Optical control of Akt to analyze cellular metabolic signalling pathways

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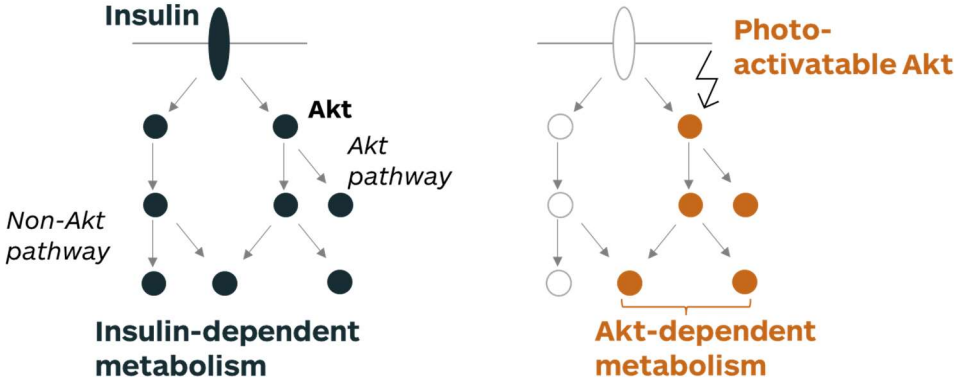
Insulin is a hormone secreted during feeding that promotes cellular metabolism. Insulin initiates cellular metabolism by activating intracellular signaling pathways, including the kinase Akt. Previous studies have shown that different temporal pattern of insulin concentration leads to selective metabolic pathway activation accompanied by the phosphorylation of Akt.[1,2] However, the link between Akt activity and metabolic pathway regulation remains elusive. Here, we aimed to identify the role of Akt in metabolic signaling pathways by specifically activating Akt with an optogenetic tool, the photoactivated Akt system.[3]

Regulation of metabolic processes involves a variety of reactions, including post-translational modification of metabolic enzymes, changes in metabolic enzyme abundance through transcriptional regulation, and allosteric regulation of metabolic enzyme. Thus, a comprehensive analysis of biomolecules is necessary to elucidate Akt-dependent cellular metabolism. In this study, we collected large-scale data for three types of molecules by RNA-seq, LC-MS, and Western blotting, upon stimulation. The collected omics data were integrated to construct a signaling network corresponding to Akt-specific activation. From the constructed network, we revealed the metabolic signaling that is attributed to Akt activation. We found distinctive regulation in the selectivity of metabolic pathways between Akt-specific activation and insulin stimulation: the glycolytic pathway was not regulated by Akt-specific activation, and nucleotide metabolism was regulated in a similar pattern to insulin stimulation. Taken together, our findings reveal the mechanism of metabolic pathway regulation that is dependent on Akt activation.



References: 1) Kubota et al., *Mol. Cell*, 46, 820 (2012). 2) Kubota et al. Cell Systems, 7, 118–128 (2018). 3) Katsura et al. *Sci. Rep.*, 5, 14589 (2015).