

Glucose regulation and Snf1 protein kinase in *Saccharomyces cerevisiae*

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Abstract

The conserved Snf1/AMPK (AMP-activated protein Kinase) family in eukaryotes is one of the central components in nutrition sensing and regulation of carbon metabolism. In mammals, AMPK was shown to be a potential target of treatment for metabolic disorder diseases such as obesity and type II diabetes (Ref 1). In yeast *S. cerevisiae*, the Snf1 protein kinase is composed of a catalytic subunit Snf1p, a scaffolding β -subunit (Sip1p, Sip2p or Gal83p) and a regulatory subunit Snf4p (Fig. 1). Snf1 also plays an important role in several other processes such as stress resistance, invasive growth and ageing (Ref 2, 3, 4). Although the redundancy of the β -subunit is not understood well, it was reported that the β -subunit can mediate subcellular localization of the Snf1 protein kinase under derepressing conditions, for example, low glucose (Ref 5) and therefore may indicate distinct functions of specific β -subunit in signaling transduction and regulation.

In order to study the roles of the β -subunit in the signal transduction and regulation, we constructed three β -subunit mutants, $\Delta sip1$, $\Delta sip2$ and $\Delta gal83$ and carried out batch fermentations on defined medium with glucose as the sole carbon source to characterize the physiology. Genome-scale microarray experiments were also performed to investigate the cellular transcriptional response to the loss of one β -subunit protein. Batch fermentation data showed that compared with $\Delta sip1$ and $\Delta sip2$ (which were similar with the reference), the strain $\Delta gal83$ showed longer diauxic shift after glucose was exhausted and lower growth rate on non-fermentable carbon sources (i.e., mixture of ethanol, glycerol, acetate, etc.), indicating a change in the enzymes corresponding to those metabolic pathways. The gene expression data showed that deletion of Gal83p caused bigger changes than deletion of Sip1p or Sip2p, in terms of both the number of genes affected and the fold-change of expression level. Principle component analysis (Fig. 2) also shows that $\Delta sip1$ and $\Delta sip2$ had similar transcription profiles and the differences between $\Delta gal83$ and $\Delta sip1/\Delta sip2$ might be due to the different sub-cellular localization of the Snf1 protein kinase and therefore a different signal transduction mechanism.

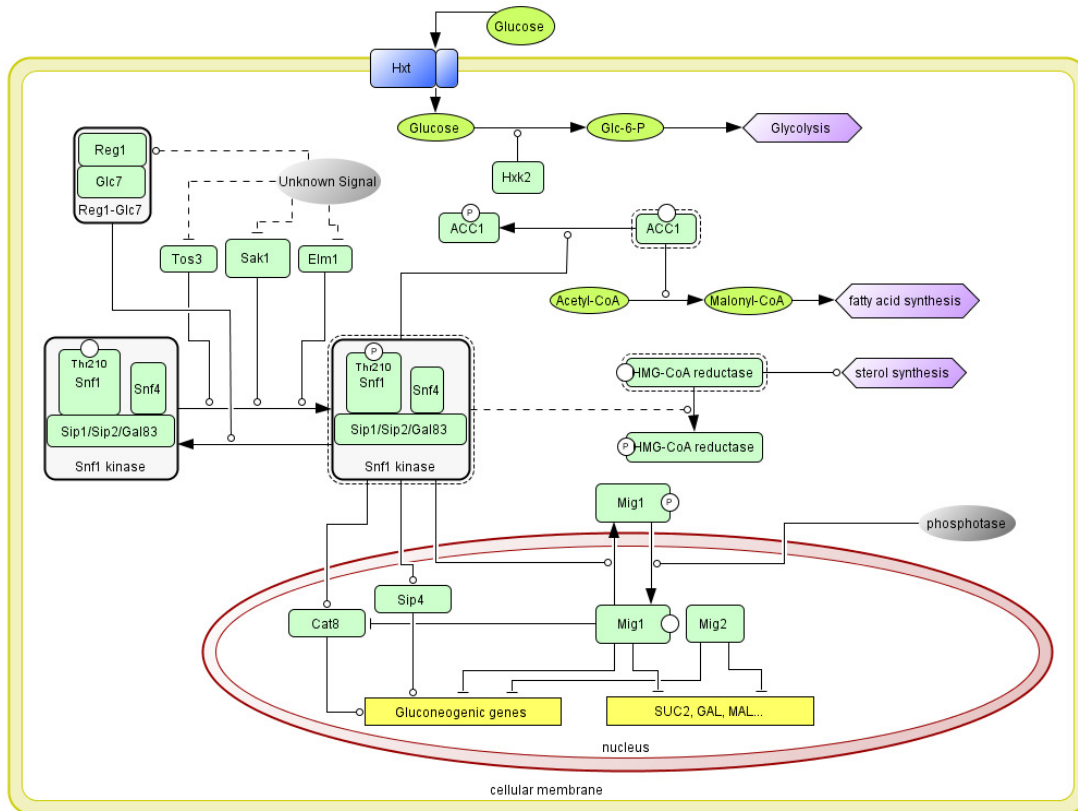


Fig. 1 A simplified scheme of Snf1 pathway

Activated by its upstream kinase (Sak1, Tos3 or Elm1) upon glucose depletion, Snf1 further phosphorylates Mig1, a transcriptional repressor for those genes involved in the utilization of alternative sugars, such as maltose and sucrose, and non-fermentable carbon sources such as glycerol and ethanol. When glucose is abundant, Snf1 is unphosphorylated by the Reg1-Glc7 protein phosphatase, probably triggered by an unidentified signal.

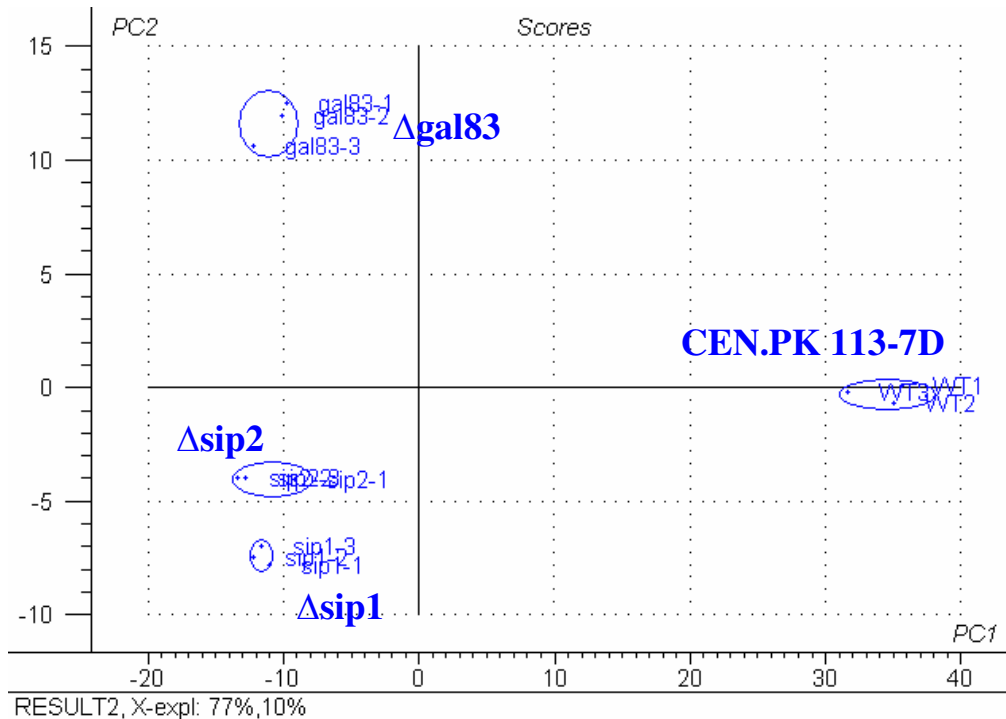


Fig. 2 PCA plot shows that $\Delta sip1$, $\Delta sip2$ and $\Delta gal83$ are separated from the reference CEN.PK113-7D on the first principle component and on the second principle component, $\Delta sip1$ and $\Delta sip2$ are co-localized and $\Delta gal83$ is separated from them.

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