GÖTEBORGS UNIVERSITET

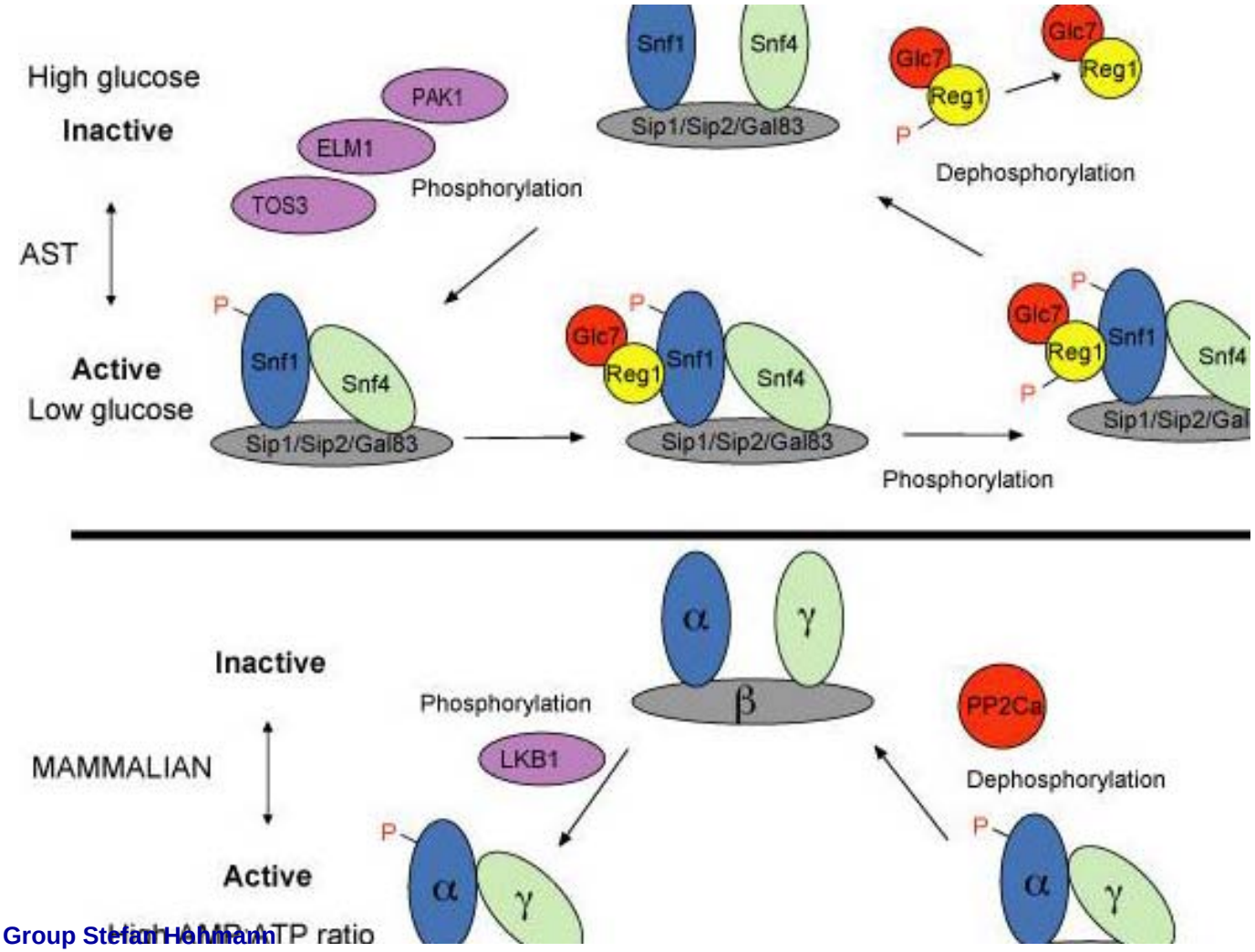
Systems biology of the yeast Snf1 pathway

Stefan HOHMANN
Göteborgs Universitet

hohmann@gmm.gu.se

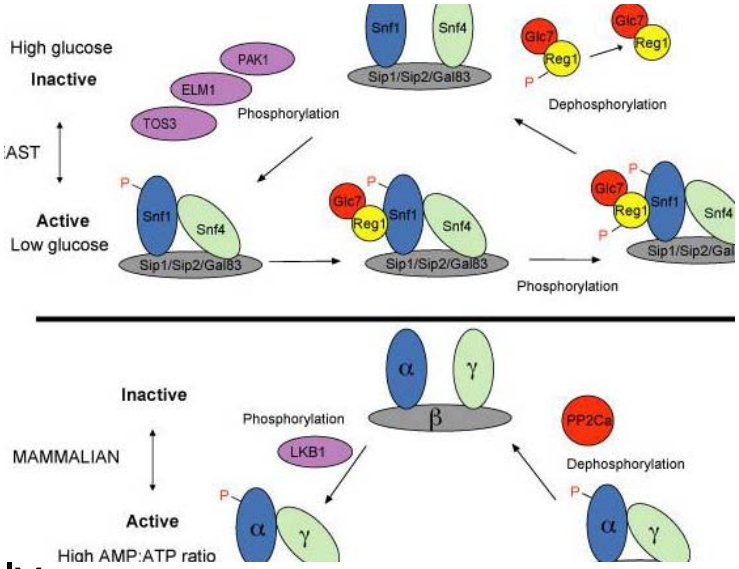
GÖTEBORGS UNIVERSITET

Snf1 is an AMP-activated protein kinase: highly conserved eukaryotic signalling module



GÖTEBORGS UNIVERSITET

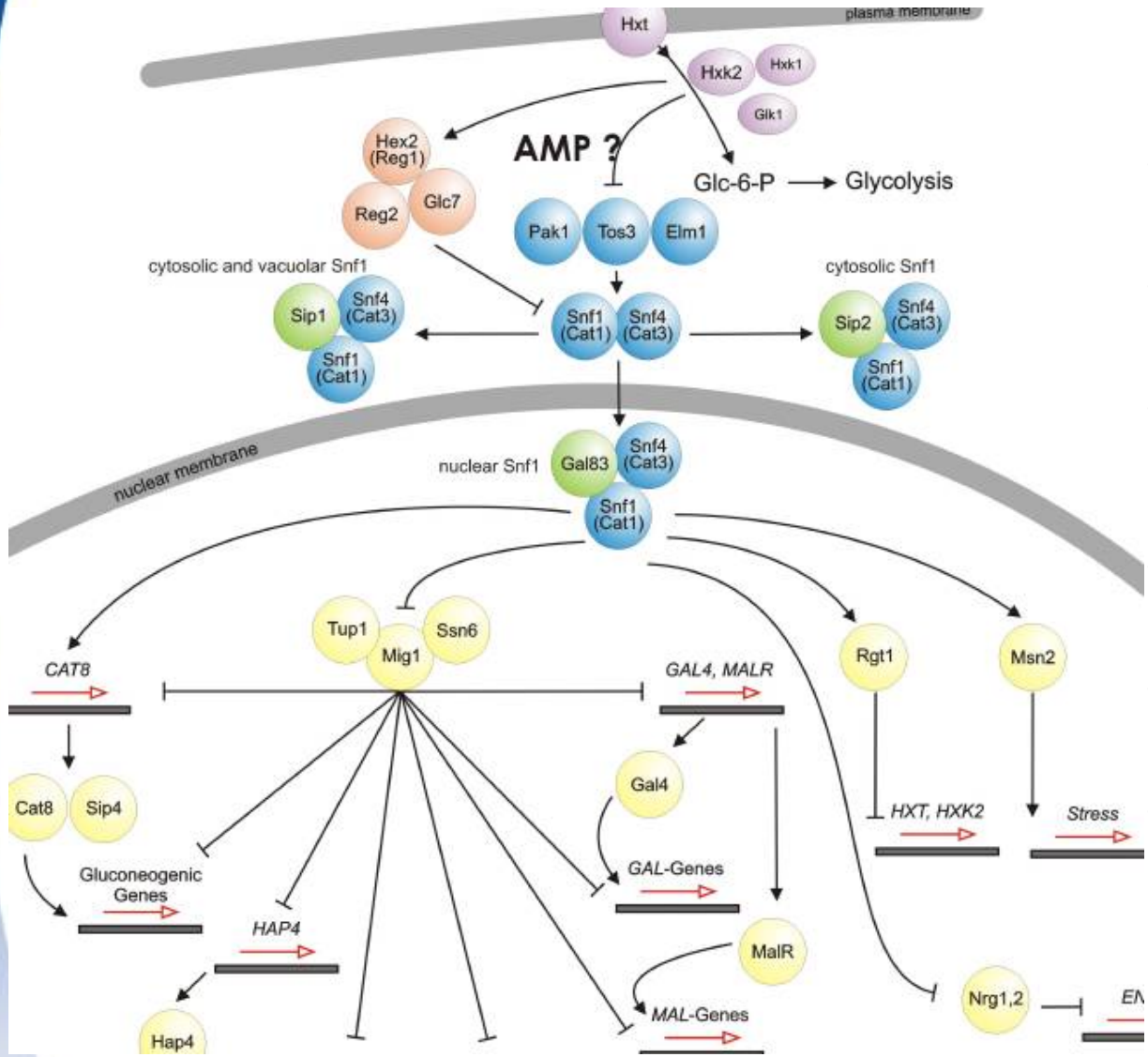
Snf1 and AMPK



- Inactive under optimal energy supply
- Activated under conditions of energy demand
- Controlling production and consumption of energy
- Snf1 is best known for its role in glucose-derepression
- Active Snf1 promotes (and is required for) utilisation of carbon sources other then glucose
- AMPK activation could be a means against conditions like metabolic syndrome and diabetes type 2

GÖTEBORGS UNIVERSITET

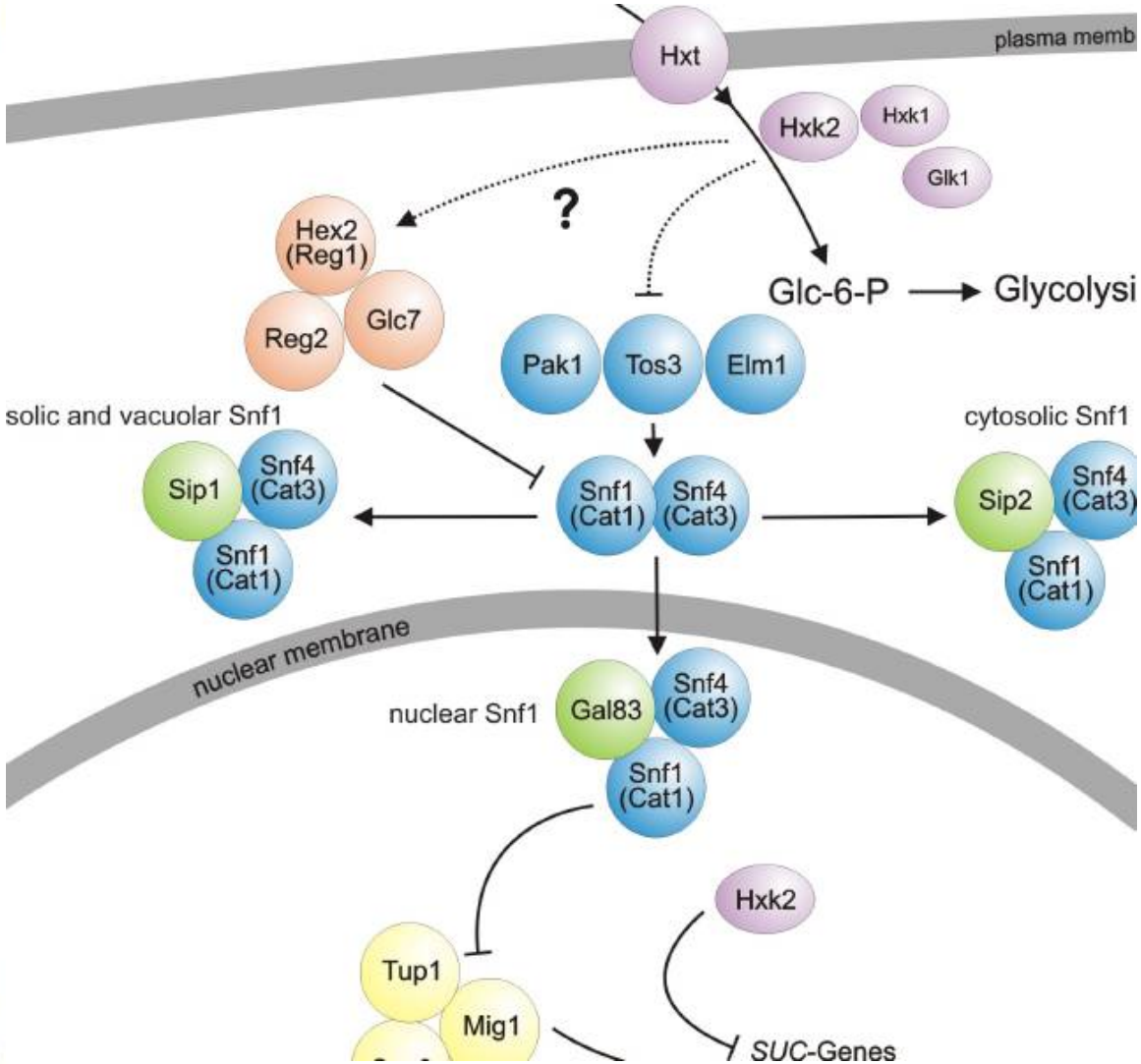
Yeast Snf1 system



- **Active Snf1 is a negative regulator of Mig1: glucose derepression**
- **Active Snf1 activates Cat8: gluconeogenesis**
- **Active Snf1 may activate the Rgt1 repressor: downregulation of sugar uptake/phosphorylation**
- **Active Snf1 may contribute to Msn2 activation: general stress response**
- **Control of *ENA1* and ion homeostasis, probably via Nrg1, 2**
- **Little is known about cytosolic targets**

GÖTEBORGS UNIVERSITET

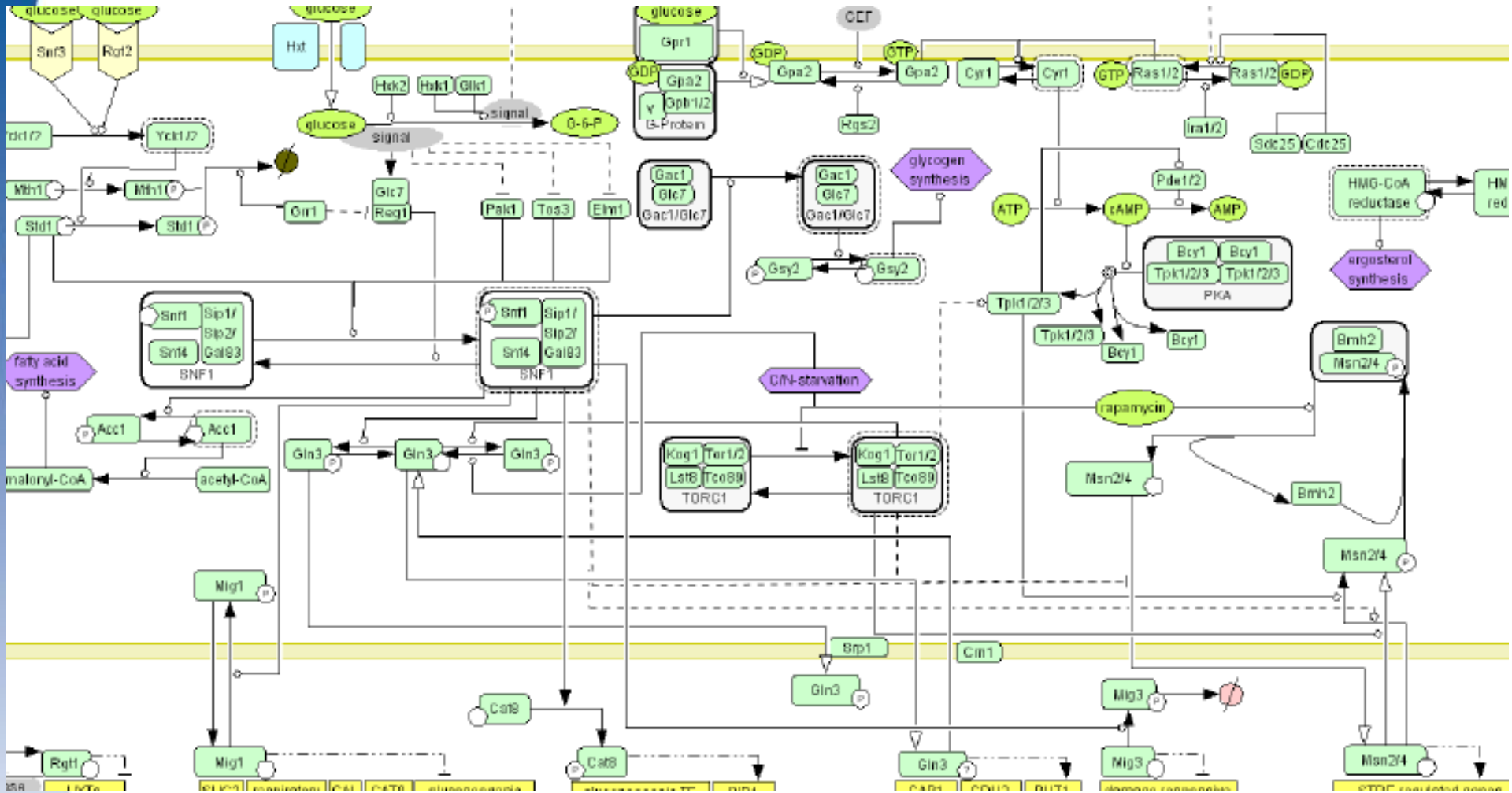
Some open questions



- **Does hexokinase signal via Snf1 and/or via a parallel pathway in the nucleus?**
- **Does signalling occur via upstream kinases or phosphatases or both?**
- **Link between metabolism and Snf1 activity – sensing?**
- **Precise role and regulation of different Snf1 complexes?**
- **How does Snf1 interact with other glucose-regulated pathways?**

GÖTEBORGS UNIVERSITET

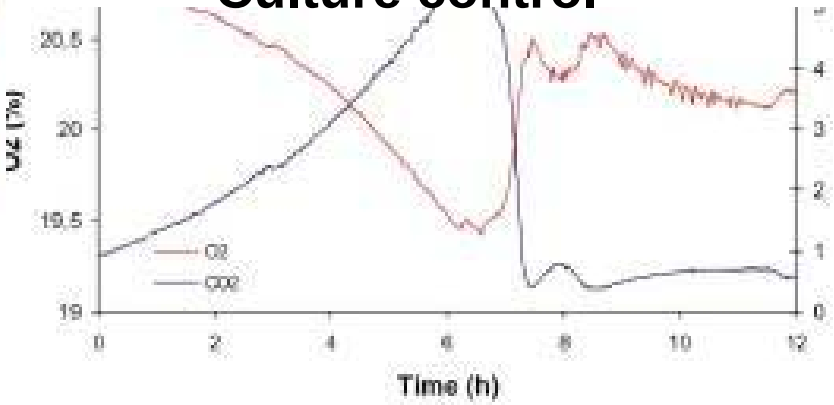
Glucose signalling network



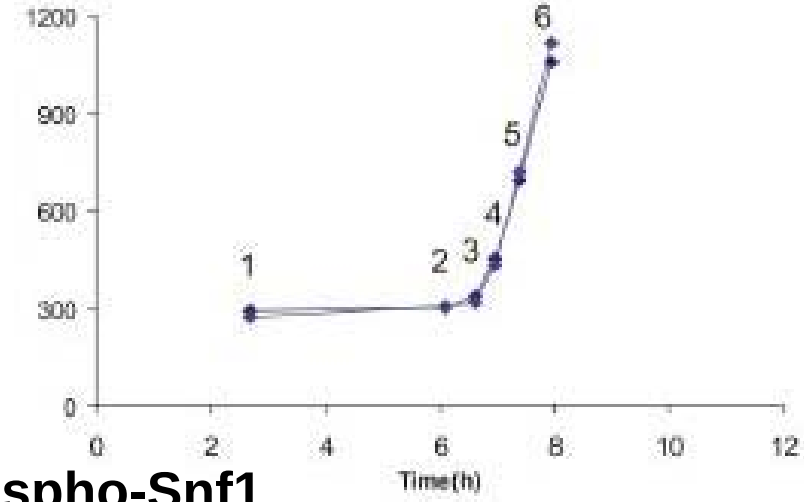
GÖTEBORGS UNIVERSITET

Generating quantitative data on pathway activation - deactivation

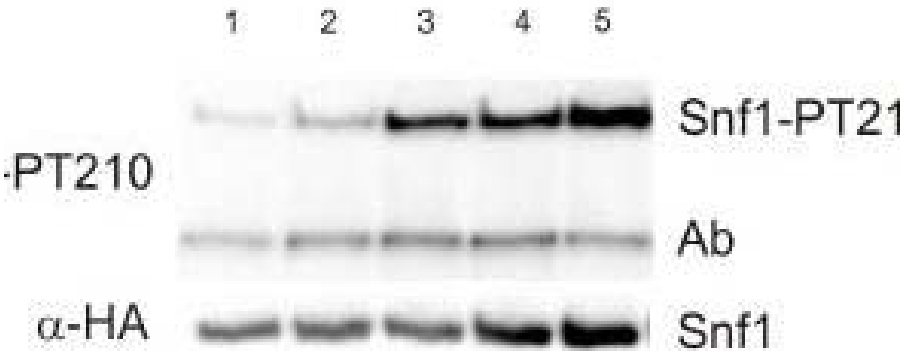
Culture control

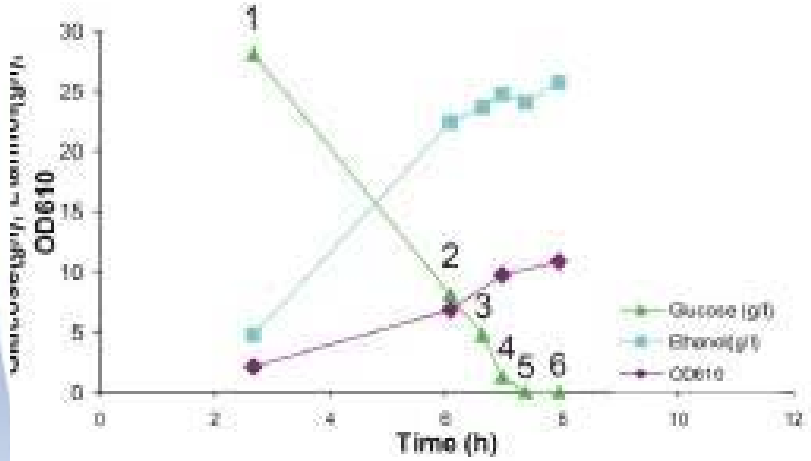


Gene expression



Phospho-Snf1





Metabolic data

GÖTEBORGS UNIVERSITET

Assessing cell-to-cell variation

- Using a *SUC2*-eGFP fusion and flow cytometry – response profiles of culture distribution
- Use of Mig1-GFP fusion (nuclear shuttling) and microscopy combined with microfluidics – monitoring signalling in real time and assessing cell-to-cell variations

GÖTEBORGS UNIVERSITET

AMPKIN EC project

- **Stefan Hohmann, Yeast biology, Göteborg**
- **Dag Hanstorp, Physics, Göteborg**
- **Dave Carling, Mammalian biology, London**
- **Jens Nielsen, Yeast physiology, Lyngby/Copenhagen**
- **Olaf Wolkenhauer, Theoretician, Rostock**
- **Thomas Svensson, Drug development, Biovitrum AB, Göteborg**

GÖTEBORGS UNIVERSITET

Group spring 2007

- **Head: Prof. Stefan Hohmann**
- **Group leaders: Docent Markus Tamás (independent team: arsenite tolerance), Dr. Karin Lindqvist (independent team: structure/function aquaporins and glucose transporters), Dr. Karin Elbing (AMPKIN), Dr. Bodil Nordlander (MAPK)**
- **Lab manager/technician: Peter Dahl, Takako Furukawa**
- **Bioinformaticians: Abraham Nahmany (PhD student)**
- **Post-docs: Carl Tiger, Gemma Beltran, Kentaro Furukawa, Julia Ilyina (MT), Raúl Salcedo**
- **PhD students: Tian Ye, Dominik Mojzita, Cecilia Geijer, Ivan Pirkov, Michael Thorsen, Elzbieta Petelenz, Madelene Palmgren, Daniel Bosch, Doryaneh Ahmadpour, Lars-Göran Ottosson, Sylwia Zoltowska, Jimmy Kjellén**