

Reconstruction of insulin-dependent metabolic regulatory networks from phosphoproteome and metabolome data

YUGI, Katsuyuki

- 1) YCI Laboratory for Trans-Omics, RIKEN Center for Integrative Medical Sciences
- 2) PRESTO, Japan Science and Technology Agency
- 3) Institute for Advanced Biosciences, Keio University
- 4) Department of Biological Sciences, University of Tokyo

Advances in comprehensive measurement technologies such as the mass spectrometry and the new generation sequencer are providing landscapes of each ‘omic’ layer. We have been developing methodologies for ‘trans-omic’ analysis [1,2] that allows reconstruction of global mechanistic molecular networks that come across multiple omic layers based on multiple omic data with the supports of public databases and software. To elucidate global regulatory pathways of the hepatic metabolism by the insulin-dependent signaling, a trans-omic analysis that integrates phosphoproteome and metabolome was performed [3]. Consequently, we found that the insulin signal flows through the trans-omic network involving 13 protein kinases, 26 phosphorylated metabolic enzymes, and 35 allosteric effectors, resulting in quantitative changes in 44 metabolites. Particularly, the 26 phosphorylated metabolic enzymes include 48 novel phosphorylation sites out of 71. This implies that the insulin signal could be transmitted to broader targets than ever thought. Mathematical modeling analysis predicted selective control of a subnetwork around phosphofructokinase by specific phosphorylation and allosteric regulation. Thus, we provide an unbiased method that reconstructs the trans-omic network from phosphoproteome and metabolome data, which will be potentially applicable to other cellular responses.

References

- [1] Yugi *et al.*, *Trends. Biotechnol.*, 34, 276-290 (2016).
- [2] Yugi and Kuroda, *Cell Syst.*, 4, 19-20 (2017).
- [3] Yugi *et al.*, *Cell Rep.*, 8, 1171-1183 (2014).