**To the Editor:** In their comprehensive review of genetic disorders of renal phosphate transport, Prié and Friedlander (June 24 issue) claim that the role of NPT2a in renal phosphate handling has been shown by the association between heterozygous mutations in NPT2a and renal phosphate leak. However, Virkki et al. found no dominant negative effect of these NPT2a variants, which indicates that they are polymorphisms. Lapointe et al. also identified NPT2a variants in patients with renal phosphate leak, but ruled out their functional significance by the finding of normal renal phosphate balance in family members carrying the same variants. The major contribution of NPT2a to renal phosphate balance was definitively established in a recent article in the Journal that reported autosomal recessive hypophosphatemic rickets with renal Fanconi’s syndrome secondary to a loss-of-function mutation in SLC34A1 (also known as NPT2a), the gene that encodes NPT2a (also known as NaPi-IIa).  

Daniella Magen, M.D.  
Israel Zelikovic, M.D.  
Kari Skorecki, M.D.  
Rambam Health Care Campus  
Haifa, Israel  
danmag@tx.technion.ac.il

No potential conflict of interest relevant to this letter was reported.


**The Authors Reply:** Magen et al. reported on two relatives with a Fanconi’s syndrome, renal insufficiency, and a homozygous mutation in SLC34A1, which encodes NPT2a. This phenotype was more complex than that of patients with heterozygous NPT2a mutations. It is surprising that...
the decrease in NPT2a expression alone could explain the whole phenotype. These unexpected features might result from intracellular accumulation of this particular mutant protein and thereby in a toxic effect on renal cells. This property is not necessarily shared with other NPT2a mutants. In these highly consanguineous patients, additional mutations in genes other than NPT2a could also participate. This important paper was published while our review article was at an advanced stage of the publication process, thereby preventing us from discussing it.

We previously reported the association between heterozygous NPT2a mutations and renal phosphate loss. These mutations decreased phosphate transport; the coexpression of wild-type and mutated NPT2a proteins in oocytes resulted in phosphate transport that was lower than expected, a result that we interpreted as a dominant negative effect of mutant NPT2a. Virkki et al. confirmed that the mutations we had identified markedly decreased NPT2a activity. These authors did not, however, detect a dominant negative effect of the NPT2a mutants by introducing a cysteine residue in NPT2a, under the assumption that this modification would reveal an interaction between wild-type and mutant NPT2a. However, the validity of an interaction between wild-type and mutant NPT2a is unknown.

Lapointe et al. found no association between hypophosphatemia and a previously unidentified variant of NPT2a. No definitive conclusion can be drawn, however, regarding the consequences of other mutations.

The data reported by Levchenko et al. suggest that NPT2a haploinsufficiency can induce hypophosphatemia, an observation consistent with the defect of renal phosphate transport seen in patients with NPT2a heterozygous mutations.

As detailed in our most recent review, mutations in genes other than NPT2a may lead to decreased NPT2a expression and thus to renal phosphate loss and hypophosphatemia. This enlightens the central role of NPT2a in phosphate homeostasis.

Gérard Friedlander, M.D., Ph.D.
Dominique Prié, M.D., Ph.D.
Paris Descartes University
Paris, France
gerard.friedlander@inserm.fr

Since publication of their article, the authors report no further potential conflict of interest.


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**Acupuncture for Chronic Low Back Pain**

**TO THE EDITOR:** In their review article, Berman et al. (July 29 issue) discuss the use of acupuncture for chronic low back pain. Acupuncture, which originated in China, has been practiced there and in other Asian countries for thousands of years. The selection of acupuncture points and manual manipulation are performed according to the diagnosis and as determined by the theories of traditional Chinese medicine. However, when acupuncture is studied by practitioners of conventional medicine, insertion points are selected from lists of commonly used points on the basis of the diagnosis as determined by conventional medicine.

In traditional Chinese medicine, the diagnosis, which is based on inquiry, inspection, olfaction, auscultation, percussion, palpation, and pulse examination, guides point selection and manual manipulation for every acupuncture point in each treatment session. The lack of a correct diagnosis on this basis could explain the reported result that real acupuncture was no more effective than sham acupuncture in the clinical trials that were cited by Berman et al.

The diagnostic assessments of both conventional and traditional Chinese medicine are required for tailored acupuncture treatment. Further studies to evaluate the efficacy of acupuncture should incorporate the diagnosis according to traditional Chinese medicine.