Mechanism of human renal sodium dependent phosphate transporter gene expression regulated by inorganic phosphate

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Summary

Reabsorption of inorganic phosphate (Pi) in the kidney is mediated largely by sodium dependent phosphate (Na^+/Pi) transporters in the brush border membrane of the proximal tubule, and is regulated by a variety of hormones such as parathyroid hormone, 1,25-dihydroxyvitamin D3, or growth hormone, and dietary Pi. Na^+/Pi transporters have been divided into types I and II on the basis of their predicted amino acid sequence.

In this study, the mechanism of Na^+/Pi transporter gene expression regulated by Pi was investigated. Type II transporter mRNA was increased by dietary Pi depletion, while the level of type I transporter mRNA remained unchanged in these conditions. Thus, type II transporters were hypothesized to play an important role to maintain Pi homeostasis in the kidney.

Sequence analysis of human type II Na^+/Pi transporter (NaPi-3) gene indicated the presence of Pho 4 binding motif (CACGTG) which was identified as Pi responsive sequence in *Saccharomyces cerevisiae*. Binding protein to this sequence was detected in nuclear extracts of Pi depleted rat kidney by gel mobility shift assay. Furthermore, the binding activity of protein to Pho 4 binding motif was reciprocally proportional to serum phosphorus concentrations. Transient transfection study with OK cells demonstrated that luciferase gene expression showed 5-fold of control vector in CACGTG driving vector, and lower in mutant CACGAA driving vector.

These findings indicated that CACGTG sequence in NaPi-3 gene had important role in basal expression of type II Na^+/Pi transporter gene and its regulation by Pi.