
Sujet de thèse

Laboratoire: Institut Fresnel

Superviseur de thèse : Loïc Le Goff, Directeur de thèse : Hervé Rigneault

Email : legoff@fresnel.fr

Adresse : Institut Fresnel, Domaine Universitaire de Saint Jérôme, 13397 Marseille

Titre : Metabolic requirements of cancer stem cells activities.

Central carbon metabolism is the bio-energetic function that provides energy for cell functions and building blocks for cell growth. It is a highly regulated process both in space and time, and both in normal and abnormal development¹. For example, in cancer development, mass increase of the tumor relies on a metabolism geared towards efficient production of macromolecules, while migration of invasive cells in a physically challenging environment (ECM), requires efficient ATP production to meet with the high energetic demands of migration².

To address this experimentally, it is essential to develop methods to quantify metabolism in a spatio-temporally resolved manner. In this context, the MOSAIC team, at Institut Fresnel, has recently demonstrated the use of deuterated compounds, and their imaging through coherent Raman Imaging to image metabolic fluxes at a subcellular resolution in yeast, cultured cells and growing *Drosophila* tissues^{3,4}.

In the proposed project, we will investigate biosynthetic and energetic metabolism in the context of the development of tumors. Our group is involved in a collaborative effort (with Institut Paoli Calmette and IBDM in Marseille) to understand the role of mechanical forces in tumor growth and the initiation of metastasis, which are both driven by cancer stem cells (CSCs)^{7,8}. We will use advanced imaging and mechanical investigation of CSCs to establish if their two seemingly different characteristics – growth on the one hand and the production of mechanical work to migrate on the other hand- are linked with a reprogramming of their metabolic activity.

References

1. Miyazawa & Aulehla. Revisiting the role of metabolism during development. *Development* 2018.
2. Zanotelli et al. Energetic costs regulated by cell mechanics and confinement are predictive of migration path during decision-making. *Nature Comm* (2019)
5. Heuke et al. submitted
6. Gasecka et al. In preparation
7. Charafe-Jauffret, E. et al. Breast Cancer Cell Lines Contain Functional Cancer Stem Cells with Metastatic Capacity and a Distinct Molecular Signature. *Cancer Res.* (2009).
8. Ginestier, C. et al. ALDH1 Is a Marker of Normal and Malignant Human Mammary Stem Cells and a Predictor of Poor Clinical Outcome. *Cell Stem Cell* (2007). doi:10.1016/j.stem.2007.08.014