
Talk

Systems medicine approach to model cell signaling activity uncovers disease mechanisms and predicts cancer outcome



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Keywords: Signaling pathways; mathematical models; systems medicine

ABSTRACT

Motivation: Gene expression measurements (microarray or RNA-seq) are affordable ways to survey cell activity. However, they constitute low-informative, decontextualized values that often lack a mechanistic link with real cell functional outcomes. Mathematical modeling of biological pathways is emerging as a useful tool to understand the molecular mechanisms that govern the cell behavior or fate, revealing disease mechanisms and drug mechanisms of action, and providing guidance on therapeutic decisions (Gustafsson et al., 2014).

Methods: Signaling KEGG pathways are used as basic maps of cell functionality over which gene expression values are modeled to obtain probabilities of signal transduction and, consequently, cell function activations (Hidalgo et al, 2017).

Results: Here we propose a new method that models cell signaling using biological knowledge on signal transduction (Hidalgo et al., 2017). The method recodes individual gene expression values (and/or gene mutations) into accurate measurements of changes in the activity of signaling circuits, which ultimately constitute high-throughput estimations of cell functionalities caused by gene activity within the pathway. Signaling circuit activities can predict cancer outcome and have also demonstrated to be excellent predictors of drug response (Amadoz et al., 2015)

Conclusions: A comprehensive, systems-based understanding of the way in which genes interact to shape the phenotype is required to realistically manage complex diseases.

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