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An metabolomic approaches to identify the endogenous substrate of OCT1

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Proliferating cancer cells require abundant energy, building blocks for macromolecules, as well as reducing power to counteract high oxidative stress. Glutamine is essential for the survival of cancer cells by providing carbon, nitrogen, NADPH and participating in regulatory pathways such as mTORC1 and MAPK signaling. Several transporters belonging to SLC1, 6, 7 and 38 families mediate absorption of glutamine across the plasma membrane. We focus on several members of the SLC38 family and have utilized metabolomics approach to analyze the effect of glutamine transporter on cancer cell metabolism. After overexpressing specific SLC38 transporters (SLC38A3 and SLC38A5) in pancreatic ductal adenocarcinoma cells, we analyzed alterations of metabolites with HILIC-LC/ESI-MS. We found that over expression of glutamine transporter indeed influenced TCA cycle, GSH production and nucleotide synthesis. Abundance of the intermediates of TCA cycle, glycolysis, GSH and nucleotide synthesis was changed. In addition, changes in the amount of urea cycle intermediates including citrulline and ornithine were observed, which introduces new perspective on the relationship between glutamine and ammonia metabolism in cancer cells. Intriguingly, significant rise of the amount of glutamine itself was not demonstrated in any analyzed cancer cell line, which suggests concomitant up-regulation of glutamine consumption through biosynthetic and regulatory pathways. Though more experiments are required to illuminate mechanisms contributing to the influence of glutamine transporter on relevant metabolites, metabolomics as a powerful tool strengthens our understanding of glutamine's effect on key metabolic processes and helps to identify noncanonical metabolic pathways in glutamine metabolism.

Biography

Ligong Chen has completed his PhD from University of California at Berkeley and Postdoctoral studies from UCSF School of Medicine and Pharmacy. He is the Principal Investigator in Pharmacology and Toxicology of Tsinghua University School of Medicine, a premier University in China. He has published more than 20 papers in reputed journals including *Nature Genetics*, *PNAS*, and *JBC* et al. He is an expert in Transporter Physiology and Pharmacology. His lab is working on various transporters' role in human diseases, using metabolomics, genomics and proteomics as major tools.

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