Master Biologie Moléculaire et Cellulaire 'BMC',
Université de Paris - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
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Fiche de Projet de Stage M2, Année 2026-2027

Unité INSERM ou CNRS ou Université : CIRB, Collège de France, CNRS UMR 7241, INSERM U1050 **Intitulé Equipe : Oocyte Mechanics and Morphogenesis** **ED d'appartenance : ED SDV PSL (ED 657)** **Responsable de l'Equipe : Marie-Émilie Terret et Marie-Hélène Verlhac**	**Responsable du Stage : Maria Almonacid** **Contacts** **maria-elsa.almonacid@college-de-france.fr**

Titre du projet : Organization of the mouse oocyte genome at the nuclear periphery

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

LADs (Lamina Associated Domains) are specific heterochromatin regions, which interact directly and indirectly with Lamins in the nucleus, and are major players in the spatial organization of the interphase genome (1). In mouse oocytes, where chromatin has a very peculiar architecture, mostly wrapped around the large and unique nucleolus, genome organization is not very well understood. However, LADs are still present on specific chromosomes (2,3).
The project aims at understanding the impact of forces exerted on the nucleus on LADs, which may also broaden our understanding of genome organization in mouse oocytes. We discovered that in absence of actin forces in the cytoplasm, nuclei are asymmetric in shape, bilobed, and present an important indentation (4). This indentation is due to the presence of numerous microtubules (MTs) locally contacting the nuclear envelope and nucleated from a major Microtubule Organizing Center (MTOC) localized close by. Strikingly, we observed that the contacts between chromatin and the nuclear envelope are increased locally at the indentation in oocytes lacking a cytoplasmic actin meshwork (4). Using live probes for both the MTOC and LADs, we clearly detected a major LAD at the indentation and in close proximity to the MTOC, which could be the X chromosome. Indeed, in mouse oocytes, genomic sequencing approaches showed an enrichment of LADs on the X chromosome, compared to autosomes (3).
During the internship, the student will investigate this potential connection between the MTOC and this major LAD. She/he will look at the distribution of the Lamin B Receptor, and other proteins that tether chromatin to the nuclear lamina, along the nuclear envelope. She/he will also target specific histone marks, such as H3K36me2 (enriched on the X chromosome) and H3K27me3 (involved in Xist locus silencing), as well as components of the LINC (LInker of the Nucleoskeleton and Cytoskeleton) complex. This will allow to decipher the molecular signature of the indentation, thereby contributing to address the impact of cytoskeletal forces and nuclear shape on genome organization in mouse oocytes.

(1) doi: 10.1016/j.cell.2017.04.022. PMID : 28525751
(2) doi: 10.1038/s41586-019-1233-0. PMID: 31118510
(3) doi: 10.1038/s41467-022-32141-2. PMID: 35922445
(4) doi: 10.1016/j.devcel.2019.09.010. PMID: 31607652

Publications de l'équipe, relatives au stage proposé (max 5)

Letort G, Mailly P, Al Jord A*, Almonacid M*. Capturing Cytoskeleton-Based Agitation of The Mouse Oocyte Nucleus Across Spatial Scales. J Vis Exp. 2024 Jan 12;(203). doi: 10.3791/65976. *co-corresponding authors
Almonacid M* and Verlhac MH. A new mode of mechano-transduction shakes the oocyte nucleus, thereby fine tunes gene expression modulating the developmental potential. C R Biol 2021 Feb4; 343(3), 223-234. doi: 10.5802/crbiol.24. *corresponding author
Almonacid M et al. Active fluctuations of the nuclear envelope shape the transcriptional dynamics in oocytes. Developmental Cell 2019 Oct 21;51(2):145-157. doi: 10.1016/j.devcel.2019.09.010.