GALNT3 Gene

Subjects: Genetics & Heredity
Contributor: Vivi Li

Polypeptide N-acetylgalactosaminyltransferase 3

Keywords: genes

1. Normal Function

The *GALNT3* gene provides instructions for making a protein called ppGalNacT3, which is found in many types of cells. This protein plays a major role in regulating 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.

The ppGalNacT3 protein regulates the activity of a protein called fibroblast growth factor 23, which is produced in bone cells and whose function is to signal the body to decrease phosphate reabsorption by the kidneys. The ppGalNacT3 protein attaches sugar molecules to particular regions of fibroblast growth factor 23 through a process called glycosylation. These sugar molecules are required for the protein's transport out of cells and to protect the protein from being broken down. When phosphate levels are increased, ppGalNacT3 glycosylates fibroblast growth factor 23 so it will not be broken down. Signaling from fibroblast growth factor 23 leads to a decrease in phosphate reabsorption, which helps to maintain normal phosphate levels in the body.

2. Health Conditions Related to Genetic Changes

2.1 Hyperphosphatemic Familial Tumoral Calcinosis

At least 25 mutations in the *GALNT3* gene have 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. *GALNT3* gene mutations result in the production of ppGalNacT3 protein with little or no function. As a result, ppGalNacT3 cannot glycosylate fibroblast growth factor 23. Fibroblast growth factor 23 becomes trapped within the cell and is broken down rather than being released from cells (secreted) as usual. Without fibroblast growth factor 23, more phosphate is reabsorbed back into the bloodstream by the kidneys, leading to hyperphosphatemia. Calcinosis results when the excess phosphate combines with calcium to form deposits that build up in soft tissues.

3. Other Names for This Gene

- GalNAc transferase 3
- GalNAc-T3
- GALT3_HUMAN
- polypeptide GalNAc transferase 3
- polypeptide GalNAc-transferase T3
- pp-GaNTase 3
- protein-UDP acetylgalactosaminyltransferase 3
- UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase 3

- UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 3 (GalNAc-T3)

References

1. Chefetz I, Kohno K, Izumi H, Uitto J, Richard G, Sprecher E. GALNT3, a geneassociated with hyperphosphatemic familial tumoral calcinosis, istranscriptionally regulated by extracellular phosphate and modulates matrixmetalloproteinase activity. Biochim Biophys Acta. 2009 Jan;1792(1):61-7. doi:10.1016/j.bbadis.2008.09.016.
2. Chefetz I, Sprecher E. Familial tumoral calcinosis and the role ofO-glycosylation in the maintenance of phosphate homeostasis. Biochim BiophysActa. 2009 Sep;1792(9):847-52. doi: 10.1016/j.bbadis.2008.10.008.
3. 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.
4. Ichikawa S, Baujat G, Seyahi A, Garoufali AG, Imel EA, Padgett LR, Austin AM, Sorenson AH, Pejin Z, Topouchian V, Quartier P, Cormier-Daire V, Dechaux M,Malandrinou FCh, Singhellakis PN, Le Merrer M, Econs MJ. Clinical variability of familial tumoral calcinosis caused by novel GALNT3 mutations. Am J Med Genet A.2010 Apr;152A(4):896-903. doi: 10.1002/ajmg.a.33337.
5. 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.
6. Yancovitch A, Hershkovitz D, Indelman M, Galloway P, Whiteford M, Sprecher E, Kılıç E. Novel mutations in GALNT3 causing hyperphosphatemic familial tumoralcalcinosis. J Bone Miner Metab. 2011 Sep;29(5):621-5. doi:10.1007/s00774-011-0260-1.