KL Gene

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klotho

genes

1. Normal Function

The *KL* gene provides instructions for making the protein alpha-klotho, which is found primarily in kidney cells. This protein plays a major role in regulating the phosphate levels within the body (phosphate homeostasis). 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 rid the body of excess phosphate by excreting it in urine, and they reabsorb this mineral into the bloodstream when more is needed.

Alpha-klotho attaches (binds) to and turns on (activates) a protein called FGF receptor 1 that spans the membrane of many types of cells, including kidney cells. Once the receptor is active, another protein called fibroblast growth factor 23 can also bind to it. Binding of fibroblast growth factor 23 to its receptor stimulates signaling that stops phosphate reabsorption into the bloodstream.

2. Health Conditions Related to Genetic Changes

2.1. Hyperphosphatemic familial tumoral calcinosis

At least one mutation in the *KL* gene has been found to cause hyperphosphatemic familial tumoral calcinosis (HFTC), a condition characterized by an increase in the levels of phosphate in the blood (hyperphosphatemia) and abnormal deposits of phosphate and calcium (calcinosis) in the body's tissues. The *KL* gene mutation that causes HFTC replaces the protein building block (amino acid) histidine with the amino acid arginine at position 193 in the protein sequence (written as His193Arg or H193R). This mutation results in a shortage of functional alpha-klotho. As a result, FGF receptor 1 is not activated, making it unavailable for fibroblast growth factor 23 binding. The fibroblast growth factor 23 protein is normal, but it cannot bind to its receptor and cannot send out signals to stop phosphate reabsorption. As a result, too much phosphate is reabsorbed into the bloodstream, leading to hyperphosphatemia and subsequent calcinosis.

2.2. Kidney stones

3. Other Names for This Gene

- alpha-klotho
- KLOT_HUMAN
- klotho precursor

References

1. Farrow EG, Imel EA, White KE. Miscellaneous non-inflammatory musculoskeletalconditions. Hyperphosphatemic familial tumoral calcinosis (FGF23, GALNT3 andαKlotho). Best Pract Res Clin Rheumatol. 2011 Oct;25(5):735-47. doi:10.1016/j.berh.2011.10.020. Review. Citation on PubMed or Free article on PubMed Central
2. Ichikawa S, Imel EA, Kreiter ML, Yu X, Mackenzie DS, Sorenson AH, Goetz R,Mohammadi M, White KE, Econs MJ. A homozygous missense mutation in human KLOTHOcauses severe tumoral calcinosis. J Clin Invest. 2007 Sep;117(9):2684-91. Citation on PubMed or Free article on PubMed Central
3. Razzaque MS. The FGF23-Klotho axis: endocrine regulation of phosphatehomeostasis. Nat Rev Endocrinol. 2009 Nov;5(11):611-9. doi:10.1038/nrendo.2009.196. Review. Citation on PubMed or Free article on PubMed Central
4. Sprecher E. Familial tumoral calcinosis: from characterization of a rarephenotype to the pathogenesis of ectopic calcification. J Invest Dermatol. 2010Mar;130(3):652-60. doi: 10.1038/jid.2009.337. Epub 2009 Oct 29. Citation on PubMed or Free article on PubMed Central