2-years post-doc offer in Cancer-cell-on-chip in Lyon

- earliest starting date : February 2024

Scientific context:

Pancreatic cancer (PDAC), 2nd leading cause of mortality from malignancy by 2030, has only 10% 5-yr survival, due to a dense immunosuppressive tumour microenvironment (TME) supporting tumor development. With 50% of PDAC patients having a local or locally advanced disease at first diagnosis, a rationale exists for a locally administered physical agent modifying TME to improve chemosensitivity and trigger immune response. Pulsed Electric Fields (PEFs) have been used for tumor ablation in PDAC and shown to trigger immune response in other types of cancers. The potential of PEFs to remodel TME has also been proven, and the combination of reversible electroporation and chemotherapy (electrochemotherapy, ECT), has been used with promising results [1]. We hypothesize that a combination of PEFs applied within the tumor volume can both disrupt TME and facilitate drug intake by ECT.

In order to reproduce in vitro the structure of tumoral tissues, spheroids appear has a relevant minimal three-dimensional model to reproduce key aspects of tumor environment (cell-cell cohesion, gradient of nutriments, pH, ….). Using such 3D model, Ampère and ILM teams have recently co-developed an integrated hydrogel-based microsystem enabling culture, monitoring, and electroporation of hundreds of spheroids in parallel [1] (**Fig. 1**).

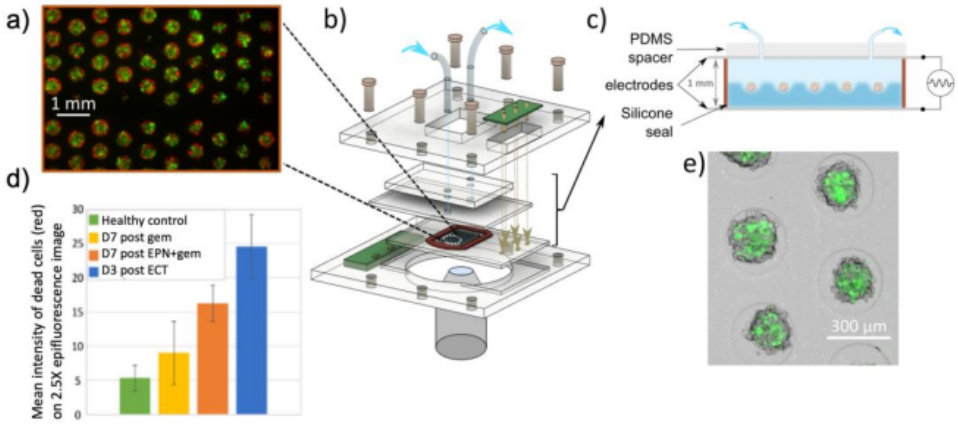

Fig. 1. (a) Epifluorescence image (2.5X) of PANC1 cell spheroids 7 days after EPN at 700 V/cm with 5 µM of gemcitabine (green = living cell, red = dead cell). (b) Exploded view of the microsystem. (c) Schematic drawing of the microfluidic chamber, sided view. (d) Mean intensity of dead cells (red) measured on 2.5X epifluorescence Images. Green = Healthy control, Yellow = 7 days after adding 5 µM of gemcitabine, Orange = 7 days after EPN at 700 V/cm with 5 µM of gemcitabine, Blue = 3 days after ECT (14 µM of bleomycin). (e) Image of co-culture spheroids after 3 days (5X). Green = fibroblasts (MRC5), Gray = PANC1

Within the frame work of an ITMO Cancer funded project, the 2-years post-doc objective is to optimize PEF therapy conditions incorporating key aspects of the TME (extracellular matrix, fibroblasts, endothelial cells and/or immune cells) for both spheroids and tumoroids. It will include microsystem preparation, optimization of the heterotypic culture condition, optimization of the

electroporation parameters, and quantitative analysis using confocal microscopy combined with transparisation protocols.

Scientific environment: The project, funded by ITMO-Cancer, is a collaborative project between Paris University Hospital (AP-HP), and 3 laboratory in Lyon : ILM, Ampère and LGEF. The candidate will share his/her time between the ILM and the Ampère Lab (both situated in Lyon).

Profil: Highly interdisciplinary project. We are searching for a candidate with a PhD either in quantitative approach in biology, biophysics or bioengineering.

Contact: Candidate should send a CV and a motivation letter to Marie Frénéa-Robin, Julien Marchalot and Charlotte Rivière

marie.robin@univ-lyon1.fr; julien.marchalot@insa-lyon.fr, charlotte.riviere@univ-lyon1.fr

---

[1] Geboers, B. et al. High-Voltage Electrical Pulses in Oncology: Irreversible Electroporation, Electrochemotherapy, Gene Electrotransfer, Electrofusion, and Electroimmunotherapy. Radiology 295, 254–272 (2020)

[2] P. Bregigeon, C. Rivière, L. Franqueville, C. Vollaire, J. Marchalot, M. Frénéa-Robin (2022). Integrated platform for culture, observation and parallelized electroporation of spheroids, **Lab on a Chip**, 22, 2489-2501. https://doi.org/10.1039/d2lc00074a