FILLING THE GAP BETWEEN EXPERIMENTALISTS AND MODELERS BY DETERMINING A MAMMALIAN CELL'S METABOLIC CAPABILITIES BASED ON TRANSCRIPTOMIC DATA

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Large-scale omics experiments are now standard in many biological studies, and many methods exist to interpret these data. One emerging approach uses genome-scale metabolic models (GEMs) for model-guided data analysis, since they provide cellular context to these large data sets by establishing a mechanistic link from genotype to phenotype. GEMs include all reactions in an organism, but not all enzymes are active in each tissue, cell line or culture condition. Therefore, algorithms have been developed to build context-specific models that recapitulate the metabolism of specific cell types under specific conditions, based on omics data measurements1. While these context-specific models improve the ability to predict genotype-phenotype relationships, the physiological accuracy and relevance of these models are often overlooked, due to gaps in our knowledge of context-specific metabolism functionalities. Indeed, many cell types have unique metabolic functions they natively accomplish. However, since these functions are often poorly defined for specific cell types, it can be difficult to evaluate a cell's metabolic activities in an unbiased fashion within a modeling context. To overcome this, we curated a list of previously published metabolic tasks2,3 and obtained a collection of 210 tasks covering 7 major metabolic activities of a cell (energy generation, nucleotide, carbohydrates, amino acid, lipid, vitamin & cofactor and glycan metabolism). Using published genome-scale metabolic models for human and CHO cells, we identified all metabolic genes that are used for each metabolic function. Thus, by using these lists of genes to analyze omics data (e.g., RNA-Seq), one can estimate the metabolic capabilities of a cell without modeling.

Therefore, this list of metabolic tasks provides a framework for modelers to develop more physiologically accurate models by identifying key reactions that need to be included in a model to capture each specific metabolic task in a cell. It can also serve as a tool for experimentalists to contextualize the omics data by evaluating the activity of metabolic functions captured in the data.

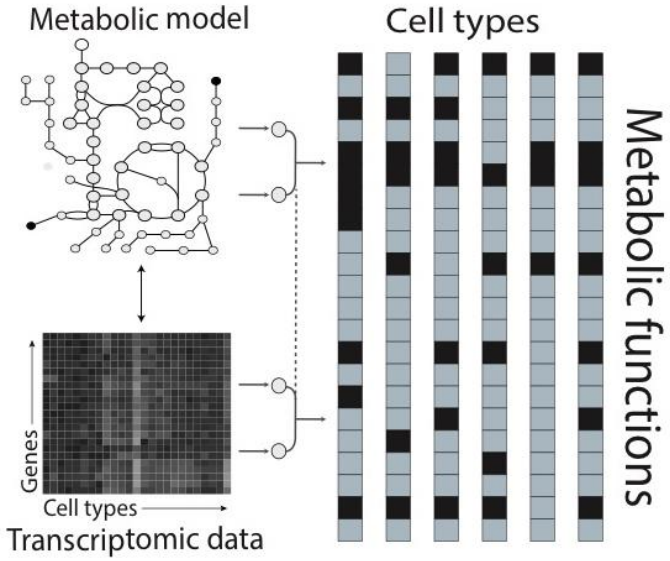

Figure 1 – The task collection allows the evaluation of the functionalities enclosed in a given mammalian cell metabolic model and the further assessment of the metabolic functions activities based on transcriptomic data.

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