



Master project 2021-2022

Personal Information

Supervisor	Iñaki Martin-Subero
Email	imartins@clinic.cat
Institution	IDIBAPS
Website	https://www.clinicbarcelona.org/en/idibaps/research-areas/oncology-and-haematology/biomedical-epigenomics
Group	Biomedical Epigenomics

Project

Computational genomics

Project Title:

Dissecting the single cell chromatin architecture of normal and neoplastic B-cells.

Keywords:

Bioinformatics, Single-cell, CLL, B-cells, Epigenetics

Summary:

Over the last years, our group has been characterizing the molecular features of normal B-cell subpopulations and pools of leukemic cells from chronic lymphocytic leukemia (CLL), the most frequent leukemia in Western countries. We have explored the epigenetic, genetic and transcriptional relationships during normal B-cell differentiation and upon B-cell malignancies, and identified potential drivers that can be linked to the origin, progression and aggressiveness of the disease. Now, the recent development of single cell technologies has opened up the possibility of providing a detailed characterization of individual cells with unprecedented resolution. Therefore, we aim to use primary samples from healthy and oncologic patients to generate a comprehensive single cell epigenetic map to study the different maturation states of B cells, and the regulatory mechanisms that govern their tumorigenesis, to decipher the cellular diversity and clonal architecture of CLL. The successful candidate will be part of the BCLL@tlas project (2018 ERC Synergy Grant) to study how the chromatin architecture is modulated during normal B-cell differentiation and upon neoplastic transformation by applying an integrative computational analysis of single cell Multiome data (scRNA-seq and scATAC-seq). She/he will learn how to use the main bioinformatic tools to analyze and interpret single cell data such as Seurat/Signat, MOFA+ among others. We provide the opportunity to work in a highly dynamic environment with top-level collaboration (CNAG-CRG, Holger Heyn) to empower the candidate towards deeper learning of single cell data analysis with the possibility to transfer basic research into clinically relevant knowledge. Furthermore, we offer the possibility to extend the master's project to a future doctoral thesis.

References:

- Kulis, M., Merkel, A., Heath, S., Queirós, A. C., Schuyler, R. P., Castellano, G., ... & Martin-Subero, J. I. (2015). Whole-genome fingerprint of the DNA methylome during human B cell differentiation. *Nature genetics*, 47(7), 746. - Queirós, A. C., Beekman, R., Vilarrasa-Blasi, R., Duran-Ferrer, M., Clot, G., Merkel, A., ... & Martin-Subero, J. I. (2016). Decoding the DNA methylome of mantle cell lymphoma in the light of the entire B cell lineage. *Cancer cell*, 30(5), 806-821. - Beekman, R., Chapaprieta, V., Russiñol, N., Vilarrasa-Blasi, R., Verdaguer-Dot, N., Martens, J. H., ... & Martin-Subero, J. I. (2018). The reference epigenome and regulatory chromatin landscape of chronic lymphocytic leukemia. *Nature medicine*, 24(6), 868-880. - Massoni-Badosa, R., Iacono, G., Moutinho, C., Kulis, M., Palau, N., Marchese, D., ... & Heyn, H. (2020). Sampling time-dependent artifacts in single-cell genomics studies. *Genome biology*, 21, 1-16. - Duran-Ferrer, M., Clot, G., Nadeu, F., Beekman, R., Baumann, T., Nordlund, J., ... & Martin-Subero, J. I. (2020). The proliferative history shapes the DNA methylome of B-cell tumors and predicts clinical outcome. *Nature Cancer*, 1(11), 1066-1081. - Mereu, E., Lafzi, A., Moutinho, C., Ziegenhain, C., McCarthy, D. J., Álvarez-Varela, A., ... & Heyn, H. (2020). Benchmarking single-cell RNA-sequencing protocols for cell atlas projects. *Nature biotechnology*, 38(6), 747-755. - Vilarrasa-Blasi, R., Soler-Vila, P., Verdaguer-Dot, N., Russiñol, N., Di Stefano, M., Chapaprieta, V., ... & Martin-Subero, J. I. (2021). Dynamics of genome architecture and chromatin function during human B cell differentiation and neoplastic transformation. *Nature communications*, 12(1), 1-18.

Expected skills::

- Degree in relevant discipline (eg. Computational Biology, Genetics, Bioinformatics, etc) - Experience in computer programming (R, Python) - Knowledge on genome-wide data set analysis, including ATAC-seq, RNA-seq, ChIP-seq and single cell data will be a valuable asset. - Strong motivation for planning and executing research projects. - Initiative to acquire new bioinformatics, statistical or programming skills. - Communication skills to allow the efficient collaboration within the group and across multiple institutions. - Good English level

Possibility of funding::

No

Possible continuity with PhD: :

Yes
