INTERNSHIP PROPOSAL

Laboratory **Matière et Systèmes Complexes**
Université Paris Cité - CNRS - UMR 7057
Internship director's name: **Sylvie Hénon & Jean-Baptiste Manneville**
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Thesis possibility after internship: YES If YES, which type of funding: ED 564

Regulation of nuclear rigidity by lysine methyltransferases: a biomechanical study

Nuclear stiffness is a key factor in the ability of cancer cells to migrate, to deform, notably during the extravasation phase, and thus to form metastases. While the cell membrane and cytoplasm are quite deformable, the ability of the nucleus to squeeze through small spaces is limited by its size and rigidity. Nuclear stiffness depends on Lamin proteins and on levels of H3K9me3-enriched rigid heterochromatin, established by the lysine methyltransferases SETDB1 and SUV39H. Our biologist collaborators have recently highlighted the essential and multiple roles of SETDB1-regulated chromatin architecture in the determining oncogenic programs [1]. The aim of the internship is to study how SETDB1 and SUV39H regulate nuclear mechanical properties and cell migration under confinement. The intern will measure the stiffness of the nuclei of different cell lines developed by our collaborator, using an optical tweezers rheometer [2] (see Figure A). She/He will also quantitatively characterize their migration abilities (speed, directionality, persistence …), in free *vs* confined environments (see Figure B). A correlation will be sought between nuclear rigidity, migration properties and the levels and spatial organization of H3K9me3 in the different cell lines.

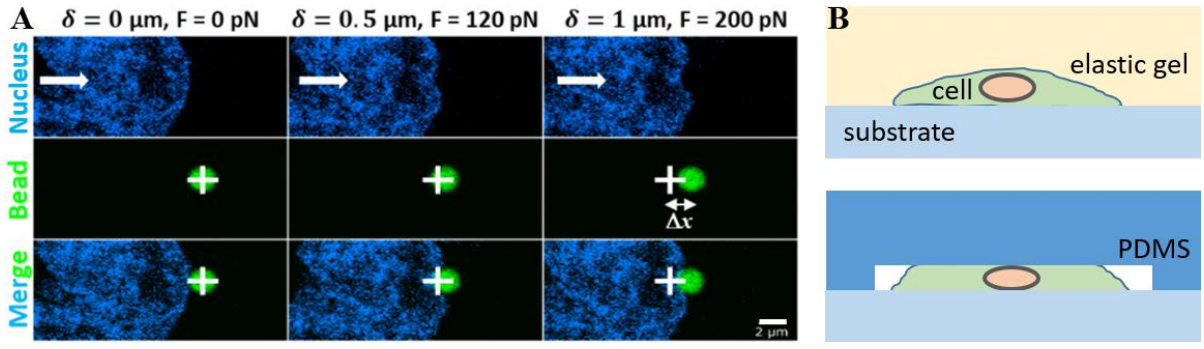

Figure:. ***A.*** *Measurement of the viscoelasticity of the nucleus of a living cell by indentation. The white cross represents the centre of the optical tweezers in which the 2 µm diameter bead (green) is trapped. The nucleus (blue) is indented by moving the cell to the right (white arrow) which displaces the bead away from the trap centre by a distance Δx, from which the applied force is inferred.* ***B****. Cells confined by a visco-elastic gel or in PDMS micro-channels.*

[1] Zakharova et al. *Nucleic Acids Research* 2022
[2] Alibert at al. *Biomaterials* 2021