

PHEX Gene

Subjects: Genetics

Submitted by:  Lily

Guo

(This entry belongs to Entry Collection "[MedlinePlus](#)")

Definition

phosphate regulating endopeptidase homolog X-linked

1. Introduction

The *PHEX* gene provides instructions for making an enzyme that is active primarily in bones and teeth. Studies suggest that it cuts (cleaves) other proteins into smaller pieces; however, the proteins cleaved by the PHEX enzyme have not been identified.

The PHEX enzyme could be involved in regulating the balance of phosphate in the body. Among its many functions, phosphate plays a critical role in the formation and growth of bones in childhood and helps maintain bone strength in adults. Phosphate levels are controlled in large part by the kidneys. The kidneys normally excrete excess phosphate in urine, and they reabsorb this mineral into the bloodstream when more is needed.

Studies suggest that the PHEX enzyme may be involved in the regulation of a protein called fibroblast growth factor 23 (which is produced from the *FGF23* gene). This protein normally inhibits the kidneys' ability to reabsorb phosphate into the bloodstream. Although the PHEX enzyme is thought to have some effect on the activity of fibroblast growth factor 23, no direct link has been established. It remains unclear how the PHEX enzyme helps control phosphate reabsorption and what role it plays in the formation and growth of bones.

2. Health Conditions Related to Genetic Changes

2.1. Hereditary hypophosphatemic rickets

More than 200 mutations in the *PHEX* gene have been found to cause the most common form of hereditary hypophosphatemic rickets, which is known as X-linked hypophosphatemic rickets. These mutations inactivate the PHEX enzyme, leaving it unable to cleave other proteins.

Researchers are uncertain how mutations in the *PHEX* gene lead to low levels of phosphate in the blood (hypophosphatemia) and related problems with bone growth in people with X-linked hypophosphatemic rickets. Because many affected individuals have increased levels of fibroblast growth factor 23, it is likely that *PHEX* gene mutations somehow alter the production of that protein. An increase in fibroblast growth factor 23 reduces phosphate reabsorption by the kidneys, leading to hypophosphatemia. However, because some affected individuals have normal levels of fibroblast growth factor 23, researchers are also considering other pathways by which a mutated *PHEX* gene could result in X-linked hypophosphatemic rickets.

3. Other Names for This Gene

- HPDR
- HPDR1
- HYP
- HYP1
- metalloendopeptidase homolog PEX
- PEX
- PHEX_HUMAN

- phosphate regulating endopeptidase homolog, X-linked
- phosphate-regulating neutral endopeptidase
- vitamin D-resistant hypophosphatemic rickets protein
- X-linked hypophosphatemia protein
- XLH

References

1. A gene (PEX) with homologies to endopeptidases is mutated in patients with X-linked hypophosphatemic rickets. The HYP Consortium. *Nat Genet.* 1995 Oct;11(2):130-6.
2. Clausmeyer S, Hesse V, Clemens PC, Engelbach M, Kreuzer M, Becker-Rose P, Spital H, Schulze E, Raue F. Mutational analysis of the PHEX gene: novel point mutations and detection of large deletions by MLPA in patients with X-linked hypophosphatemic rickets. *Calcif Tissue Int.* 2009 Sep;85(3):211-20. doi:10.1007/s00223-009-9260-8.
3. Gaucher C, Walrant-Debray O, Nguyen TM, Esterle L, Garabédian M, Jehan F. PHEX analysis in 118 pedigrees reveals new genetic clues in hypophosphatemic rickets. *Hum Genet.* 2009 May;125(4):401-11. doi: 10.1007/s00439-009-0631-z.
4. Ichikawa S, Traxler EA, Estwick SA, Curry LR, Johnson ML, Sorenson AH, Imel EA, Econs MJ. Mutational survey of the PHEX gene in patients with X-linked hypophosphatemic rickets. *Bone.* 2008 Oct;43(4):663-6. doi:10.1016/j.bone.2008.06.002.
5. Quarles LD. FGF23, PHEX, and MEPE regulation of phosphate homeostasis and skeletal mineralization. *Am J Physiol Endocrinol Metab.* 2003 Jul;285(1):E1-9. Review.
6. Rowe PS. The role of the PHEX gene (PEX) in families with X-linked hypophosphatemic rickets. *Curr Opin Nephrol Hypertens.* 1998 Jul;7(4):367-76. Review.
7. Rowe PS. The wrinkled pathways of FGF23, MEPE and PHEX. *Crit Rev Oral Biol Med.* 2004 Sep 1;15(5):264-81. Review.

Keywords

genes