TNFRSF11B gene

TNF receptor superfamily member 11b

Normal Function

The *TNFRSF11B* gene provides instructions for making a protein called osteoprotegerin. This protein plays an important role in bone remodeling, a normal process in which old bone is broken down and new bone is created to replace it. Osteoprotegerin is involved in the regulation of specialized cells called osteoclasts, which break down bone tissue during bone remodeling.

Osteoprotegerin is one of two receptor proteins that can attach (bind) to a protein called receptor activator of NF-κB ligand (RANKL). The other receptor protein is called receptor activator of NF-κB (RANK). Because RANKL can only bind to one receptor at a time, osteoprotegerin and RANK compete with one another. When RANKL is bound to RANK, it sets off a series of chemical signals that trigger immature osteoclasts to mature and become fully functional. When RANKL is bound to osteoprotegerin, it blocks these chemical signals and prevents the activation of osteoclasts. Because no chemical signals are transmitted when RANKL is attached to osteoprotegerin, osteoprotegerin is often called a "decoy" receptor.

By reducing the amount of RANKL that is available to bind to RANK, osteoprotegerin plays a critical role in regulating the process of bone remodeling.

Health Conditions Related to Genetic Changes

Paget disease of bone

Studies suggest that several normal variations (polymorphisms) in the *TNFRSF11B* gene may increase the risk of developing classic Paget disease of bone, particularly in women. These genetic changes could affect the amount or function of osteoprotegerin. However, it is unclear how polymorphisms in this gene influence disease risk.

Juvenile Paget disease

At least six mutations in the *TNFRSF11B* gene have been found to cause juvenile Paget disease. Each of these mutations greatly reduces the function of osteoprotegerin or prevents cells from making any of this protein. Without osteoprotegerin, RANKL binds only to RANK. The resulting increase in chemical signaling stimulates the production of

too many osteoclasts and triggers these cells to break down bone abnormally. In people with juvenile Paget disease, bone is broken down and replaced much faster than usual. When the new bone tissue grows, it is weaker and less organized than normal bone. These problems with bone remodeling cause bones throughout the skeleton to become unusually large, misshapen, and easily broken (fractured).

Other Names for This Gene

- MGC29565
- OCIF
- OPG
- osteoclastogenesis inhibitory factor
- osteoprotegerin
- osteoprotegerin precursor
- TR1
- TR11B_HUMAN
- tumor necrosis factor receptor superfamily member 11b
- tumor necrosis factor receptor superfamily, member 11b

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of TNFRSF11B (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4982[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28TNFRSF11B%5BTIAB%5D%29+OR+%28osteoprotegerin%5BTI%5D%29+OR+%28OPG%5BTI%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

- TUMOR NECROSIS FACTOR RECEPTOR SUPERFAMILY, MEMBER 11B; TNFRSF11B (https://omim.org/entry/602643)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4982)

- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=TNFRSF11B[gene])

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Genomic Location

The *TNFRSF11B* gene is found on chromosome 8 (https://medlineplus.gov/genetics/chromosome/8/).

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