Parathyroid Hormone 1 Receptor

Alternative Names
PTH1R
Parathyroid Hormone Receptor 1
PTHR1
PTH Receptor
PTHR
Parathyroid Hormone/Parathyroid Hormone-Related Protein Receptor
PTH/PTHRP Receptor

Record Category
Gene locus

WHO-ICD
N.B.:Classification not applicable to gene loci.

Incidence per 100,000 Live Births
N/A to gene loci

OMIM Number
168468

Mode of Inheritance
N/A

Gene Map Locus
3p21.31

Description
The Parathyroid Hormone 1 Receptor (PTH1R) gene codes for a member of the G-protein coupled receptor family 2, which is a receptor for both parathyroid hormone and parathyroid-like hormone. The protein functions to regulate calcium ion homeostasis through activation of adenylate cyclase as well as a phosphatidylinositol-calcium second messenger system. The signal transduction cascade associated with the receptor stimulates osteoclasts to increase the resorption rate of calcium. In addition, it also mediates the paracrine activities of parathyroid-like hormone, which is involved in the process of endochondral bone development and epithelial-mesenchymal interactions during teeth and mammary gland formation. The gene is primarily expressed in the bones and kidneys.

Mutations in the PTHR1 gene have been associated with a number of disorders. These include Blomstrand Type chondrodysplasia, a skeletal dysplasia with advancement of bone maturation, Jansen metaphyseal chondrodysplasia, a form of short-limb dwarfism characterized by a retarded differentiation of chondrocytes, Ollier disease, characterized by multiple cartilage tumors and skeletal deformity, Eiken syndrome, a form of skeletal dysplasia characterized by multiple epiphyseal dysplasia and extremely retarded ossification, and Primary Failure of Tooth Eruption (PFE).

Molecular Genetics
The PTH1R gene is located on the short arm of chromosome 3. The gene contains 15 exons and spans approximately 32 kb. The PTHR1 protein is a transmembrane protein made up of 593 amino acids with a molecular mass of 66 kDa. The protein consists of a 27-amino acid signal recognition sequence, a 150 amino acid extracellular domain with a hormone binding site, seven helical transmembrane regions, and an intracellular interaction domain. Disulphide bridges between Cys-48 and 117, Cys 108 and 148, and Cys 131 and 170 form part of the tertiary structure of the protein. Post translational modifications to the protein include N-linked glycosylation at Asn-151, 161, 166, and 176. The functional protein exists as a dimer with a combined molecular weight of 119 kDa.

Epidemiology in the Arab World

Saudi Arabia
Jelani et al., (2016) studied a 5-generation consanguineous Saudi Arabian family originating from the southwestern region in a study looking for the causative gene causing PFE. This family had four affected girls with tooth eruption failure. Jelani et al., (2016) utilized whole exome sequencing and identified a homozygous pathogenic (c.611T>A: p.Val204Glu) mutation in the PTH1R gene. The patients' mother was heterozygous and the unaffected healthy siblings were homozygous for the wild-type allele. This mutation was absent in 200 matched controls and was not seen in exome database (ExAc). This

novel mutation expanded the spectrum of PTH1R pathogenicity.

References

Jelani M, Kang C, Mohamoud HS, Al-Rehaili R, Almramhi MM, Serafi R, Yang H, Al-Aama JY, Naeem M, Alkhiary YM. A novel homozygous PTH1R variant identified through whole-exome sequencing further expands the clinical spectrum of primary failure of tooth eruption in a consanguineous Saudi family. Arch Oral Biol. 2016; 67:28-33. PMID: 27019138.

Related CTGA Records

Failure of Tooth Eruption, Primary

External Links

https://www.genecards.org/cgi-bin/carddisp.pl?gene=PTH1R
https://www.ncbi.nlm.nih.gov/gene/5745

Contributors

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