PHEX gene

phosphate regulating endopeptidase X-linked

Normal Function

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.

Health Conditions Related to Genetic Changes

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.

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

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PHEX (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5251[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28PHEX%5BTIAB%5D%29+OR+%28%28PEX%5BTIAB%5D%29+AND+%28rickets%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- PHOSPHATE-REGULATING ENDOPEPTIDASE, X-LINKED; PHEX (https://omim.org/entry/300550)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/5251)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=PHEX[gene])

References

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Genomic Location

The *PHEX* gene is found on the X chromosome (https://medlineplus.gov/genetics/chromosome/x/).

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