Studying cancer cells phenotypes integrating omics data in human reduced genome-scale metabolic models

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Cancer is a leading cause of death in the world, and the mechanisms underlying this disease are still not completely understood. In the last decades, altered tumour metabolism has been recognized as a hallmark of cancer. This has created a resurgence of interest in the field of systems biology and metabolic modelling to analyse and understand the metabolic changes occurring in cancer cells. Modelling the different phenotypes of healthy and cancer cells will help to make predictions to create effective therapies to prevent, diagnose and treat cancer.

The reconstruction of genome-scale models (GEMs) enables the computation of phenotypic traits based on the genetic composition of a target organism. Therefore, we use the human genome-scale model *Recon 2* to build cancer cell-specific human GEMs by integrating experimental data (fluxomics, metabolomics, genomics, transcriptomics) and thermodynamic data. To overcome the well-known challenges when working with large networks, we generate systematically reduced models around specific subsystems, considering the composition and usage of the extracellular medium metabolites, and the biosynthesis of the biomass precursor metabolites. Furthermore, we apply pathway enrichment to study the regulation of the pathways under study. The reduced models can be used for a broad range of applications ranging from *omics* data integration to kinetic models.

The proposed pipeline will enhance the comparison and understanding, at the stoichiometric and kinetic level, of the main metabolic differences that emerge in cancer development and progression. Furthermore, predicting the network responses will help to design experiments to find new targets for therapies and drugs.