Application of gene expression profiles of mouse nephron-segments to analyze renal functions including NaCl handling

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Summary

We had constructed expressed genes data bases termed expression profiles of mouse proximal tubules and inner medullary collecting ducts. The information of the expression profiles were applied to identify and characterize nephron segment specific or predominantly expressed genes. In inner medullary collecting ducts, αB-crystallin was the most abundantly expressed gene. This is a family member of small stress proteins and has been known as a major protein in vertebra lens. αB-crystallin mRNA expression was upregulated significantly in the kidney by dehydration for three days, while there were no induction by NaCl loading. Among two thousands clones which we analyzed, over one thousand six hundreds genes were identified. The variation of expressed genes in inner medullary collecting ducts was larger than those of any other tissues or cells, but in relatively small amounts. From the subtraction procedures using a computer, GS (gene signature) 5219 appeared to be specific to this nephron segment. The full length cloning of GS5219 revealed that this gene was a new member of glutathione-S-transferase class theta.

In kidney cortex and the lumen of proximal tubules, it has been shown that the concentration of angiotensinogen, angiotensin (Ang) I and II were ten to thousands times higher than those in serum. They are much greater than can be explained by the glomerular filtration. It has demonstrated that there are angiotensionogen and its mRNA in epithelial cells of proximal tubules, suggesting that they are secreted and converted in the vicinity of the proximal tubules or in themselves. The precise mechanisms, however, remains to be unclear. One of the proximal tubules specific gene, GS4001, has been cloned. The sequence revealed that this transcript encoded a protein of the family member of aspartic proteinases including renin and cathepsin D. There was a leader sequence at the N terminal site, suggesting that this protein could be secreted. We hypothesized that GS4001 protein might be involved in the mechanisms of high concentration of Ang in the kidney cortex and proximal tubular lumen. The full length of GS4001 cDNA with tag was transfected into the culture cells and the secretion of GS4001 protein was confirmed in the culture medium. The medium of cultured cells transfected GS4001 were harvested. The production of AngI from angiotensionogen was identified in the medium collected from transfected cells, suggesting that GS4001 had renin-like activity.

The expression profiles of renal nephron-segments would be feasible to analyze and characterize new genes and their functions.