

Chromosomal Localization of the Human Renal Sodium-Phosphate Transporter to Chromosome 5: Implications for X-Linked Hypophosphatemia

Phosphorus and sodium are absorbed across the luminal membrane of the renal tubule utilizing a cotransporter protein whose gene has been cloned.¹ The present investigators employed 3 methods for localizing the chromosomal site of this gene: (1) probing of somatic cell hybrid panels with a radiolabeled DNA genomic fragment that revealed a signal on human chromosome 5; (2) PCR amplification of DNA from somatic cell hybrids to localize the sodium-phosphate cotransporter gene to chromosome 5; and (3) utilizing a fluorescein-labeled DNA probe for the sodium-phosphate cotransporter gene and fluorescent in situ hybridization on metaphase chromosome spreads from human peripheral blood lymphocytes, which located the gene at chromosome 5q13. The location of the sodium-phosphate cotransporter gene on chromosome 5 was unexpected because the trait for human familial hypophosphatemic rickets in which renal phosphorus reabsorption is decreased is X-linked and has been assigned to Xp22.1-p21.3. Therefore, there may be a second phosphorus transporter isoform whose gene is on the short arm of the X chromosome, or the X chromosomal product may regulate expression of the gene on chromosome 5 or the function of its product.

United States. Although it is clearly X-linked, the gene for the function that is defective in these patients (ie, renal phosphorus transport) is not on the X chromosome. In the animal model of this disorder, the X-linked Hyp mouse, there is a decrease in the renal tubular content of mRNA and protein for the sodium-phosphate cotransporter that probably accounts for decreased renal tubular transport of phosphorus.² The chromosomal site of the mouse sodium-phosphate cotransporter gene has not as yet been reported, but there are data suggesting the presence of a humoral factor (whose gene may possibly be on the X chromosome) in these animals that inhibits phosphorus transport, perhaps by downregulating transcription of the sodium-phosphate cotransporter gene.² A "knock-out" experiment in which the calcium-phosphate transporter gene is eliminated and the effect on phosphorus transport observed would be of interest.

A second study has been published that localizes the human sodium-phosphate cotransporter gene to chromosome 5q35.³ Thus, both reports assign this gene to the long arm of chromosome 5, but its specific sublocation is not certain.

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Ghishan FK, et al. *Pediatr Res* 1994;35:510-513.

Editor's comment: *Familial hypophosphatemic rickets is the most common form of rickets presently encountered in the*

1. Magagnin S, et al. *Proc Nat Acad Sci USA* 1993;90:5979-5983.

2. Tenenhouse HS, et al. *J Clin Invest* 1994;93:671-676.

3. Kos CH, et al. *Genomics* 1994;19:176-177.