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Regulation of AMP-activated protein kinase by glucose: from yeast to humans

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Cells respond to environmental stimuli by adjusting their internal machinery to cope with these external changes. One of these environmental stimuli is the presence/absence of glucose. This monosaccharide acts as a pseudo-hormone since it is able to trigger specific signalling cascades that affect metabolism, gene expression and cell growth. Some of the glucose signalling pathways are conserved from yeast to humans, indicating the importance of these events in cell physiology. One of the main signalling cascades regulated by glucose is the pathway governed by the AMP-activated protein kinase (AMPK in mammals; SNF1 in yeast), a sensor of the cellular energy status. AMPK is activated by two mechanisms namely allosteric activation by AMP and phosphorylation of Thr172 within the catalytic domain by upstream kinases. Once activated, AMPK leads to the inhibition of anabolic pathways, in order to save energy, and to the activation of catabolic pathways in order to produce energy. In this way, AMPK senses the cellular energy status and balances anabolic and catabolic pathways in order to maintain energy levels.

Glucose is able to inhibit AMPK activation both by increasing the levels of ATP (therefore it decreases the intracellular AMP/ATP ratio) and also by triggering the dephosphorylation of Thr172 by specific protein phosphatases. The glucose-induced downregulation of the activity of AMPK is conserved from yeast to humans, and has a profound impact in cell physiology. In this presentation I will review the current knowledge on the regulation of AMPK and how yeast has helped us to understand this complex mechanism.