Protein metabolite interaction and metabolic flux sensing are involved in glucose control of Snf1/AMPK activity

Milanesi R.[1], Tripodi F.[1], Coccetti P.

E-mail: r.milanesi2@campus.unimib.it
[1]University of Milano-Bicocca, Piazza della Scienza 2, Milan, Italy

Keywords: Snf1/AMPK, Ras/PKA, glucose metabolism, protein metabolite interaction, signal transduction, flux sensing.

Abstract:

Snf1/AMPK is a highly conserved protein kinase required for energy homeostasis among all eukaryotes. In Saccharomyces cerevisiae it is essential for the growth on carbon sources alternative to glucose, condition in which it is active and highly phosphorylated on threonine 210 (T210). Snf1 phosphorylation is controlled by glucose catabolite repression and decrease in cells grown in high glucose condition. Despite this evidence the molecular mechanism connecting Snf1 phosphorylation state to the availability of glucose is still lacking.

Recent reports suggest that microbial metabolism is linked with rate at which carbon sources is imported within the cell. In *E. coli* and *S. cerevisiae* the choice between respiration and fermentation of glucose is inversely correlated with glucose uptake rate. This implies the existence of a “flux sensing” mechanism able to perceive sugars transport rates and properly tune genes expression and enzymes activity towards fermentation or respiration.

A different line of evidence suggests that the coordination of cellular metabolism and signal transduction is achieved through Protein Metabolite Interactions (PMIs). These molecular events consist in physical interactions between key metabolites and regulatory proteins, resulting in a change in the activity of these proteins.

In the present work, we investigate the hypothesis that glucose control of Snf1 phosphorylation implies the sensing of glucose uptake rate, that could take place through a direct interaction of Snf1 complex with one of the glycolytic metabolites.
We also speculate that the engineering of such a mechanism could allow to control *S. cerevisiae* metabolism, releasing yeast choice between fermentation or respiration from the availability of glucose.