Post-doc Position:
Cell biology and biophysics of PML nuclear bodies structure and dynamics
Group V. Lallemand-Breitenbach & H. de Thé

Research Context

PML nuclear bodies (NBs) are stress-regulated membrane-less organelles controlling multiple biological functions, such as metabolism or senescence. PML NBs assembly is stimulated by oxidative stress. From a cell biology perspective, PML oxidation drives the assembly of NBs, forming a spherical shell structures that recruits multiple partner proteins within their inner core, a remarkable, but unconventional, assembly mechanism. Functionally, NBs control a critical post-translational modification, sumoylation. Mechanistically, the shell-structure and stress-controlled dynamics of PML NBs likely control enzymatic sumoylation function of core-associated proteins in response to stress. Yet to date, **how structure, assembly dynamics and function of PML NBs are linked remains poorly understood from cell biological and biophysical perspectives.**

We want to revisit the biogenesis of PML NBs within the framework of liquid-liquid phase separation. The formation of a shell structure without co-condensation of associated proteins, and the gel-like response of the PML scaffold upon stress hint toward a complex interplay between architecture and assembly dynamics. In collaboration with H. Turlier's group at the College de France for physical modeling, the aim of project is to decipher the physical driving forces underlying structure, dynamics and sumoylation function of PML NBs.

Candidate skills

Candidates should have good experience in live cell biology, confocal microscopy analysis (fixed and live microscopy, FRAP, photoconversion etc.), as well as cell culture. Candidates with quantitative background (computational imaging, some biophysics knowledge) and super-resolution microscopy or cryo-EM are particularly encouraged to apply. Skills in molecular biology & cloning will be a plus. We are seeking an interactive and collaborating personality, as well as good communication skills combined to autonomy, since the project will be conducted side by side with our physicist partner.

Situation & scientific environment

The team is located at the *Center for Interdisciplinary Research in Biology (CIRB*), on the prestigious Collège de France site, located in the *quartier Latin* of Paris.

The CIRB provides an original and integrated environment to address key questions in Life Sciences. Its originality and strength reside in the association of people with different scientific culture and expertise, developing both experimental and theoretical approaches. It promotes collaboration and scientific exchanges between its 18 research teams, interested in fundamental or applied questions in microbiology, developmental biology, neuroscience, oncology, biophysics, cancer biology or cardio-vascular physiology. The CIRB benefits from the extremely rich scientific environment of the Montagne Sainte-Geneviève, where are also located *Ecole Normale Supérieure*, *ESPCI* and *Curie* Institute.

How to apply

The position is funded by the labex *Memolife* - for two years.

Applications should include a CV, the academic achievements, a brief statement of research interests including your past experience and names of at least 2 referees. Applications will be accepted until positions are filled. Interviews will be arranged on a rolling basis.

Center for Interdisciplinary Research in Biology
Group « Nuclear organization and post-translational control in pathology »
Collège de France - Inserm U1050 - Cnrs UMR7241- Université PSL

Contact: Valérie Lallemand-Breitenbach (valerie.lallemand@inserm.fr)

Selected relevant publications of the group

- Tessier S. et al. *Unbiased in vivo exploration of nuclear bodies-enhanced sumoylation reveals that PML orchestrates embryonic stem cell fate.* **BioRxiv, 26 June 2021,** (in revision **Nat. Commun**)
- Wu, H.C. et al. *Actinomycin D targets NPM1c-primed mitochondria to restore PML-driven senescence in AML therapy.* **Cancer Discov**, **2021 Jul 23. doi: 10.1158/2159-8290.CD-21-0177**
- Dagher, T. et al. *JAK2V617F myeloproliferative neoplasm eradication by a novel interferon/arsenic therapy involves PML.* **J Exp Med, 2021**. 218(2).
- Lallemand-Breitenbach, V. & H. de The, *PML nuclear bodies: from architecture to function.* **Curr Opin Cell Biol, 2018.** 52: p. 154-161.
- de The, H., *Differentiation therapy revisited***. Nat Rev Cancer, 2018.** 18(2): p. 117-127.
- Wang, P., et al. *RING tetramerization is required for nuclear body biogenesis and PML sumoylation.* **Nat Commun**, **2018**. 9(1): p. 1277.
- Niwa-Kawakita, M. et al., *PML is a ROS sensor activating p53 upon oxidative stress.* **J Exp Med**, **2017**. 214(11): p. 3197-3206.