

Differential metabolic activity and discovery of therapeutic targets using summarized metabolic pathway models

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In spite of the increasing availability of genomic and transcriptomic data, there is still a gap between the detection of perturbations in gene expression and the understanding of their contribution to the molecular mechanisms that ultimately account for the phenotype studied. Alterations in the metabolism are behind the initiation and progression of many diseases, including cancer. The wealth of available knowledge on metabolic processes can therefore be used to derive mechanistic models that link gene expression perturbations to changes in metabolic activity that provide relevant clues on molecular mechanisms of disease and drug modes of action (MoA). In particular, pathway modules, which recapitulate the main aspects of metabolism, are especially suitable for this type of modeling.

Here we present a simple model of metabolic activity based on pathway modules. The model has been implemented in a web-based application, Metabolizer, which offers an intuitive, easy-to-use interactive interface to analyze differences in pathway module metabolic activities that can also be used for class prediction and in silico prediction of Knock-Out (KO) effects. Moreover, Metabolizer can automatically predict the optimal KO intervention for restoring a diseased phenotype. We provide different types of validations of some of the predictions made by Metabolizer.

Metabolizer can be found at: <http://metabolizer.babelomics.org>.

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