SOST gene

sclerostin

Normal Function

The *SOST* gene provides instructions for making the protein sclerostin. Sclerostin is produced in osteocytes, which are a type of bone cell. The main function of sclerostin is to stop (inhibit) bone formation. The maintenance of bone over time requires a balance between the formation of new bone tissue and the breakdown and removal (resorption) of old bone tissue. Inhibition of bone formation is necessary to ensure that bones are of the correct shape, size, and density. Research suggests that sclerostin exerts its effects by interfering with a process called Wnt signaling, which plays a key role in the regulation of bone formation. Sclerostin may also promote the self-destruction (apoptosis) of bone cells, further inhibiting bone growth.

Health Conditions Related to Genetic Changes

SOST-related sclerosing bone dysplasia

At least six mutations in or near the *SOST* gene have been found to cause *SOST*-related sclerosing bone dysplasia. There are two forms of *SOST*-related sclerosing bone dysplasia: sclerosteosis and van Buchem disease. Sclerosteosis, the more severe type, is most common in the Afrikaner population of South Africa, while the milder van Buchem disease occurs most often in people of Dutch ancestry.

Most mutations that cause sclerosteosis result in a premature stop signal in the instructions for making sclerostin. These mutations prevent the production of any functional protein.

The most common mutation that causes van Buchem disease in people of Dutch ancestry is a deletion of 52,000 DNA building blocks (nucleotides) in a region of DNA neighboring the *SOST* gene. This region, called a regulatory region, normally controls the gene's activity (expression). This deletion within the regulatory region reduces the expression of the *SOST* gene, leading to a shortage of functional sclerostin protein.

A shortage or absence of sclerostin in bone cells disrupts the protein's inhibitory effect on bone growth, causing excessive bone formation. As a result, bones are denser and wider than usual, particularly the bones of the skull. These bone abnormalities are characteristic of *SOST*-related sclerosing bone dysplasia.

Other Names for This Gene

- sclerosteosis
- sclerostin precursor
- SOST_HUMAN
- VBCH

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SOST (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=50964[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SOST%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

- SCLEROSTIN; SOST (https://omim.org/entry/605740)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/50964)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SOST[gene])

References

- Balemans W, Van Hul W. Human genetics of SOST. J Musculoskelet NeuronalInteract. 2006 Oct-Dec;6(4):355-6. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17185822)
- ten Dijke P, Krause C, de Gorter DJ, Lowik CW, van Bezooijen RL.Osteocyte-derived sclerostin inhibits bone formation: its role in bonemorphogenetic protein and Wnt signaling. J Bone Joint Surg Am. 2008 Feb;90 Suppl1:31-5. doi: 10.2106/JBJS.G.01183. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18292354)
- van Bezooijen RL, ten Dijke P, Papapoulos SE, Lowik CW. SOST/sclerostin, anosteocyte-derived negative regulator of bone formation. Cytokine Growth FactorRev. 2005 Jun;16(3):319-27. doi: 10.1016/j.cytogfr.2005.02.005. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15869900)

Genomic Location

The *SOST* gene is found on chromosome 17 (https://medlineplus.gov/genetics/chromosome/17/).

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