SMC1A gene

structural maintenance of chromosomes 1A

Normal Function

The *SMC1A* gene provides instructions for making a protein that is part of the structural maintenance of chromosomes (SMC) family. Within the nucleus, SMC proteins help regulate the structure and organization of chromosomes.

The protein produced from the *SMC1A* gene (which is usually called the SMC1 protein) helps control chromosomes during cell division. Before cells divide, they must copy all of their chromosomes. The copied DNA from each chromosome is arranged into two identical structures, called sister chromatids, which are attached to one another during the early stages of cell division. The SMC1 protein is part of a protein group called the cohesin complex that holds the sister chromatids together.

Researchers believe that the SMC1 protein, as a structural component of the cohesin complex, also plays important roles in stabilizing cells' genetic information, repairing damaged DNA, and regulating the activity of certain genes that are essential for normal development.

Health Conditions Related to Genetic Changes

Cornelia de Lange syndrome

More than 35 mutations in the *SMC1A* gene have been identified in people with Cornelia de Lange syndrome, a developmental disorder that affects many parts of the body. Researchers estimate that mutations in this gene account for about 5 percent of all cases of this condition.

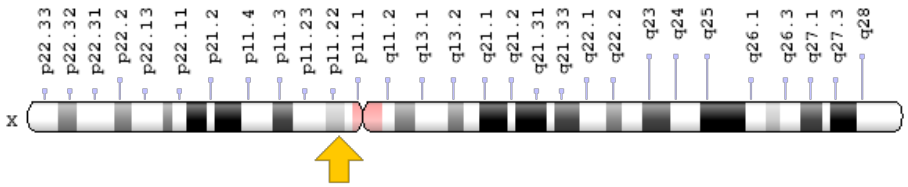
Most of the *SMC1A* gene mutations that cause Cornelia de Lange syndrome change single protein building blocks (amino acids) in the SMC1 protein. These mutations alter the structure and function of the protein, which likely interferes with the activity of the cohesin complex and impairs its ability to regulate genes that are critical for normal development. Although researchers do not fully understand how these changes cause Cornelia de Lange syndrome, they suspect that altered gene regulation probably underlies many of the developmental problems characteristic of the condition.

Studies suggest that mutations in the *SMC1A* gene tend to cause a form of Cornelia de Lange syndrome with relatively mild features. Compared to mutations in the *NIPBL* gene, which are the most common known cause of the disorder, *SMC1A* gene mutations often cause less significant delays in development and growth and are less likely to cause major birth defects.

Chromosomal Location

Cytogenetic Location: Xp11.22, which is the short (p) arm of the X chromosome at position 11.22

Molecular Location: base pairs 53,374,149 to 53,422,728 on the X chromosome (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- DXS423E
- KIAA0178
- segregation of mitotic chromosomes 1
- SMC1
- SMC1-alpha
- SMC1A_HUMAN
- SMC1L1
- SMCB

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): Cohesins and Condensins Help Configure Replicated Chromosomes for Segregation https://www.ncbi.nlm.nih.gov/books/NBK26931/#A3334

Clinical Information from GeneReviews

- Cornelia de Lange Syndrome https://www.ncbi.nlm.nih.gov/books/NBK1104

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SMC1A%5BTIAB%5D%29+OR+%28SMC1L1%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+2160+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- STRUCTURAL MAINTENANCE OF CHROMOSOMES 1A
  http://omim.org/entry/300040

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SMC1A.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SMC1A%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:11111
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:8243
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/8243
- UniProt
  https://www.uniprot.org/uniprot/Q14683

Sources for This Summary

- Borck G, Zarhrate M, Bonnefont JP, Munnich A, Cormier-Daire V, Colleaux L. Incidence and clinical features of X-linked Cornelia de Lange syndrome due to SMC1L1 mutations. Hum Mutat. 2007 Feb; 28(2):205-6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17221863
- Deardorff MA, Kaur M, Yaeger D, Rampuria A, Korolev S, Pie J, Gil-Rodríguez C, Arnedo M, Loeys B, Kline AD, Wilson M, Lillquist K, Siu V, Ramos FJ, Musio A, Jackson LS, Dorsett D, Krantz ID. Mutations in cohesin complex members SMC3 and SMC1A cause a mild variant of cornelia de Lange syndrome with predominant mental retardation. Am J Hum Genet. 2007 Mar;80(3):485-94. Epub 2007 Jan 17.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17273969
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1821101/
- Deardorff MA, Noon SE, Krantz ID. Cornelia de Lange Syndrome. 2005 Sep 16 [updated 2016 Jan 28]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from http://www.ncbi.nlm.nih.gov/books/NBK1104/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301283

- Gervasini C, Russo S, Cereda A, Parenti I, Masciadri M, Azzollini J, Melis D, Aravena T, Doray B, Ferrarini A, Garavelli L, Selicorni A, Larizza L. Cornelia de Lange individuals with new and recurrent SMC1A mutations enhance delineation of mutation repertoire and phenotypic spectrum. Am J Med Genet A. 2013 Nov;161A(11):2909-19. doi: 10.1002/ajmg.a.36252. Epub 2013 Oct 2.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24124034
- Liu J, Feldman R, Zhang Z, Deardorff MA, Haverfield EV, Kaur M, Li JR, Clark D, Kline AD, Waggoner DJ, Das S, Jackson LG, Krantz ID. SMC1A expression and mechanism of pathogenicity in probands with X-Linked Cornelia de Lange syndrome. Hum Mutat. 2009 Nov;30(11):1535-42. doi: 10.1002/humu.21095.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19701948
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2783874/
- Mannini L, Cucco F, Quarantotti V, Krantz ID, Musio A. Mutation spectrum and genotype-phenotype correlation in Cornelia de Lange syndrome. Hum Mutat. 2013 Dec;34(12):1589-96. doi: 10.1002/humu.22430. Epub 2013 Sep 16. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24038889
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3880228/
- Mannini L, Liu J, Krantz ID, Musio A. Spectrum and consequences of SMC1A mutations: the unexpected involvement of a core component of cohesin in human disease. Hum Mutat. 2010 Jan;31(1):5-10. doi: 10.1002/humu.21129. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19842212
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2797832/
- Musio A, Selicorni A, Focarelli ML, Gervasini C, Milani D, Russo S, Vezzoni P, Larizza L. X-linked Cornelia de Lange syndrome owing to SMC1L1 mutations. Nat Genet. 2006 May;38(5):528-30. Epub 2006 Apr 9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16604071
- Revenkova E, Focarelli ML, Susani L, Paulis M, Bassi MT, Mannini L, Frattini A, Delia D, Krantz I, Vezzoni P, Jessberger R, Musio A. Cornelia de Lange syndrome mutations in SMC1A or SMC3 affect binding to DNA. Hum Mol Genet. 2009 Feb 1;18(3):418-27. doi: 10.1093/hmg/ddn369. Epub 2008 Nov 7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18996922
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2722190/

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/SMC1A

Reviewed: September 2015
Published: May 14, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services