S-D7

세포외 삼투질농도변화가 신집합관에 미치는 영향 : 융합 오믹스연구

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Patterns of Gene and Metabolite Define the Effects of Extracellular Osmolality on Kidney Collecting Duct

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Despite the well-established vasopressin-induced urine concentration and sodium reabsorption in the kidney collecting ducts, the effects of altered extracellular microenvironment on the collecting duct cells are poorly understood. To investigate the direct effect of a variety of different extracellular osmolalities, we generated transcriptome and metabolome profiles of primary cultured inner medullary collecting duct (IMCD) cells that were grown in hyperosmolar culture medium (640 mOsm) for 4 d and then exposed to either reduced (300 mOsm) or same osmolality for 1 or 2 d more. The integrated analysis of omics data demonstrated that 1) a number of metabolites were changed, including organic osmolytes, branched chain amino acids (BCAA), glucose, and intermediates of citric acid (CA) cycle; 2) 768 differentially expressed genes (DEGs) were observed, which were categorized into 5 clusters based on their expression patterns, and 31 GO biological processes (GOBPs) of interest were selected; 4) both the genes belonging to the 31 GOBPs and the differentially expressed metabolites were analyzed, demonstrating 40 DEGs involved in the changes of metabolites; 5) among them, 22 DEGs were associated with the metabolism of organic osmolytes, glucose and intermediates of CA cycle, and BCAA; and 6) quantitative real-time RT-PCR confirmed their transcript levels, and immunoblotting revealed significantly decreased expression of selected proteins: P-type transporters, ABC transporters and proteins in the insulin signaling pathways. In conclusion, extracellular osmolality per se changes a broad spectrum of cellular processes by affecting transcriptome and metabolome, and hence possibly the functions of IMCD cells including water and sodium reabsorption.

Key Words: 시스템생물학,대사체, 유전체
Systems biology, Osmolyte, Osmolality