1) How to cost-efficiently leverage hIPSCs to organoids through a multi-omics approach

Human induced pluripotent stem cells (hiPSCs) can differentiate into any cell type of the human body, rendering them a valuable resource for personalized medicine, research, and disease modeling. This project investigates the maintenance of pluripotency during the reprogramming process and subsequent differentiation potential from hiPSCs to organoids to establish a fast-track generation of fully functional organoids in microfluidic platforms. To this aim, a multi-omics analysis (scRNA + scATAC) approach on pooled hiPSCs from different stages enables the characterization of gene expression patterns and chromatin accessibility.
Combining scRNA and scATAC, we can perform a gene regulatory network (GRN) of transcription factors (TFs) associated with pluripotency to display their expression dynamics throughout different stages of pluripotency. The goal is to validate that early hIPSCs are pluripotent and fully established for subsequent organoid differentiation, making feasible the development of a cost-efficient methodology for generating patient-specific avatars, which accurately represent an individual's organoid model. This approach could have significant potential for personalized medicine, revolutionizing drug testing, disease modeling, and treatment.

2) Application of spatial transcriptomics for identification of potential biomarkers in cancer

Spatial transcriptomics combines scRNA-seq and spatial information with traditional morphological details can offer a comprehensive view of the tumor's molecular landscape. Such an approach has the potential to assist anatomopathologists in improving sample characterization, enabling the determination of areas of dubious origin. Pathologists can annotate areas of interest, such as the tumor core and leading edges, on matched histological images that can be further investigated to analyze the proportion of cell subtypes and distinct gene expression patterns.
Applying this technology to triple-negative cancer samples, we investigated the transcriptional profiles of different cell types within the tumor microenvironment, including cancer cells, immune cells, and vascular cells. By integrating spatial transcriptomic data with immunohistochemistry, we validated the expression of new potential marker genes. This innovative approach presents a new model for identifying potential novel markers in tumor samples, with significant implications for future research and clinical applications.

3) Population genomics for surveillance of common genetic diseases

Germline variants in specific genes play a crucial role in the development of certain types of inherited cancer, such as breast and ovarian cancer syndromes, as well as some genetic-based diseases like cardiomyopathies. Within families affected by these hereditary syndromes, certain patterns can be observed. Detecting these mutations accurately can help identify individuals who have a higher-than-normal risk of developing these disorders, enabling informed treatment and management decisions. However, the expensive nature of germline genetic testing creates a barrier to effective mass screening.
In recent years, next-generation sequencing (NGS) amplicon-based approaches have revolutionized genomic sequencing in diagnostics, leading to improved personalized care. The main objective of this project is to develop a cost-effective computational approach for mass screening of germline mutations in genes commonly associated with inherited diseases. By utilizing these methodologies, we aim to overcome the limitations posed by the high cost of genetic testing and potentially expand this analysis for large-scale genomic surveillance of common hereditary diseases.