2018-03

IC-**3i** International PhD Program

PhD thesis project

2018 Call for application

Control of cell emigration in development and cancer: from single cell to integrated in vivo level

General information

Call	2018-2019
Reference	2018-03-MONSORO-BURQ_PESHKIN
Keyword(s)	Single cell transcriptomics, Single cell imaging, epithelium-to-mesenchyme transition, metastasis, cell migration

Director(s) and team

Thesis director(s)	Anne-Helene Monsoro-Burq
Research team	Signaling and Neural Crest Development
Research department	UMR 3347/U1021 – Normal & Pathological Signaling: from the embryo to the innovative therapy of cancers

Description of the PhD thesis project

The team Signaling and Neural Crest Development focuses on understanding the gene regulatory network controlling neural crest formation, an essential embryonic cell population with stem cell properties and highly migratory capacities.

Cell emigration is an essential event to shape embryos during development, and the initial step for cancer metastasis in adults. The molecular mechanisms involved in the acquisition of cell motility, and cell ability to leave its epithelium of origin, are conserved in evolution and between embryos and adults: they involve a group of transcription factors (TFs) which control cell-cell adhesion and cell invasiveness. These TFs are themselves tightly regulated in embryos. It remains unknown however, how several redundant processes may cooperate in individual cells, or if different mechanisms are activated in parallel in the cell population. Using the model of neural crest cells in embryos, one of the best understood models for cell emigration, this Ph. D. project will explore the mechanisms that control cell migrations at the single cell level, and integrate them within the in vivo context. This project takes advantage of the team strong knowledge of pre-migratory and migrating NC biology, combining it with single cells technologies (transcriptomics, epigenomics, imaging) and other recent approaches (molecular embryology, migration assays) in xenopus and zebrafish embryos.

This project is highly interdisciplinary with biostatistics and informatics; embryology and cell biology; and advanced multiplex imaging at the single cell level. The PhD student will be trained by specialized supervisors thus acquire truly pluridisciplinary competence. The candidate will register at University Paris-Saclay, with co-direction with Prof. Peshkin, USA. The candidate will benefit from a large network of collaborations and the many technological platforms in Institut Curie to fulfill the different aspects of the project.

International, interdisciplinary & intersectoral aspects of the project

This project stems from a joint effort between the Monsoro-Burq Team, Institut Curie, Orsay, France, and the Peshkin Team, Harvard Medical School, HMS, MA, USA, to push the limits of single cell transcriptomics analyses applied to embryonic and cancer cells. Based primarily in Institut Curie, the candidate will spend significant research time in Peshkin team to develop the analysis on single cells, accompanied by long term visits of Prof. Peshkin to Institut Curie. In addition, for the biological validation of results, powerful imaging tools will be developed in collaboration with the Azelead SME, Montpellier (France). This triple link will provide a rich and interdisciplinary environment allowing the candidate to develop academic and industrial skills and international connections.

Recent publications

Monsoro-Burq Team
1. Plouhinec JL, Medina-Ruiz S, Borday C, Bernard E, Vert JP, Eisen MB, Harland RM, **Monsoro-Burq AH***. A molecular atlas of the developing ectoderm defines neural, neural crest, placode, and nonneural progenitor identity in vertebrates. PLoS Biol. 2017 Oct 19;15(10):e2004045. doi: 10.1371/journal.pbio.2004045. PMID: 29049289;

2. Cécile Milet, Frédérique Maczkowiak, Daniel D. Roche and **Anne H. Monsoro-Burq***. Pax3 and Zic1 drive induction and differentiation of multipotent, migratory and functional neural crest in Xenopus embryos. Proc Natl Acad Sci U S A. 2013 Apr 2;110(14):5528-33. doi: 10.1073/pnas.1219124110. PMID:23509273.

3. de Crozé N, Maczkowiak F, **Monsoro-Burq AH***. Reiterative AP2a activity controls sequential steps in the neural crest gene regulatory network. Proc Natl Acad Sci U S A. 2011 Jan 4;108(1):155-60. doi: 10.1073/pnas.1010740107.

Peshkin Team
4. Briggs JA, Weinreb C, Wagner DE, Megason S, **Peshkin L**, Kirschner MW, Klein AM. The dynamics of gene expression in vertebrate embryogenesis at single-cell resolution. Science. 2018 Jun 1;360(6392). pii: eaar5780. doi:10.1126/science.aar5780. PMID: 29700227.

5. **Peshkin L**, Wühr M, Pearl E, Haas W, Freeman RM Jr, Gerhart JC, Klein AM, Horb M, Gygi SP, Kirschner MW. On the Relationship of Protein and mRNA Dynamics in Vertebrate Embryonic Development. Dev Cell. 2015 Nov 9;35(3):383-94. doi:10.1016/j.devcel.2015.10.010. PMID: 26555057.

Expected profile of the candidate

Applicants should have a strong motivation to explore cell biological phenomena in an in vivo context, and should show solid capacity for independent and creative thinking, as well as enjoy team work. Background in cell and molecular biology is strongly recommended. Bachelor level knowledge in biostatistics is appreciated. Background in developmental biology is a plus but not compulsory. The project highly relies on the preparation and analysis of large datasets and live imaging techniques, for which the applicant should have either experience or a strong motivation to learn.