

## Identification of intestinal sodium dependent phosphate transporter and its activation by vitamin D

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### Summary

Transcellular inorganic phosphate (Pi) in the small intestine is increased in animals with increased 1,25-dihydroxyvitamin D (1,25(OH)<sub>2</sub>D) levels. Three sodium dependent phosphate (Na/Pi) transporters have been identified as type I and II mainly expressed in renal proximal tubule and type III ubiquitously expressed in many organs. Recently, Murer et al have cloned from a rabbit small intestinal cDNA library a novel cDNA (PiUS) encoding a protein stimulating Na/Pi uptake into *Xenopus laevis* oocytes, but which is not a Na/Pi transporter itself. In this study, Na/Pi transporters expressed in intestine were identified and the mechanism by which vitamin D stimulated intestinal Na/Pi transport was elucidated in the rat.

We have used homology cloning technique to search for rat cDNA using rabbit PiUS cDNA as a probe. The identified rat PiUS cDNA codes for a protein of 425 amino acids. Hydropathy analysis suggests a lack of transmembrane segments. The derived protein sequence has multiple consensus sites: For cyclic nucleotide dependent kinase (2 sites), for protein kinase C (6 sites) and for prenyl group binding site (5 sites). The expression of type III Na/Pi transporters such as PiT-1 and PiT-2 were also observed in rat intestine and the effect of 1,25(OH)<sub>2</sub>D<sub>3</sub> on Na/Pi transport activity and on the expression of related molecules were investigated. Administration of 1,25(OH)<sub>2</sub>D<sub>3</sub> into vitamin D deficient rat lead to 7-fold stimulation of intestinal Na/Pi uptake. After 1,25(OH)<sub>2</sub>D<sub>3</sub> administration, PiT-1 mRNA level slightly increased at 12 h but not changed at 24 h and 48 h, PiT-2 mRNA level significantly increased at 24 h and 48 h. However, rat PiUS mRNA level was not affected by 1,25(OH)<sub>2</sub>D<sub>3</sub>.

It is concluded from present study that PiT-2 is regulated by 1,25(OH)<sub>2</sub>D<sub>3</sub> and that PiUS is suggested to be Na/Pi transport regulating protein in rat intestine.