ILM (Institut Lumière Matière), UCBL,
Bât. Brillouin, 43 Boul. du 11 novembre,
69622 Villeurbanne France.
http://ilm.univ-lyon1.fr

M2 Internship, ILM (Biophysic and FENEC group)

Title : ***Multicellular Tumor Spheroid (MCTS) model for evaluation of the efficiency of nanoparticle drug delivery***

Advisors: Charlotte Rivière and François Lux
Tél.: 04 72 43 27 96 (CR)
Email : charlotte.riviere@univ-lyon1.fr; françois.lux@univ-lyon1.fr

Possible to continue with a phD : eventually

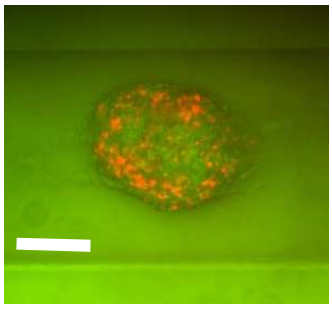
Key words: Nanoparticles, Cell aggregates (Spheroids), Time-lapse microscopy, Image analysis

Abstract, General context of the project

In most current treatment of cancer, only a few percentage of the injected drug is actually reaching the tumour cell. The rest is just diluted in all part of the body and is responsible of many side effects. This impairs the use of a high drug concentration and decrease treatment efficiency. It is then rather difficult to translate a dose showing a therapeutic activity *in-vitro* into *in-vivo* drug concentration to be injected in the patient. One approach to overcome this issue is to use nanoparticles as drug carriers or therapeutic agents. FENNEC team of ILM has developed sub-5 nm ultrasmall nanoparticles made of polysiloxane that can be visualized in MRI and are effective radiosensitizers for radiotherapy.
Before in-vivo model, the quantification of anti-tumor effects of nanoparticles are classically performed using 2D cell culture. However, such monolayer cultures do not represents physical and biological barriers encountered *in vivo.*
One of the earliest and still the most popular and prospective 3D cellular models is the multicellular tumour spheroid (MCTS). These structures contain a lot of in-vivo like factors, e.g. spatial cell-to-cell interactions and oxygen, nutrient and metabolite gradients. They can be embedded in collagen gels for example to mimic the extracellular matrix, and they can be made of different type of cells to mimic tumour heterogeneity. The Biophysic group of ILM have now a recognized expertise in 3D imaging of MCTS[1] and quantification of cell response under different stimuli (drug treatment or mechanical constraints). In particular, the biophysic group is currently developing a hydrogel-based micro-array for drug screening[2].
We plan to join the expertise of the FENEC and Biophysic group to quantify nanoparticles penetration within MCTS and subsequent drug treatment efficacy in this 3D cellular model.

Internship work

- nanoparticles synthesis
- MCTS fabrication
- 3D imaging using different type of microscopy (epifluorescence, confocal, 2-photon, single Plane Illumination Microscopy).
- quantification of nanoparticles uptake
- quantification of nanoparticle therapy



MCTS submitted to a gradient of drug concentration in a microfluidic device.

Scale Bar = 100 µm

[1] Using 2-photons Imaging or Single Plane Illumination Microscopy (Plan Cancer project under progress).
P. Marmottant, A. Mgharbel, K. Jos, B. Audren, J. P. Rieu, J.-C. Vial, B. Van Der Sanden, A. F. M. Maree, F. Graner and H. Delanoe-Ayari, *Proc. Natl. Acad*, 2009, **106**, 17271–17275.
A. Virgone-Carlotta, M. Lemasson, H. C. Mertani, J.-J. Diaz, S. Monnier, T. Dehoux, H. Delanoë-Ayari, C. Rivière and J. Rieu, *Submitt. to Plos one*.
[2] Patent under study with SATT Pulsalys.