SOX9

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SRY-box 9

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1. Normal Function

The *SOX9* gene provides instructions for making a protein that plays a critical role during embryonic development. The SOX9 protein is especially important for development of the skeleton and plays a key role in the determination of sex before birth. The SOX9 protein attaches (binds) to specific regions of DNA and regulates the activity of other genes, particularly those that control skeletal development and sex determination. On the basis of this action, the SOX9 protein is called a transcription factor.

2. Health Conditions Related to Genetic Changes

2.1. Campomelic dysplasia

More than 70 mutations involving the *SOX9* gene have been found to cause campomelic dysplasia, a disorder that affects skeletal development, sex determination, and other processes in the body and is often life-threatening in the newborn period. Most cases of campomelic dysplasia are caused by mutations within the *SOX9* gene. These mutations prevent the production of the SOX9 protein or result in a protein with impaired ability to function as a transcription factor. About 5 percent of cases are caused by chromosome abnormalities that occur near the *SOX9* gene. These chromosome abnormalities disrupt regions of DNA called enhancers that normally regulate the activity of the *SOX9* gene. All of these genetic changes prevent the SOX9 protein from properly controlling the genes essential for normal development of the skeleton, reproductive organs, and other parts of the body. Abnormal development of these structures causes the signs and symptoms of campomelic dysplasia.

Individuals with milder forms of campomelic dysplasia are more likely to have chromosome abnormalities near the *SOX9* gene rather than mutations within the gene.

2.2. Isolated Pierre Robin sequence

Genetic changes that occur near the *SOX9* gene cause some cases of isolated Pierre Robin sequence. Individuals with this condition have a small lower jaw (micrognathia) and a tongue that is placed further back than normal (glossoptosis), which can block the airways. Most affected individuals are also born with an opening in the roof of the mouth (a cleft palate). These cases of Pierre Robin sequence are described as isolated because they occur without other signs and symptoms.

The genetic changes associated with isolated Pierre Robin sequence are thought to disrupt enhancer regions that normally regulate the activity of the *SOX9* gene during development of the lower jaw, which reduces *SOX9* gene activity. As a result, the SOX9 protein cannot properly control the genes essential for normal jaw development, causing micrognathia. Underdevelopment of the lower jaw affects placement of the tongue and formation of the palate, leading to glossoptosis and, often, cleft palate.

3. Other Names for This Gene

- SOX9_HUMAN
- SRA1
- SRY (sex determining region Y)-box 9
- SRY (sex-determining region Y)-box 9 protein

- SRY box 9
- transcription factor SOX9

The entry is from https://medlineplus.gov/genetics/gene/sox9

References

1. Alankarage D, Lavery R, Svingen T, Kelly S, Ludbrook L, Bagheri-Fam S, KoopmanP, Harley V. SOX9 regulates expression of the male fertility gene Ets variantfactor 5 (ETV5) during mammalian sex development. Int J Biochem Cell Biol. 2016Oct;79:41-51. doi: 10.1016/j.biocel.2016.08.005. Epub 2016 Aug 4.
2. Amarillo IE, Dipple KM, Quintero-Rivera F. Familial microdeletion of 17q24.3upstream of SOX9 is associated with isolated Pierre Robin sequence due toposition effect. Am J Med Genet A. 2013 May;161A(5):1167-72. doi:10.1002/ajmg.a.35847. Epub 2013 Mar 26.
3. Benko S, Fantes JA, Amiel J, Kleinjan DJ, Thomas S, Ramsay J, Jamshidi N,Essafi A, Heaney S, Gordon CT, McBride D, Golzio C, Fisher M, Perry P, Abadie V, Ayuso C, Holder-Espinasse M, Kilpatrick N, Lees MM, Picard A, Temple IK, ThomasP, Vazquez MP, Vekemans M, Roest Crollius H, Hastie ND, Munnich A, Etchevers HC, Pelet A, Farlie PG, Fitzpatrick DR, Lyonnet S. Highly conserved non-codingelements on either side of SOX9 associated with Pierre Robin sequence. Nat Genet.2009 Mar;41(3):359-64. doi: 10.1038/ng.329. Epub 2009 Feb 22.
4. Bien-Willner GA, Stankiewicz P, Lupski JR. SOX9cre1, a cis-acting regulatoryelement located 1.1 Mb upstream of SOX9, mediates its enhancement through the SHHpathway. Hum Mol Genet. 2007 May 15;16(10):1143-56. Epub 2007 Apr 4.
5. Fonseca AC, Bonaldi A, Bertola DR, Kim CA, Otto PA, Vianna-Morgante AM. Theclinical impact of chromosomal rearrangements with breakpoints upstream of theSOX9 gene: two novel de novo balanced translocations associated with acampomelic campomelic dysplasia. BMC Med Genet. 2013 May 7;14:50. doi:10.1186/1471-2350-14-50.
6. Gordon CT, Attanasio C, Bhatia S, Benko S, Ansari M, Tan TY, Munnich A,Pennacchio LA, Abadie V, Temple IK, Goldenberg A, van Heyningen V, Amiel J,FitzPatrick D, Kleinjan DA, Visel A, Lyonnet S. Identification of novelcraniofacial regulatory domains located far upstream of SOX9 and disrupted inPierre Robin sequence. Hum Mutat. 2014 Aug;35(8):1011-20. doi:10.1002/humu.22606.
7. Hill-Harfe KL, Kaplan L, Stalker HJ, Zori RT, Pop R, Scherer G, Wallace MR.Fine mapping of chromosome 17 translocation breakpoints > or = 900 Kb upstream ofSOX9 in acampomelic campomelic dysplasia and a mild, familial skeletal dysplasia.Am J Hum Genet. 2005 Apr;76(4):663-71.
8. Kobayashi A, Chang H, Chaboissier MC, Schedl A, Behringer RR. Sox9 in testisdetermination. Ann N Y Acad Sci. 2005 Dec;1061:9-17. Review.
9. Leipoldt M, Erdel M, Bien-Willner GA, Smyk M, Theurl M, Yatsenko SA, LupskiJR, Lane AH, Shanske AL, Stankiewicz P, Scherer G. Two novel translocationbreakpoints upstream of SOX9 define borders of the proximal and distal breakpointcluster region in campomelic dysplasia. Clin Genet. 2007 Jan;71(1):67-75.
10. Mead TJ, Wang Q, Bhattaram P, Dy P, Afelik S, Jensen J, Lefebvre V. Afar-upstream (-70 kb) enhancer mediates Sox9 auto-regulation in somatic tissuesduring development and adult regeneration. Nucleic Acids Res. 2013Apr;41(8):4459-69. doi: 10.1093/nar/gkt140. Epub 2013 Feb 28.
11. Velagaleti GV, Bien-Willner GA, Northup JK, Lockhart LH, Hawkins JC, Jalal SM,Withers M, Lupski JR, Stankiewicz P. Position effects due to chromosomebreakpoints that map approximately 900 Kb upstream and approximately 1.3 Mbdownstream of SOX9 in two patients with campomelic dysplasia. Am J Hum Genet.2005 Apr;76(4):652-62. Epub 2005 Feb 22.