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세포외 삼투질농도변화에 따른 신집합관 세포의 대사체 및 유전체 변화

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Metabonomics and Transcriptomics of Primary Cultured Kidney Inner Medullary Collecting Duct Cells Exposed to Different Osmolalities

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Renal tubular epithelial cells are exposed to a variety of different microenvironment. We recently demonstrated that luminal fluid shear stress induces F-actin reorganization and AQP2 trafficking in the renal collecting duct cells despite the absence of vasopressin stimulation (Jang et al. Integr Biol, 2011). Transepithelial difference of osmolality may also be an important microenvironment to kidney tubular cells. In diuretic conditions (e.g., nephrogenic diabetes insipidus or diuretics treatment), luminal plasma membrane of inner medullary collecting duct (IMCD) cells is exposed to significantly lower tubular fluid osmolality. We hypothesized that changes in luminal osmolality could affect cellular metabolism and gene profiles. Primary cultured IMCD cells of rat kidney were grown in hypertonic culture medium (640 mOsm/KgH2O) for 4 days, and then cells were exposed to either low osmolality (340 mOsm/KgH_2O) or the same osmolality (640 mOsm/KgH_2O) for 1 day or 2 days more. We applied a novel method of 1H-NMR-based metabonomics to integrate the metabolic profiling and to identify the changes of the levels of metabolites in the IMCD cells exposed to different osmolalities. Moreover, transcriptome analysis (Affymetrix GeneChip® Rat Gene 1.0 ST array) was applied to profile different gene expression at the mRNA level in rat kidney. The accurate concentrations of metabolites in cell lysate were rapidly measured using the target profiling procedure and the difference in the levels of metabolites was compared using multivariate analysis such as PCA. Major endogenous metabolites for cell lysate contained products of glycolysis (glucose, lactate) and amino acids, as well as organic osmolytes (e.g., betaine, myo-inositol, taurine, sorbitol, and glycerophosphocholine). Many metabolites revealed changes in their levels, including significantly decreased levels of organic osmolytes and amino acids in the IMCD cells exposed to low osmolality. Moreover, gene expression of transporters for organic osmolytes (e.g., inositol, betaine, taurine) and aldose reductase for sorbitol production was significantly reduced in IMCD cells exposed to low osmolality. Taken together, metabonomics and transcriptomics of the IMCD cells provide insight into the effects of different osmolality on the cellular metabolism and gene profiles.

Key Words: 대사체 유전체
Transcriptome meatbolome