University / lab: University of Lyon / Stem cell and Brain Research Institute (SBRI) – Inserm U1208

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Supervisor (to be contacted for applying):

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Internship title: Single cell RNA-Seq analysis of neural progenitor's diversity

Keywords: bioinformatic meta-analysis, validation, transcriptome, cortical progenitors, embryonic development, postnatal forebrain, single cell RNA sequencing

Internship description:

Stem cells produce all cells from our organism during development and persist in most adult tissues to replace dying cells. This is also true for the central system, where they are named "neural stem cells, or NSCs". These NSCs produce different cell types depending on their location (spatial identity), and their age (temporal identity). For example, NSCs located in the dorsal most regions of the developing brain produce the excitatory neurons of our cortex during early embryonic development, then switch to producing glial cells at later stages.

The transcriptional coding of NSCs' spatial and temporal identity is starting to be unravelled. Several laboratories, including our, have recently performed single cell and bulk RNA-Seq of progenitors isolated from different location and at different times. The intern will bring skills and creativity in bioinformatics and statistics to integrate and compare these datasets. In particular, several key biological questions will be addressed using bioinformatics tools such as tSNE clustering, minimum spanning tree, etc... :

- Are distinct NSCs populations observed at early and late developmental timepoints?
- Are distinct NSCs biased towards a neuronal or glial fate observed at late developmental times?
- Are progenitors present in the adult brain distinct from those active during development?

Some background work from the lab can be found in:

- Donega, V., Marcy, G., Lo Giudice, Q., Zweifel, S., Angonin, D., Fiorelli, R., Abrous, D. N., Rival-Gervier, S., Koehl, M., Jabaudon, D. et al. (2018). Transcriptional Dysregulation in Postnatal Glutamatergic Progenitors Contributes to Closure of the Cortical Neurogenic Period. Cell Reports 22, 2567-2574.
- Azim, K., Angonin, D., Marcy, G., Pieropan, F., Rivera, A., Donega, V., Cantu, C.,

Williams, G., Berninger, B., Butt, A. M. et al. (2017). Pharmacogenomic identification of small molecules for lineage specific manipulation of subventricular zone germinal activity. PLoS Biol 15, e2000698.

- Fiorelli, R., Azim, K., Fischer, B. and Raineteau, O. (2015). Adding a spatial dimension to postnatal ventricular-subventricular zone neurogenesis. Development 142, 2109-2120.

Other published work relevant to the project:

- Yuzwa S, Borrett MJ, Innes BT, Voronova A, Ketela T, Kaplan DR, Bader GD, Miller FD. (2017). Developmental Emergence of Adult Neural Stem Cells as Revealed by Single-Cell Transcriptional Profiling. Cell Reports 21, 3970-3986.
- Mayer C, Hafemeister C, Bandler RC, Machold R, Batista Brito R, Jaglin X, Allaway K, Butler A, Fishell G, Satija R. (2018). Developmental diversification of cortical inhibitory interneurons. Nature 555, 457-462.

Allowance: ~500 €/Month