Modelling Snf1 regulation in *Saccharomyces cerevisiae*

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**Background**

The AMP-activated-protein-kinase (AMPK) signaling pathway plays a central role in monitoring the cellular energy status and controlling energy production and consumption. The yeast AMPK orthologue Snf1 is best known for its role in glucose repression/derepression. One ultimate goal of the study of these pathways is to generate a computational model able to support drug development, targeted at advancing diseases such as obesity and type II diabetes. In this work, we focus on a quantitative dynamic model describing the Snf1 activation/deactivation pathway.

**Model**

Snf1 plays a main role in transcriptional activation and repression of gene expression:

- Glucose depletion → Snf1 activation by phosphorylation through its upstream kinases Sak1, Tos3, Elm1. Activation of Snf1 → Inactivation of the repressor Mig1 via phosphorylation → Expression of genes involved in alternative carbon utilization.
- Glucose abundance → Snf1 deactivation by dephosphorylation through its upstream phosphatase Req1/Glc7. Deactivation of Snf1 → Mig1 remains active → Repression of genes involved in the utilization of alternative carbon sources.

**Key Questions**

- Does regulation of Snf1 occur via its phosphatase or its kinase or both?
- How are the kinase and phosphatase of Snf1 regulated?
- Which role do the hexokinases play?
- Can the huge variety of hexosetransporters (Hxts) be summarized in one pool?

**Hypotheses**

1. **Regulation by complex formation:**
   - Snf1 binds to Mig1 and regulates its activity.
2. **Regulation directly from Hxts:**
   - Hxts provide glucose and activate Snf1.
3. **Regulation directly from Hxts with respect to the X-factor:**
   - X-factor (e.g., stress) affects the activity of Snf1.

**Results**

- Experimental data for extracellular glucose, OD, and Snf1P provided the basis for modelling.
- The model correctly reproduces the experimentally measured Snf1 activation and deactivation responses.
- To reproduce *in silico* the glucose correctly, we included synthesis and degradation reactions for the Hxts.

**Acknowledgments**

S.F., O.W. and S.H. are supported by EU FP6 project “Systems biology of the AMP-activated protein kinase” (AMPKIN; grant LSH-CT-2005-518181).

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