties cells. (2) Establishing the causal links between the properties of membrane-free RNA organelles and the regulations of RNA (translation, degradation, …) in mammalian cells. (3) Applications for unraveling the transcriptomic/proteomic of pathological organelles (neurodegenerative diseases).
This project benefits from several key collaborators based in France (Biologists at IBENS / SU / Collège de France) and in Japan (CiRA, Kyoto University). The Laboratory is developing interdisciplinary research between Biophysics, Biology, and Chemical Biology. The Master student will benefit from strong preliminary experiments.

4. Références

1. Liquid phase condensation in cell physiology and disease. Shin Y, Brangwynne CP. *Science*. 2017.
2. Biomolecular condensates: organizers of cellular biochemistry. Banani. Nature Rev Mol Cell Biol. 2017.

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3. Garcia-Jove Navarro M, Kashida S, Chouaib R, Souquere S, Pierron G, Weil D, Gueroui Z. *Nature Communications. 2019.* https://www.nature.com/articles/s41467-019-11241-6.

https://inc.cnrs.fr/fr/cnrsinfo/utiliser-des-organelles-artificielles-pour-etudier-lorganisation-des-cellules

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