SH3BP2 gene

SH3 domain binding protein 2

Normal Function

The *SH3BP2* gene provides instructions for making a protein whose exact function is unclear, although it is known to interact with other proteins within cells. The SH3BP2 protein plays a role in transmitting chemical signals, particularly in certain immune system cells and cells involved in the replacement of old bone tissue with new bone (bone remodeling).

Studies suggest that the SH3BP2 protein helps regulate signaling pathways that turn on (activate) immune system cells called B cells and macrophages. The protein is also involved in the production of osteoclasts, which are specialized cells that break down bone tissue when it is no longer needed. Osteoclasts play a central role in bone remodeling.

Health Conditions Related to Genetic Changes

Cherubism

At least 15 mutations in the *SH3BP2* gene have been identified in people with cherubism. Each of these mutations changes a single protein building block (amino acid) in a critical region of the SH3BP2 protein. These genetic changes lead to the production of an abnormal protein that does not get broken down when it is no longer needed. Too much SH3BP2 protein likely increases signaling in certain cells, causing an immune reaction (inflammation) in the bones of the jaw and also triggering the production of an increased number of osteoclasts. An excess of these bone-destroying cells contributes to the abnormal breakdown of bone tissue in the upper and lower jaws. A combination of bone loss and inflammation likely underlies the cyst-like growths characteristic of cherubism.

Other Names for This Gene

- 3BP-2
- 3BP2
- 3BP2_HUMAN
- CRBM

- CRPM
- FLJ42079
- RES4-23
- SH3-domain binding protein 2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SH3BP2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6452[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28SH3BP2%5BTIAB%5D%29+OR+%28SH3-domain+binding+protein+2%5BTIAB%5D%29%29+OR+%283BP2%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- SH3 DOMAIN-BINDING PROTEIN 2; SH3BP2 (https://omim.org/entry/602104)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/6452)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SH3BP2[gene])

References

- Chen G, Dimitriou ID, La Rose J, Ilangumaran S, Yeh WC, Doody G, Turner M, Gommerman J, Rottapel R. The 3BP2 adapter protein is required for optimal B-cellactivation and thymus-independent type 2 humoral response. Mol Cell Biol. 2007Apr;27(8):3109-22. doi: 10.1128/MCB.01014-06. Epub 2007 Feb 5. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17283041) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1899947/)
- de la Fuente MA, Kumar L, Lu B, Geha RS. 3BP2 deficiency impairs the responseof B cells, but not T cells, to antigen receptor ligation. Mol Cell Biol. 2006Jul;26(14): 5214-25. doi: 10.1128/MCB.00087-06. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16809760) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1592712/)
- de Lange J, van Maarle MC, van den Akker HP, Redeker EJ. A new mutation in theSH3BP2 gene showing reduced penetrance in a family affected with cherubism.

OralSurg Oral Med Oral Pathol Oral Radiol Endod. 2007 Mar;103(3):378-81. doi:10.1016/j.tripleo.2006.05.012. Epub 2006 Sep 26. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17321449)

- Guettler S, LaRose J, Petsalaki E, Gish G, Scotter A, Pawson T, Rottapel R,Sicheri F. Structural basis and sequence rules for substrate recognition byTankyrase explain the basis for cherubism disease. Cell. 2011 Dec9;147(6):1340-54. doi: 10.1016/j.cell.2011.10.046. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22153077)
- Levaot N, Voytyuk O, Dimitriou I, Sircoulomb F, Chandrakumar A, Deckert M, Krzyzanowski PM, Scotter A, Gu S, Janmohamed S, Cong F, Simoncic PD, Ueki Y, LaRose J, Rottapel R. Loss of Tankyrase-mediated destruction of 3BP2 is theunderlying pathogenic mechanism of cherubism. Cell. 2011 Dec 9;147(6):1324-39.doi: 10.1016/j.cell.2011.10.045. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22153076) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3475183/)
- Li CY, Yu SF. A novel mutation in the SH3BP2 gene causes cherubism: casereport. BMC Med Genet. 2006 Dec 5;7:84. doi: 10.1186/1471-2350-7-84. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17147794) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1764878/)
- Lietman SA, Kalinchinko N, Deng X, Kohanski R, Levine MA. Identification of anovel mutation of SH3BP2 in cherubism and demonstration that SH3BP2 mutationslead to increased NFAT activation. Hum Mutat. 2006 Jul;27(7):717-8. doi: 10.1002/humu.9433. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16786512)
- Lo B, Faiyaz-Ul-Haque M, Kennedy S, Aviv R, Tsui LC, Teebi AS. Novel mutationin the gene encoding c-Abl-binding protein SH3BP2 causes cherubism. Am J MedGenet A. 2003 Aug 15;121A(1):37-40. doi: 10.1002/ajmg.a.20226. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12900899)
- Morice A, Kadlub N, Coudert A. Cherubism. 2007 Feb 26 [updated 2025 Mar 20].In: Adam MP, Bick S, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA): University of Washington,Seattle; 1993-2025. Available from http://www.ncbi.nlm.nih.gov/books/NBK1137/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20301316)
- Novack DV, Faccio R. Jawing about TNF: new hope for cherubism. Cell. 2007 Jan12;128(1):15-7. doi: 10.1016/j.cell.2006.12.019. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17218248)
- Ueki Y, Lin CY, Senoo M, Ebihara T, Agata N, Onji M, Saheki Y, Kawai T, Mukherjee PM, Reichenberger E, Olsen BR. Increased myeloid cell responses toM-CSF and RANKL cause bone loss and inflammation in SH3BP2 "cherubism" mice.Cell. 2007 Jan 12;128(1):71-83. doi: 10.1016/j.cell.2006.10.047. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17218256)
- Ueki Y, Tiziani V, Santanna C, Fukai N, Maulik C, Garfinkle J, Ninomiya C, doAmaral C, Peters H, Habal M, Rhee-Morris L, Doss JB, Kreiborg S, Olsen BR, Reichenberger E. Mutations in the gene encoding c-Abl-binding protein SH3BP2cause cherubism. Nat Genet. 2001 Jun;28(2):125-6. doi: 10.1038/88832.

Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11381256)

Genomic Location

The *SH3BP2* gene is found on chromosome 4 (https://medlineplus.gov/genetics/chromosome/4/).

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