INSTITUT DE GÉNOMIQUE FONCTIONNELLE

M2 Bioinformatics stage proposal (~6 months)

Tracking colorectal cancer relapse using circulating tumor DNA: analytical proof-of-concept

Compétences à acquérir ou à développer

- Computational analysis of genomic sequencing data (Oxford Nanopore sequencing)
- Understanding and use of bioinformatics tools and statistical/data visualization methods for cancer genomics analysis
- Pipeline development (including bash programming and especially R programming)
- Understanding of colorectal cancer biology

Description du projet

The leading cause of death from colorectal cancer (CRC) is tumor recurrence and metastasis, which affect half of patients within five years of initial treatment. Recurrent CRC can occur without symptoms and is initially undetected by standard surveillance methods. Thus, it is crucial to improve surveillance of CRC to identify patients showing evidence of persistent minimal residual disease (MRD) that cannot be detected through routine post-treatment evaluations.

Cell-free DNA (cfDNA) analysis from **liquid biopsies** is an emerging tool for minimally invasive and personalized monitoring of disease dynamics. In cancer patients, cfDNA contains cancer-derived circulating tumor DNA (ctDNA) shed by tumor cells, which can be utilized to identify clinically significant tumor characteristics while also providing the opportunity for continuous patient monitoring with greater sensitivity than conventional imaging. This may allow a better detection of crucial aspects such as tumor dormancy, disease evolution and therapeutic resistance. However, ctDNA analysis is particularly challenging due to its low levels in the blood, especially during post-treatment remission, and standard next-generation sequencing methods (e.g., Illumina) are poorly scalable, time-consuming and expensive.

In this context, our research focuses on **improving the detection and characterization of ctDNA in CRC** using the innovative nanopore sequencing technology and an unbiased sequencing approach. Our objective is to **explore the feasibility and efficiency of nanopore technology in a preclinical context** by examining its ability to perform **ctDNA genomic analysis from CRC blood samples** in a cost-efficient manner. We suggest that by using nanopore **whole-genome sequencing (WGS)**, we can efficiently and accurately track CRC by continuously assessing **ctDNA-associated genomic copy number alterations (CNAs)**, which are a hallmark of solid tumors. The broad scope of WGS, along with the simplicity, versatility and speed of nanopore technology, may represent a significant improvement over current monitoring approaches. This includes shorter analysis time, lower cost, higher sensitivity, and the possibility to incorporate patients with different tumor subtypes. **These advances are vital in clinical oncology, as they promise faster diagnosis, universal inclusion, and accelerated discovery of treatment-resistant mechanisms**.

Activité du candidat

- Generation of *in-silico* simulated nanopore datasets

- Application of different bioinformatic tools for the detection of tumor-specific genomic alterations (i.e., CNAs) from simulated and real nanopore sequencing data
- Identification of critical parameters influencing ctDNA genomic analysis with nanopore technology
- Statistical analysis and data visualization of results

Établissement d'accueil

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