

Postdoctoral position available in the team « Stemness in Gliomas »

Location : Cancer Research Centre of Lyon, Lyon, France. (<http://www.crcl.fr/>)

Laboratory : The team « Stemness in Gliomas » is headed by François DUCRAY, MD-PhD, neuro-oncologist and Mathieu GABUT PhD, Inserm Researcher.

Duration : 18 months

Objective : Decipher the molecular pathways controlling glioblastoma stem cell self-renewal in 3D culture models using single cell approaches.

Context : Glioblastomas (GBM) are the most aggressive primary brain tumors. Despite decades of research, the standard care has not significantly improved overall patient survival (<5% five years after diagnosis), and GBM almost systematically relapse with no efficient treatments available. GBM tumors display an important intra- and inter-tumoral cellular heterogeneity, which is likely a major driver of treatment resistance. In this context, a specific population of GBM neoplastic cells, the glioblastoma stem cells, drew a lot of attention in the past 5-10 years as their activity is sufficient to recapitulate several features of GBM including cellular hierarchy, treatment resistance as well as tumor recurrence. Our goal is to better characterize the populations of GSCs at the genomic, transcriptomic and molecular level using in 3D culture models (tumorspheres and organoids) as patient avatars.

Description : In collaboration with the Institut Pasteur in Paris, we are conducting a single cell RNAseq study to characterize the populations of cancer cells that constitute tumorspheres and organoids obtained after culture of biopsies of glioblastoma patients in 3D conditions. More precisely, we are aiming at isolating GSC populations and precise their proliferative status, their resistance capacities to TMZ, the main chemotherapy used to treat GBM, as well as to identify signalling pathways and molecular pathways controlling their self-renewal capacities in 3D culture conditions. The models have been established in the Ducray-Gabut laboratory in collaboration with the CRCL Organoid platform. The single cell transcriptomics and computational analyses will be carried out by our collaborators from the Institut Pasteur.

The objectives of the project will be to:

- identify candidate genes/pathways enriched in GSC based on scRNAseq analysis.
- Conduct functional approaches to characterize the role of these factors in GSC maintenance in 3D models by KD or KO approaches.
- Characterize the molecular function of selected candidate genes in GSCs.

The prospective postdoctoral fellow will be in charge of the development of the project. He/she will develop new cellular models from patient derived 3D cultures and perform molecular/biochemical assays to define the function of selected genes/pathways. As the project is at the interface of the single cell transcriptomics and cancer stem cell fields, **the candidate must demonstrate prior experience in these research fields**. The applicant should have a Ph.D. degree in cell and molecular biology, biochemistry, or genetics and should be proficient in modern molecular and cellular biology procedures and have an excellent knowledge in computational scRNAseq analysis. A track record (as evidenced by publications in peer-viewed journals) in relevant fields is required. Applicants must be able to fluently communicate in English (oral and written skills). He/she must be able to communicate his/her results to the team, to our internationally recognized collaborators from the Institut Pasteur and during seminars or conferences.

Candidates must provide a CV, a cover letter stating research interests and qualifications, as well as recommendation letters and references to Dr. Mathieu GABUT : mathieu.gabut@inserm.fr