

## **Development of an Analytical Framework for the Integration of Genomic and Metabolomic Profiles to Characterise Mixed Systems.**

### **Introduction**

In the past decade several new technologies have provided the basis for a better understanding of the molecular mechanisms at the cell level. With the advent of Next Generation Sequencing (NGS), we are now capable of capturing system-wide phenomena by multi -region and -time sequencing. In parallel, the application of metabolomics research has allowed an ever more precise holistic characterisation of the systemic effects of cell “production” via the characterisation of metabolism. However, currently no reliable framework exists that integrates these different types of data to accurately characterize mixed system. **The ability to characterise a molecular heterogeneity at the genomic and metabolic level in an integrative approach is key to the monitoring of progression of mixed systems in patients under treatment.**

### **Data available**

- Genomic and metabolomic (NMR) profile of Cancer patients

### **Overall aim**

We propose to take advantage of the diversity and heterogeneity of the data types to better identify rare events and their interaction with the environment. To this end **we will develop a mathematical, statistical and computational framework to integrate genomic and metabolic data.** We will first analyse existing genomic and metabolic profiles from patients to establish a mechanistic correlation between genomic mutations and metabolomics alterations. This will reveal their commonalities and provide candidate driver mutations. We then further assess the underlying genomic heterogeneity at the functional metabolome level, further narrowing what is common. The metabolome is the endpoint of biochemistry and provides a dynamic and sensitive snapshot of the phenotype. In other words, integrating data from multiple biological sources within individual patients will reveal complex genomic structures and better characterise heterogeneity at the molecular and phenotypic level. As metabolomics data generation relies on an entirely different technology than NGS, we expect to gather complementary data while benefiting from an altogether different error model. Using an exhaustive profiling of patients, this novel framework should place us ideally to understand not only the mixture of cells, but track their progression and response to treatment via the provision of new robust biomarkers.

### **Specific questions**

- 1) Genomic Analysis
- 2) Metabonomic Analysis
- 3) Integration of Genomic and Metabonomic approaches

### **Prospects for a follow-on PhD project**

If successful, this project would extend into a PhD to study further dimensions of the problem: We can use Whole Genome Sequencing (WGS) or Transcriptomics (RNASeq) at multiple sites, including their immediate surroundings and circulating DNA (ctDNA) in a subset of high-risk patients.

### **Approach in mini-project**

We are going to use available concept and software in Genomics, Metabonomics, Bioinformatics, Statistics and Mathematical Modelling.

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