Postdoctoral position:

Deciphering the crosstalk between tumor and immune cells mediating resistance to immunotherapy in metastatic melanoma

A postdoctoral position is available in the "Cancer Cell Plasticity in Melanoma" lab (Dr Julie Caramel and Pr Stéphane Dalle) at the Cancer Research Center in Lyon. Our research team is dedicated to the study of metastatic melanoma, the treatment of which has been recently revolutionized by targeted and immune-therapies. However, a significant part of patients still develop resistance, and melanoma is the proof-of-concept tumor model for studying resistance mechanisms. Our lab is focused on non-genetic mechanisms of resistance to treatment, which rely on melanoma cells adaptation, through transcriptional and epigenetic mechanisms. Based on our previous results pointing at EMT-inducing transcription factors as major regulators of melanoma phenotype plasticity and intra-tumor heterogeneity, our projects aim at further characterizing the mechanisms underlying the adaptation of melanoma tumors, viewed as complex ecosystems, and the acquisition of resistance to immunotherapies. Based on the complementary expertise of basic researchers and physicians, we develop basic and translational research projects, facilitated by a privileged access to large cohorts of melanoma samples (Hospices Civils de Lyon). In this project, we will use innovative methods *in vitro*, *in vivo* in mouse models, as well as in cohorts of human samples, to:

(i) decipher the crosstalk of tumor cells with their immune microenvironment, the mechanisms of immune evasion and resistance, including a detailed characterization of intra-tumor heterogeneity in patient samples (in responders versus non-responders to anti-PD1 alone or in combination with anti-LAG3). Spatial multiplexed immunofluorescence analyses will be combined with transcriptomic analyses. Relevant targets will then be knocked-down in tumor cells and consequences on tumor growth and on immune cells function will be studied in melanoma mouse models.

(ii) develop original strategies for targeting cancer cell plasticity in order to overcome melanoma resistance to current therapeutic strategies, which will in turn provide a strong rationale to the development of new combination therapies in the treatment of malignant melanoma.

A background in immune-oncology is preferred. Previous experience in mouse handling and flow-cytometry, is required.
The position is funded for 2 years. Post-doctoral grant applications will be encouraged.

Related lab publications:

- Benboubker V, et al. Cancer cell phenotype plasticity as a driver of immune escape in melanoma. *Frontiers in Immunology*, 2022.
- Plaschka M, et al. ZEB1 transcription factor promotes immune escape in melanoma. *J Immunother Cancer*, 2022.
- Richard G, et al. ZEB1-mediated melanoma cell plasticity enhances resistance to MAPK inhibitors. *EMBO Mol Med*. 2016. 8: 1143-1161.
- Caramel J., et al. A Switch in the Expression of Embryonic EMT-Inducers Drives the Development of Malignant Melanoma. *Cancer Cell* 2013, 24, 466-480.

The CRCL environment provides state-of-the-art equipment (cell sorting and cytometry platform, imaging platform, cancer genomic platform, related technological platforms on the Lyon-Est site). More information may be found at http://www.crcl.fr

Highly motivated candidates can send an application including a cover letter, a curriculum vitae and the names of two referees, by email to julie.caramel@lyon.unicancer.fr