Biomaterials and Biodevices track (BioMAT)
Research projects 2020-2021

Biomechanics of Circulating Tumor Cells (CTCs)

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Project description :

Most Circulating Tumor Cells (CTCs) die in the blood circulation, which imposes shear stress as well as large and repetitive deformations. Unfortunately, some survive, and eventually form metastases. To elucidate how CTCs react to harsh mechanical conditions of the blood stream, we developed microfluidic devices as *in vitro* models of the microvasculature.

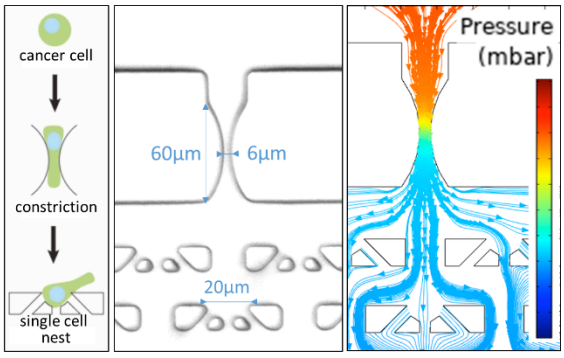

Fig.1: *Principle of microfluidic device*

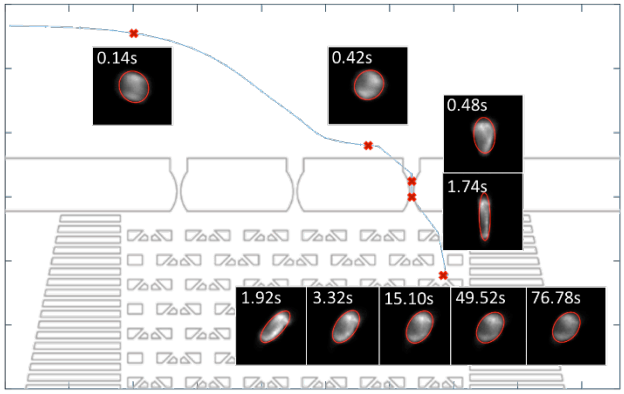

Fig.2: *Shape evolution of the cell as it cross the constriction and recovers in the trap*

In the microfluidic device above (Fig.1) we implemented flow-induced migration of suspended cancer cells into constriction mimicking the microvasculature (6µm-wide, 60µm-long). After passing through

a constriction at the price of a strong deformation, the cell is trapped in a nest structure allowing its observation during recovery in a pressure-free relaxation chamber. We in particular observed that highly metastatic cancer cells MDA-MB-231 recover their shapes according to an exponential decay in a few seconds while their nucleus come back to their original shape in less than 20ms. The internship will in particular focus on this intriguing behavior of the nucleus.

Description of the internship

The intern will carry experiments using the above described microfluidic device using cancer cell lines of different origin (breast cancer, glioblastoma) and metastatic potential. These experiments include cell culture, the fabrication of microfluidic devices and the use of pressure controllers to finely regulate the flows of medium and cells inside the chip.
Recorded images will be analyzed using ImageJ and Matlab to extract pertinent parameters of the deformation.
Experiments will include variations in the constriction width to correlate nucleus deformation and recovery to the magnitude of the deformation.
Some cell lines were transformed to stably express fluorescent markers for double strand DNA breaks and nucleus rupture. Following these markers in addition of morphological analysis will bring further insights in the dynamics and cellular pathways involved in CTCs survival to high stresses and deformations.

The intern will work on a daily basis with Emile Gasser, 2nd year PhD supervised by Catherine Villard and Jean-Yves Pierga (clinician at Curie Hospital). This internship will also benefit from a close collaboration with Jean-Baptiste Manneville, an expert in cell biomechanics at MSC.