M2 Internship Proposal

Influence of Substrate Topography on Vascular Endothelial Function and Dysfunction

Supervision: Claire Leclech (CNRS Research Scientist) and Abdul Barakat (PI), Vascular Biomechanics and Bioengineering Team, LadHyX, École Polytechnique (Palaiseau, France)

Background and Significance

Atherosclerosis is a major cardiovascular disease whose complications (heart attacks and strokes) remain the leading cause of mortality worldwide. A key early step in its development is the dysfunction of the vascular endothelium, the cellular monolayer that lines blood vessels. The preferential localization of atherosclerotic lesions in regions where endothelial cells (ECs) are cuboidal and randomly oriented suggests a strong relationship between cell shape and function, raising interest in the mechanisms controlling EC morphology.

While endothelial morphology has traditionally been attributed to the local hemodynamic environment, flow is not the only biophysical stimulus ECs experience *in vivo*. The vascular basement membrane—the substrate on which ECs rest—is not smooth but displays micro-scale roughness. Consequently, ECs are also exposed to topographical cues from their basal surface.

Our group has been investigating how such substrate topography influences EC behavior using in vitro models based on surfaces patterned with microgrooves. We have shown that ECs cultured on these substrates undergo pronounced elongation and alignment along the grooves (contact guidance) [1]. Moreover, these aligned ECs display a striking form of collective migration in the form of anti-parallel streams [2] and exhibit large-scale nuclear deformations [3]. **These findings demonstrate that substrate topography is a powerful regulator of ECs, a novel concept in vascular biology.**

Aim of the Project

Building on these results, the proposed project aims to determine **whether topography-induced changes in EC shape can also modulate endothelial functionality**, particularly in processes relevant to atherosclerosis onset.

Specifically, we will assess:

- Expression of inflammatory markers associated with early endothelial dysfunction,
- Endothelial barrier properties via permeability assays,

- Interactions between EC monolayers and circulating immune cells.

The outcomes will be directly compared to data from flow-aligned ECs, enabling us to disentangle the relative contributions of apical flow and basal topography in regulating endothelial function.

Host Laboratory

The project will be supervised by:
- Claire Leclech, CNRS researcher and expert in cellular responses to topographical cues,
- Abdul Barakat, CNRS Research Director, Professor of Mechanics and Biology at École Polytechnique, and head of the vascular biomechanics and bioengineering group at LadHyX.

The team has long-standing expertise in vascular mechanobiology, combining experimental and computational approaches, and in the design of vascular devices. Its integration within LadHyX, a leading hydrodynamics laboratory, provides a highly interdisciplinary environment fostering daily interactions between biologists, physicists, and engineers. Located on the École Polytechnique campus near Paris, the lab offers a stimulating setting with cutting-edge facilities.

Required Skills

We seek motivated students with some background in biology—ideally in **cell biology, vascular biology, or mechanobiology**, and motivated to work at the interface of disciplines. Strong interest in interdisciplinary research combining biology, physics, and biomedical engineering is essential.

The project will involve the following techniques: microfabrication, microfluidics, cell culture, molecular biology, advanced microscopy, image analysis.

A PhD project is expected to follow this internship.

Contact: claire.leclech@polytechnique.edu – abdul.barakat@polytechnique.edu

Relevant references:

[1] Leclech, C., et al. Distinct Contact Guidance Mechanisms in Single Endothelial Cells and in Monolayers. Adv. Mater. Interfaces 10, (2023).
[2] Leclech, C. et al. Topography-induced large-scale antiparallel collective migration in vascular endothelium. Nat. Commun. 13, 2797 (2022).
[3] Leclech, C. et al. Micro-Scale Topography Triggers Dynamic 3D Nuclear Deformations. Adv. Sci. (2025) doi:10.1002/advs.202410052.