The biophysical signature of AML cells cells to prognosticate response to treatment

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Duration : 6 months **Starting date** : February or March 2024.

Acute myeloid leukemia (AML) develops in the bone marrow from stem cells in particular, which are transformed into leukemic cells that proliferate and cause the production of normal hematopoietic cells to dry up. One of the major problems is resistance to treatment, which is essentially based on intensive chemotherapy (cytarabine-AraC, daunorubicin), with or without allogeneic hematopoietic stem cell transplantation.
In the context of AML, the rapid expansion of medullary leukemia cells leads to changes in the properties of the tumour environment and in the availability of space for each cell population. Indeed, the cellular transition towards a leukemic phenotype is accompanied by various mechanical modifications such as the hardening of the extracellular matrix, the increase in interstitial fluid pressure (1), and the compressive stress resulting from cellular proliferation in a confined environment (2). In addition, the intrinsic cellular rigidity of leukemia can be affected by its microenvironment through a reciprocal mechanical response. Recent preliminary results have shown that commercial AML lines resistant to chemotherapy exhibit greater deformability than their sensitive counterparts (3).

In this context, the aim of this internship is to evaluate the use of an electro-deformation platform to obtain the mechanical signature of commercial AML cells in relation to their resistance to treatment. This approach has already been used in the literature to assess the metastatic character of breast cancer cells (4). The device we propose to test (Fig. 1a) has the capacity to probe the mechanical properties of several hundred cells in parallel, enabling high-throughput analysis compatible with diagnostic and prognostic applications. In addition, a "single cell" configuration of the device (Fig. 1b) will enable analysis via impedance spectroscopy to probe the dielectric properties of membranes and cytoplasmic elements, leading to a dielectric model of AML cells. This should make it possible to explore the existence of a dielectric signature characteristic of the resistant phenotype. Obtaining a new biophysical signature combining mechanical and/or dielectric phenotypes to identify the presence of resistant cells at diagnosis, could provide a robust new tool for clinicians and provide a new personalized medicine approach for choosing the type of treatment to be implemented.

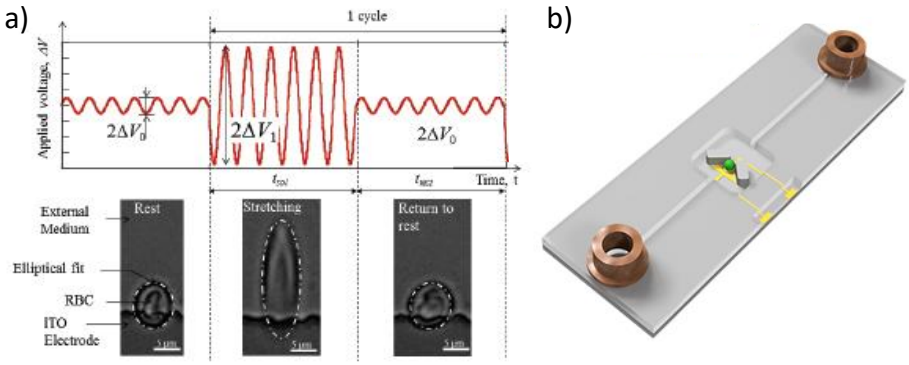

Figure 1 : a) Principle of electrodeformation illustrated on red blood cells (5). b) Illustration of the "single cell" version enabling analysis via impedance spectroscopy.

Candidate profile:
The student must have a strong taste for experimental work. Knowledge of microfabrication would be an asset. An interest in soft matter or biology is of course required. A candidate with a profile including knowledge of electrical impedance theory and measurement would also be highly appreciated.

The candidate for the M2 internship will benefit from the technological facilities provided by INL (clean room + L2 biotech zone) and will be trained in micro-nanotechnologies. It will also be an opportunity for the student to reinforce his/her theoretical and practical expertise in the field of microtechnologies.

Bibliography :
(1) Petrakis NL. J Clin Invest. 1954 Jan;33(1):27–34.
(2) Paszek MJ, Zahir N, Johnson KR, Lakins et al. Cancer Cell. 2005 Sep;8(3):241–54.
(3) Faivre et Lefort unpublished results.
(4) Teng, Y., Zhu, K., Xiong, C., & Huang, J. (2018). Analytical chemistry, 90(14), 8370–8378.
(5) Amin Amirouche. PhD thesis. Université de Lyon, 2017. ⟨tel-01707400⟩