

A systems approach toward automated metabolic phenotyping

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Abstract

The conventional approach to the metabolomic analysis of human in vitro cell cultures is for one laboratory to transfer a set of cell culture samples to another laboratory to a set of metabolomic platforms. This results in a list of quantified, and possibly identified, metabolites together with generic statistical analyses. The challenges associated with this conventional approach are discussed. An alternative approach is proposed to automatically characterise metabolism in human stem-cell derived cultures by introducing the concept of a closed-loop metabolic phenotyping apparatus. This is a physically and computationally integrated system of automated experimental and analytical chemistry components that iteratively minimises the uncertainty in a cell-type-specific, constraint-based computational model of metabolism. Progress toward construction of a closed-loop metabolic phenotyping apparatus described. In particular, automated microfluidic cell culture of stem-cell derived neurons, generation of genome-scale, cell-type-specific metabolic models from a generic human metabolic network reconstruction, and metabolic model driven metabolomic experimental design. Future aims and their relationship of automated metabolic phenotyping to personalised in vitro disease modelling will be discussed.