Universitat Pompeu Fabra Barcelona | Master in Bioinformatics for Health Sciences

Master project 2024-2025

Personal Information

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Project

Computational genomics

Project Title:

Unraveling noncoding mutations and chromatin organization in uncharacterised B cell acute leukemia

Keywords:

genomics, noncoding mutations, Hi-C, Leukemia

Summary:

Among the different types of leukemia, B-cell acute lymphoblastic leukemia (B-ALL) is the most common childhood cancer. While the cure rate in child is high, it declines with age to reach ~30% in adults. B-ALL comprises a large diversity of subtypes characterized and classified by genetic alterations more and less recurrent. In the past few years, the expansion of high throughput sequencing techniques has revolutionized our understanding of the genomic landscape of ALL by enabling a better characterization of genetic alterations allowing to refine the risk stratification and to identify new therapeutic targets. However, current leukemia mutation landscapes are far from complete and recurrent leukemia-associated genetic alterations cannot be identified in ~ 10 to 20 % of patients with B-ALL. With most somatic mutations occurring in noncoding regions, current understanding of cancer mutations will remain incomplete until a systematic examination of the noncoding genome is conducted. Although attributing a functional role to non-coding mutations has been challenging, recent studies have shown that non-coding mutations play a significant role in the development and progression of leukemia. They can modify gene expression and induce functional genomic changes by altering the binding of transcription factors or by inducing high-order chromatin structural modifications. Thus, we propose a novel approach using multilevel genomic assays to simultaneously explore the 3D epigenome landscape and identify noncoding somatic mutations in unclassified B-ALL. The study aims to achieve two objectives through specific work packages: 1. Characterize the 3D epigenome landscape of unclassified B-ALL 2. Establish an atlas of the non-coding mutations of unclassified B-ALL and their potential role in the disease For that, we will combine and integrate state-of-the-art genomic technologies (ATAC-seq, H3K27ac Cut&Run and Hi-C) to identify noncoding somatic mutations in unclassified B-ALL and to characterize their functional roles in the disease. This project will provide valuable insights into the disease's mechanisms and may lead to the development of new diagnostic and therapeutic strategies.

References:

https://doi.org/10.1038/s41577-022-00774-5

Expected skills:

Understanding of basic biological principles, including genetics, molecular biology, biochemistry, and cellular biology. Proficiency in programming languages commonly used in bioinformatics, such as Python or R.

Possibility of funding:

To be discussed

Possible continuity with PhD:

To be discussed