Post-doctoral Research Position (3 years) on
Cellular plasticity, epigenetic remodeling and resistance to treatment
"Génétique et Biologie des Cancers", Inserm U830 - Institut Curie, Paris.

Context

The laboratory “Genetics and Biology of Pediatric Tumors” directed by Olivier Delattre at Institut Curie develop several research programs to understand the biology and oncogenic transformation mechanisms of various pediatric tumors. We are particularly interested in the mechanisms that govern cellular plasticity in childhood cancers and their role in treatment resistance. Institut Curie provides an excellent scientific environment for high quality research with state-of-the-art equipments as well as a constellation of seminars covering many research areas. The successful post-doctoral applicant will join the neuroblastoma team on a collaborative research project funded by INCa and led by Isabelle Janoueix-Lerosey.

Research project

Tumor cell plasticity has now been identified as a source of intra-tumor heterogeneity that may contribute to treatment failure in several types of cancer. To further explore the mechanisms of plasticity and their link with epigenetic remodeling, we will focus on neuroblastoma, a tumor of the sympathetic nervous system, derived from multipotent neural crest cells (NCC), which accounts for around 15% of children cancer-related deaths. High-Risk neuroblastoma most often initially responds to intensive chemotherapy, however, relapses frequently occur followed by fatal outcome. Through the analysis of the super-enhancer landscape, we recently revealed two types of cell identity in neuroblastoma: a sympathetic noradrenergic identity and a NCC-like identity, driven by a module including the PHOX2B, HAND2 and GATA3 transcription factors (TFs) and a module containing AP-1 TF, respectively (Boeva et al, Nature Genetics, 2017). We showed that NCC-like cells display mesenchymal features and are less sensitive to chemotherapy. Recent evidence indicates that some neuroblastoma cells exhibit plasticity and are able to shift between a NCC-like/mesenchymal and a noradrenergic identity and vice versa.

The successful candidate will participate in the whole project that aims at investigating neuroblastoma cell identity, plasticity and heterogeneity in neuroblastoma in order to: (1) determine the fundamental mechanisms involved in cell plasticity in vitro; (2) characterize intratumor heterogeneity and plasticity upon treatments using in vivo models; (3) evaluate intratumor heterogeneity in patient samples and investigate the links between heterogeneity and clinical parameters. To answer these questions, we will use cell culture, FACS sorting based on specific markers, RNA-seq at the cell population and single cell levels and ChiP-seq. The understanding of the mechanisms underlying neuroblastoma cell identity and lineage plasticity should provide novel
insights into therapy design to improve outcome of high-risk neuroblastoma patients. It will contribute to a better characterization of the role of cellular reprogramming in tumorigenesis.

**Requirement**

We are looking for a highly motivated and innovative post-doc candidate with a PhD degree in life science, preferentially in a relevant discipline (cellular and molecular biology, cancer biology ...) with expertise in transcriptomic analysis and epigenetics and experience working with mice.

**How to apply**

The position (3 years) is available starting between November 2018 and January 2019. Applicants should send their detailed CV, a cover letter and contact information of at least two academic references to janoueix@curie.fr

**Selected publications of the team**


