

Towards a qualitative understanding of Cancer metabolism

Adaptation of metabolism is a response of many eukaryotic cells to nutrient heterogeneity in the cell microenvironment. One of these important adaptations for cancer cells is the shift from respiratory to fermentative metabolism, namely the Warburg effect. It is mostly a response to a very high nutrient increase in the cell microenvironment, even in the presence of oxygen. We use an extension of the René Thomas modelling framework for representing the regulations between the main catabolic and anabolic pathways of eukaryotic cells, and formal methods for confronting models with known biological properties in different microenvironments. Our formal model of the regulation of cell metabolism reveals the conditions under which this metabolic phenotype switch occurs. It clearly proves that currently known regulating signals within the main components of central carbon metabolism are sufficient to bring out the Warburg effect. Moreover, this model offers a valuable tool to perform in silico screening of perturbations of the central carbon metabolism in order to inventory potential innovative cancer treatments.