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Systems-level investigation of the interaction between glucose metabolism and the Snf1/Mig1 signalling pathway

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Abstract

Saccharomyces cerevisiae Snf1 and its mammalian homolog, AMPK, are members of a protein kinase family present throughout the Eukaryotic kingdom. AMPK plays an essential role in different cellular processes and is involved in diseases such as diabetes, obesity and cancer. Snf1 in yeast is a central component of metabolic switching and influences a broad spectrum of cellular processes such as lipid synthesis, glucose uptake and glucose metabolism. This kinase also plays a distinct role in other stress responses. When glucose becomes limiting, the Snf1 kinase phosphorylates, among others, the Mig1 transcriptional repressor causing it to exit the nucleus, resulting in derepression of gene expression. Many components of glucose signalling are already known, however there are still some caveats in our knowledge. Here, additional details are presented on how glucose metabolism influences the functioning of the Snf1/Mig1 pathway and how the glucose signalling interaction network is integrated with other cellular processes. Another aspect of this work centred on the individual yeast cells responses to glucose. Both empirical observations and mathematical modelling was used to predict the outcome of glucose signalling and to identify the source(s) of the significant cell-to-cell variability in the response to carbon source availability. We report a novel modelling approach to explain cell-to-cell variability in the response of individual yeast cells to glucose and reconstruct large signalling networks. Taken together, the importance of individuality of single yeast cells is highlighted by glucose signalling displaying considerable variability at the level of individuals. Furthermore, this work shows that glucose metabolism mediates a dynamic and stringent regulation of Snf1/Mig1 pathway dynamic.

Keywords: glucose signalling**,** microfluidics, *Saccharomyces cerevisiae*.