Project Proposal

Transcriptional phenotyping of breast cancer at the single-cell level to predict drug therapy for personalized medicine.

Project Description (*max 500 words*)

One of the main roadblocks in personalised medicine is the lack of biomarkers to predict which drug or drug combination could benefit the patient starting. Measurement of gene expression in tumour samples has been effective in classifying tumour types but its clinical usefulness in predicting drug sensitivity is unclear. Classic "bulk" gene expression profiling averages out tumour heterogeneity and can miss rare cancer cell populations, which may confer drug resistance. Single-cell transcriptomics enables to obtain a molecular profile of individual cells and thus take tumour heterogeneity into account. This project aims at exploring how plasticity in gene expression programs affects cell heterogeneity, and thus drug response, by comparing three breast cancer models of increasing complexity: cancer cell lines grown in 2D, in 3D (MultiCellular Tumour Spheroids - MCTS) and patients' derived Breast Cancer Organoids (BCOs). In the project, we will generate single-cell sequencing data from MCTS and BCOs to complement the data on cancer cell lines grown in 2D that were previously generated in the lab (Gambardella et al, Nature Comm, 2022), then to develop a computational approach for automated cancer diagnosis; and finally to predict the most effective drug combination therapies, starting from single-cell expression profile of a tumour sample.

Supervisor(s), Lab/Group details, other additional info. (*please provide information about the group and available facilities*)
Diego di Bernardo (DICMAPI) - Systems and Synthetic Biology Lab @ TIGEM

Funding (*how the reagents, equipments, conference and travelrs will be supported)*
Italian Association for Cancer Research (AIRC)

References

1. A single-cell analysis of breast cancer cell lines to study tumour heterogeneity and drug response. Gambardella G, Viscido G, Tumaini B, Isacchi A, Bosotti R, di Bernardo D. Nat Commun. 2022 Mar 31;13(1):1714. doi: 10.1038/s41467-022-29358-6.