Master 2 Internship Offer (5-6 months from january 2027)

Laboratory: Department *"Physics and Engineering for Living Systems"*
Centre Interdisciplinaire de Nanoscience de Marseille (CINaM), Campus de Luminy
Supervisors: *Emmanuèle Helfer* E-mail: emmanuelle.helfer@univ-amu.fr,
Pauline Lahure E-mail: pauline.lahure@cnrs.fr

Investigating the Role of Nuclear Cytoskeletal Coupling in Cancer Cell Mechanics Using Microfluidics

Context and previous work. Cell migration under confinement plays a crucial role in cancer metastasis. To migrate through narrow spaces, cell must deform. The nucleus, the largest and stiffest organelle in the cell is a major physical barrier to confined migration. Nuclear mechanical properties depend on chromatin organization and these properties influence whole-cell mechanics through the cytoskeleton, which is connected to the nucleus via a protein complex: the LINC complex.
We use in routine microfluidic devices to characterize the overall mechanical properties of cells (Fig. A-C)[1]. Recently, we investigated cancer cells with altered SETDB1 expression. SETDB1 is a histone methyltransferase involved in chromatin organization[2]. We showed that SETDB1 knockout (KO) cells show increased cellular viscosity whereas partial depletion of SETDB1 (knockdown, KD) does not[3]. This difference may reflect changes in gene expression of proteins related to cytoskeleton that are induced only by complete loss of SETDB1.

Project Description. The aim of this project is to investigate the respective contributions of the nucleus and the cytoskeleton to overall cell mechanics. To address this question, we will use the same cancer cells (control and KO) in which the LINC complex is disrupted. We will characterize their mechanical properties using microfluidic assays and compare when the LINC complex is not altered. This approach will allow us to determine the role of the connection between the nucleus and the cytoskeleton in cellular mechanics and whether it acts on the behavior observed in SETDB1 KO cells. We will also investigate the consequences of these modifications for cell migration using a new microfluidic device currently under development (fig D). This approach will allow us to explore how changes in cellular mechanics affect the ability of cancer cells to migrate under confinement

The Student will :

- Perform cell culture and maintain the different cell lines.
- Conduct microfluidic experiments using existing devices to characterize cellular mechanical properties
- Investigate cell migration under confinement using the new microfluidic device.
- Perform quantitative image analysis and analyze the experimental data.

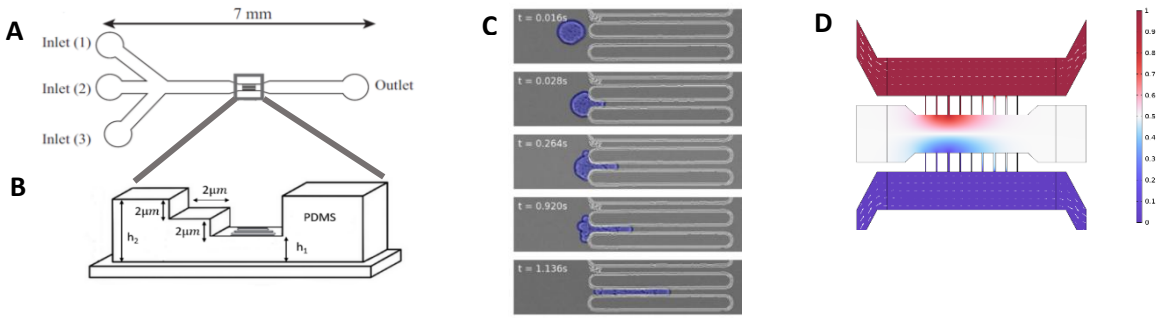

Figure : **A-B)** Schematics of the microfluidic device with constrictions, made of polydimethylsiloxane (PDMS), used to assess cell mechanical properties: **(A)** top view, and **(B)** zoomed 3D-view of the constriction region. **C)** Time-lapse sequence of a cell entering a 6-µm-wide constriction. **(D)** Microfluidic device in developpement to study confined migration under chemotactic gradient (from blue to red).

Expected Profile: We are looking for a motivated student, preferably with a background in physics or biophysics, who has a strong interest in biological questions and interdisciplinary research. An interest in microfluidics, quantitative image analysis, or mathematical modelling would be an advantage.

References

(1) **Jebane, C.**; Varlet, A.-A.; Karnat, M.; Hernandez- Cedillo, L. M.; Lecchi, A.; Bedu, F.; Desgrouas, C.; Vigouroux, C.; Vantyghem, M.-C.; Viallat, A.; Rupprecht, J.-F.; **Helfer, E.**; Badens, C. *iScience* 2023, *26* (10), 107714. https://doi.org/10.1016/j.isci.2023.107714
(2) Zakharova, V. V.; Magnitov, M. D.; Del Maestro, L.; Ulianov, S. V.; Glentis, A.; Uyanik, B.; Williart, A.; Karpukhina, A.; Demidov, O.; Joliot, V.; Vassetzky, Y. S.; Mège, R.-M.; Piel, M.; Razin, S. V.; Ait-Si-Ali, S. https://doi.org/10.1093/nar/gkac234
(3) Comunian, S.; Petit, V.; Velasco, G.; Zakharova, V.; **Jebane, C.**; **Lahure, P.**; Joliot, V.; Maestro, L. D.; Hennion, M.; Lamour, G.; Manneville, J.-B.; **Helfer, E.**; Boyarchuk, E.; Ait-Si-Ali, S. https://doi.org/10.1101/2025.11.28.690983