SOD1 Gene

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Contributor: Peter Tang

Superoxide dismutase 1

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1. Normal Function

The *SOD1* gene provides instructions for making an enzyme called superoxide dismutase, which is abundant in cells throughout the body. This enzyme attaches (binds) to molecules of copper and zinc to break down toxic, charged oxygen molecules called superoxide radicals. The molecules are byproducts of normal cell processes, and they must be broken down regularly to avoid damaging cells.

2. Health Conditions Related to Genetic Changes

2.1. Amyotrophic lateral sclerosis

At least 200 mutations in the *SOD1* gene have been found to cause amyotrophic lateral sclerosis (ALS), a condition characterized by progressive muscle weakness, a loss of muscle mass, and an inability to control movement. Most of these mutations change one of the protein building blocks (amino acids) in the superoxide dismutase enzyme. About half of all Americans with ALS caused by *SOD1* gene mutations have a particular mutation that replaces the amino acid alanine with the amino acid valine at position 5 in the enzyme, written as Ala5Val or A5V. (Because of variations in the ways amino acids are counted in proteins, this mutation is sometimes called Ala4Val or A4V.) ALS caused by the A5V mutation is generally associated with a shorter life expectancy compared with ALS caused by other genetic mutations.

ALS is caused by the death of nerve cells that control muscle movement (motor neurons). It is unclear why these cells are particularly sensitive to *SOD1* gene mutations. Researchers have suggested several ways in which the altered enzyme may cause the death of motor neurons. These possibilities include an increase in harmful superoxide radicals, increased production of other types of toxic radicals, increased cell death, or accumulation of clumps (aggregates) of misfolded superoxide dismutase that may be toxic to cells.

3. Other Names for This Gene

- ALS1
- Cu/Zn superoxide dismutase
- indophenoloxidase A
- IPOA
- SODC_HUMAN
- superoxide dismutase 1, soluble
- superoxide dismutase 1, soluble (amyotrophic lateral sclerosis 1 (adult))
- superoxide dismutase, cystolic
- superoxide dismutase-1, soluble

References

1. Barber SC, Mead RJ, Shaw PJ. Oxidative stress in ALS: a mechanism ofneurodegeneration and a therapeutic target. Biochim Biophys Acta. 2006Nov-Dec;1762(11-12):1051-67. Epub 2006 Apr 4. Review. Citation on PubMed
2. Bertolin C, D'Ascenzo C, Querin G, Gaiani A, Boaretto F, Salvoro C, Vazza G,Angelini C, Cagnin A, Pegoraro E, Sorarù G, Mostacciuolo ML. Improving theknowledge of amyotrophic lateral sclerosis genetics: novel SOD1 and FUS

variants.Neurobiol Aging. 2014 May;35(5):1212.e7-1212.e10. doi:10.1016/j.neurobiolaging.2013.10.093. Epub 2013 Oct 29. Citation on PubMed

3. Rakhit R, Chakrabartty A. Structure, folding, and misfolding of Cu,Znsuperoxide dismutase in amyotrophic lateral sclerosis. Biochim Biophys Acta. 2006Nov-Dec;1762(11-12):1025-37. Epub 2006 May 22. Review. Citation on PubMed
4. Shaw BF, Valentine JS. How do ALS-associated mutations in superoxide dismutase1 promote aggregation of the protein? Trends Biochem Sci. 2007 Feb;32(2):78-85.Epub 2007 Jan 5. Review. Citation on PubMed
5. Siddique N, Siddique T. Amyotrophic Lateral Sclerosis Overview. 2001 Mar 23[updated 2019 Oct 3]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH,Stephens K, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): Universityof Washington, Seattle; 1993-2020. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1450/ Citation on PubMed
6. Tsang CK, Liu Y, Thomas J, Zhang Y, Zheng XF. Superoxide dismutase 1 acts as anuclear transcription factor to regulate oxidative stress resistance. Nat Commun.2014 Mar 19;5:3446. doi: 10.1038/ncomms4446. Citation on PubMed or Free article on PubMed Central
7. Valentine JS, Doucette PA, Zittin Potter S. Copper-zinc superoxide dismutaseand amyotrophic lateral sclerosis. Annu Rev Biochem. 2005;74:563-93. Review. Citation on PubMed

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