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Combined metabolomic and transcriptomic profiling revealed the time-dependent effects of metformin on LoVo cells

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Metformin is a commonly used anti-diabetic drug, which has been recognized of possessing potential anticancer activities in a variety of cancer models. However, the exact mechanism is poorly understood. In current study, we performed a GC-TOFMS and LC-TOFMS-based metabolomic profiling on LoVo cells, a human derived colon cancer cell line, treated by 10 mM metformin for 8, 24 and 48h respectively. Although the significant suppression on cell viability was only observed after 24h treatment, an obvious metabolic alteration was present after 8h treatment, and these metabolic changes were further amplified after 24 and 48h metformin treatment in consistence with the time-dependent suppressive effects on cell viability. Nevertheless, we observed that most differential metabolites were up-regulated at 8h, but down-regulated at 24 and 48h by metformin compared to the corresponding control cells, indicating the different modulation in cell metabolism by metformin at different time points. We found that most of the identified differential metabolites were involved in amino acids metabolism, glycolysis, TCA cycle, and nucleic acids metabolism, suggesting that the metabolic impacts of metformin on energy metabolism were prior to the phenotypic changes in cell viability. Meanwhile, we performed a transcriptomic profile of LoVo cells which were treated by 10 mM metformin for 8 and 24h. The transcriptomic data showed there are over 100 and 3000 differentially expressed genes induced by 8 and 24h metformin treatment compared to the corresponding control cells. Interestingly, we found that the impacts of normal 24h culture were greater than 8h treatment of metformin on gene expression, which was different with the observed metabolic alterations. We observed that the main involved pathways of differentially expressed genes were not only related with classical cancer signaling pathways such as Wnt signaling, p53 signaling, MAPK pathway, cell cycle, apoptosis and ErbB signaling pathway, but also with energy metabolism process. Altogether, our current data indicate that metformin treatment results in a time-dependent metabolic and transcriptomic alteration on LoVo cells, and the results from these two omics approaches could be complementary and warrants a further investigation on these observed changes of genes and metabolic pathways.

Biography

Houkai Li has completed his PhD at the age of 32 years from Shanghai Jiao Tong University and Postdoctoral studies from University of North Carolina (2011.8-2013.5) and Chinese Academy Sciences (2008.11-2011.3) respectively. He is now a Professor at Center for Traditional Chinese Medicine and Systems Biology in Shanghai University of Traditional Chinese Medicine. He has published over 22 papers in reputed journals.

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