Analyses of renal NaCl handling using gene expression profiles of mouse renal tubules.

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Summary

An expression profile is a list based on a single pass sequences of 1000 or 2000 cDNA clones, demonstrating the genes expressed and the relative abundance of their transcripts in a given tissue. We constructed an expression profiles of mouse renal proximal tubules (PT) and inner medullary collecting ducts (IMCD) and compared the data with those of other cells and tissues.

Non-biased 3' end cDNA libraries from about 18cm of mouse PT and 20 cm of IMCD isolated by micro dissection method, were prepared. Single-pass sequence of randomly selected 1000 or 2000 cDNA clones was performed to collect the short sequences (about 250bp average) from poly (A), called gene signatures (GS). Identical sequences were joined as a single GS, and its occurrence was counted. The resulting list shows the expressed genes and their abundance.

First, by comparing the expression profile of PT with those obtained from other sources, several genes were identified only in PT. Two of the non-homologous genes were analyzed by Northern blotting and in situ hybridization, confirming that they were predominantly expressed in the kidney namely proximal tubules. The sequence analyses revealed that GS4001 was a new member of aspartic proteinases and GS 4059 was a novel gene. Another clone, GS4068, was cloned and identified as mouse uroguanylin (UG). UG has been postulated to regulate the salt and water secretion in the intestine as well as in the kidney. *In situ* hybridization demonstrated that it was located around the corticomedullary junction of the kidney. Seventy-two hours of dehydration induced the UG mRNA expression in the kidney but not in the intestine. Acute NaCl loading, however, did not induce its mRNA in the kidney as well as intestine. To examine its possible role(s) in the mouse developing and neonatal kidney, we performed *in situ* hybridization using whole body of fetuses on 14, 16 and 18 days of gestation (E14, E16, E18) and postnatal kidney on 0, 1, 7, 14 and 56 days after birth (P0, P1, P7, P14, P56), respectively. The hybridization signals have been detected in the intestine from E14 to E18, but not in the kidney from E14 up to P1. The signals, however, were increased markedly in the kidney after P14, mainly in the corticomedullary region. It was known that neonatal rodent had a tendency of negative Na balance because of the immature renal Na handling, suggesting that it may play a role in the maturation of Na handling in the neonatal kidney. The profile of IMCD showed that αB-crystallin was most abundant.

We constructed the expression profiles of renal PT and IMCD and showed that they were useful to analyze renal functions from molecular point of view.