Master M2:

A microfluidic droplet platform for high throughput screening of tumor growth and anticancer drugs action

Supervisors:

Name:Jean-Louis Viovy, DR Emeritus CNRS, UMR 168, CNRS/Institut Curie/IPGG
Phone: 06 07 67 59 62
E-mail: jean-louis.viovy@curie.fr
Claire Wilhelm, DR CNRS, UMR 168, CNRS/Institut Curie/IPGG
Phone: 06 79 73 48 98
E-mail: claire.wilhelm@curie.fr

Host Laboratory:

Affiliation: Institut Curie, CNRS, PSL
Lab Name : UMR168, Institut Pierre Gilles de Gennes pour la Microfluidique (IPGG)
Address : IPGG, 6 Rue Jean Calvin, 75005 Paris

Partners or collaborations :

Name: Prof Olivier Delattre
Phone: 0156246679
E-mail: olivier.delattre@curie.fr
Affliliation: Institut Curie
Lab Name : CHIP (U830 INSERM)
Address : 26 Rue d'Ulm 75005 Paris

Project description :

The development of precision and personalized medicine, notably in cancer, leads to an explosion in the cost of research, clinical trials, diagnosis and treatment. It calls for a change of paradigm in cell-based personalized models, allowing-high throughput screening of large panels of drugs at low cost and on minute samples. Microfluidics is a natural candidate to solve the above problem.

We are developing in the lab a new **microfluidic approach**, in which cancer drugs are screened for their efficiency on "cancer organoids" or "**tumoroids**", cultivated in droplets in microchannels (Fig1).[1] This emerging new approach to cell-based screening is the oncology variant of "organoids", in which cells are allowed to develop *in vitro* in 3D. It has been shown that it is more representative as conventional screening in 2D in microtiter plates or petri body, and the accessibility and response to drugs. Conventional tumoroid approaches based on microtiter plates, however, require a large quantity of initial cells, so they impose the intermediate use of PDX (Patient Derived Xenografts) in which tumor cells from patients are implanted in mice. This PDX technology is very long and laborious (several months), and requires to sacrifice a large number of laboratory animals[2]. Due to this cost and development time, it cannot be used efficiently for treatment orientation purposes, and is reserved to drug development by big pharma.

---

[1] Ali-Cherif, A., Begolo, S., Descroix, S., Viovy, J. L. & Malaquin, L. Programmable magnetic tweezers and droplet microfluidic device for high-throughput nanoliter multi-step assays. *Angewandte Chemie - International Edition* **51,**10765–10769 (2012).

[2] Stewart, E. *et al.* Orthotopic patient-derived xenografts of paediatric solid tumours. *Nature***549,** 96–100 (2017).

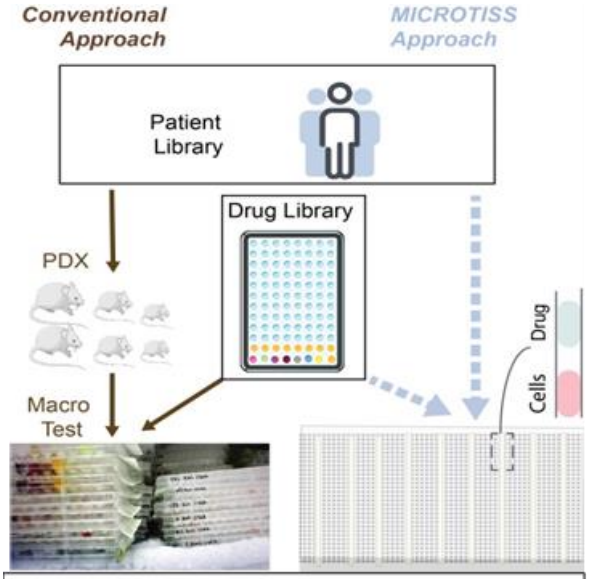

Fig 1: Principle of direct drug screening in microfluidic chips (right) à compared to the conventional approach, require a passage by PDX and multiple microtiter plates

Our new platform will allow to generate, from a single micro-biopsy, thousands of 3D tumor cell spheroids encapsulated within individual 100 nanoliters droplets, reducing the initial number of required cells by about 100, thus allowing direct screening without passage through PDX, and reducing the screening time from months to typically one week. This will first reduce considerably the cost of drug development, but most of all open the route to a real "personalized" selection of treatments. A first generation automated platform was developed, and proofs of concept of the successful growth and testing of tumoroids was made on cell lines. In this Master Internship, we shall build on this early work to develop a quantitative assay based on a test of metabolic activity, which has the advantage of screening all modes of drug actions. Besides, the platform mimics **tumor growth in confined environment**, and the cancer cell behaviour in the unique environment of droplet microfluidics, such as accelerated aggregation of cells under convection, will be studied. Importantly, this new screening platform will be compared with a more conventional approach to **patterning spheroids in microwells**, which will involve cutting-edge microfabrication techniques. Such platform can be associated to a **magnetic imprint** of the tumoroids through a labeling with nanoparticles, adding another physical dimension to the study through magnetic confinement. Ultimately, magnetic tools could be envisaged to be coupled to the droplet platform. Finally, on a more medical viewpoint, we will also consider the extension from early validations on cell lines o assays on cancer cells from patients, in collaboration with Curie Hospital.

This interdisciplinary project will be developed in the team "Macromolecules and Microsystems in Biology and Medicine, a multidisciplinary team of about 20 persons working at the interface between physics, chemistry and biology. The team is located in IPGG the first French Institute entirely dedicated to microfluidics. The project will benefit from the whole technological platform and support of the engineers of IPGG (clean room, microfabrication facility, culture rooms, microscopy), and if needed of the technological platforms and engineers of Curie Institute.

For the clinical part, it will also involve a collaboration with Prof O. Delattre, Curie Institute's Hospital, a world specialist of paediatric cancers. Finally, this project received the funding of ANR (project DROMOS), together with the startup INOREVIA, which will provide its experience in instrumentation for the maturation of the prototype, and will be a natural partner for future industrial development.

The project will require knowledge in biophysics, biomedical devices, cell biology, curiosity for new fields and ability to work in team. Those who are interested in pursuing *a* PhD are welcome.