ANKH gene

ANKH inorganic pyrophosphate transport regulator

Normal Function

The *ANKH* gene provides instructions for making a protein that is involved in skeletal development. The ANKH protein plays a role in the development and function of cells that build bones (osteoblasts) and cells that break down bone (osteoclasts). Osteoclasts are involved in bone remodeling, a normal process in which old bone is removed and new bone is created to replace it. In addition, the ANKH protein transports a molecule called pyrophosphate out of cells to the intricate network of proteins that forms in the spaces between cells (extracellular matrix). This extracellular pyrophosphate helps regulate bone formation by preventing mineralization, the process by which minerals such as calcium and phosphorus are deposited in tissues. The ANKH protein may have other, unknown functions.

Health Conditions Related to Genetic Changes

Craniometaphyseal dysplasia

More than 10 mutations in the *ANKH* gene have been found to cause autosomal dominant craniometaphyseal dysplasia, a condition characterized by thickening of bones in the skull (cranium) and widening of a region at the end of long bones known as the metaphysis. Some mutations change a single protein building block (amino acid) in the ANKH protein, whereas others insert or delete one or more amino acids in the protein. These changes disrupt the functioning of osteoblasts and osteoclasts. In particular, the maturation (differentiation) of osteoclasts is impaired, which likely disrupts bone remodeling. Reduced breakdown of bone tissue can contribute to the bone thickening characteristic of craniometaphyseal dysplasia. The altered ANKH proteins may also be less able to transport pyrophosphate out of cells. A shortage of extracellular pyrophosphate can increase bone mineralization, which may also contribute to the bone abnormalities.

Other disorders

At least five mutations in the *ANKH* gene have been found to cause a rare hereditary form of a cartilage disorder called calcium pyrophosphate dihydrate deposition disease (CPPDD). CPPDD, also called chondrocalcinosis or pseudogout, is characterized by the accumulation of calcium pyrophosphate dihydrate crystals in the cartilage, the tough but

flexible tissue that covers the ends of bones at the joints. The buildup of these crystals weakens cartilage and causes it to break down more easily. The crystals may cause inflammation in the joints, which can be painful.

Most cases of CPPDD occur in people older than 40, are not inherited, and have an unknown cause. However, inherited mutations in the *ANKH* gene have been shown to cause CPPDD in a few families. In these families, one altered copy of the *ANKH* gene in each cell is sufficient to cause the condition. Individuals with familial CPPDD caused by *ANKH* gene mutations typically form crystal deposits within multiple joints during early adulthood. Researchers believe that these mutations lead to elevated pyrophosphate levels in the extracellular matrix. High levels of pyrophosphate result in excessive formation of calcium pyrophosphate dihydrate crystals within joints.

Studies suggest that certain variations (polymorphisms) in the *ANKH* gene are associated with the normal differences in bone size and shape among individuals. These polymorphisms probably result in slight changes in the activity of the ANKH protein, affecting the levels of pyrophosphate in the extracellular matrix.

Other Names for This Gene

- ANK
- ANKH_HUMAN
- ankylosis, progressive homolog (mouse)
- FLJ27166
- HANK
- MANK
- progressive ankylosis protein
- SLC62A1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ANKH (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=56172[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ANKH%5BTIAB%5D%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

- CHONDROCALCINOSIS 2; CCAL2 (https://omim.org/entry/118600)
- ANKH INORGANIC PYROPHOSPHATE TRANSPORT REGULATOR; ANKH (https://omim.org/entry/605145)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/56172)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ANKH[gene])

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Genomic Location

The *ANKH* gene is found on chromosome 5 (https://medlineplus.gov/genetics/chromosome/5/).

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