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.
**Chromosomal Location**

Cytogenetic Location: 17q21.31, which is the long (q) arm of chromosome 17 at position 21.31

Molecular Location: base pairs 43,753,738 to 43,758,791 on chromosome 17 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

**Other Names for This Gene**

- sclerosteosis
- sclerostin precursor
- SOST_HUMAN
- VBCH

**Additional Information & Resources**

**Clinical Information from GeneReviews**

- SOST-Related Sclerosing Bone Dysplasias
  https://www.ncbi.nlm.nih.gov/books/NBK1228

**Scientific Articles on PubMed**

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?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+AND+AND+AND+AND+AND+AND+AND+AND+AND+AND+AND+AND+AND+AND+AND+AND

**Catalog of Genes and Diseases from OMIM**

- SCLEROSTIN
  http://omim.org/entry/605740
Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SOST.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SOST%5Bgene%5D
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:50964
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/Q9BQB4

Sources for This Summary

- OMIM: SCLEROSTIN
  http://omim.org/entry/605740

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