

# Homo sapiens superoxide dismutase 1, soluble (SOD1)

Biomedical Engineering 20073006 Jang Jeong Hwa

## Introduction

Superoxide dismutases (SOD) are a class of enzymes that catalyze the dismutation of superoxide into oxygen and hydrogen peroxide. As such, they are an important antioxidant defense in nearly all cells exposed to oxygen.

**Recommended Name:** Superoxide dismutase [Cu-Zn]

**Size:** 154 amino acids; 15936 Da

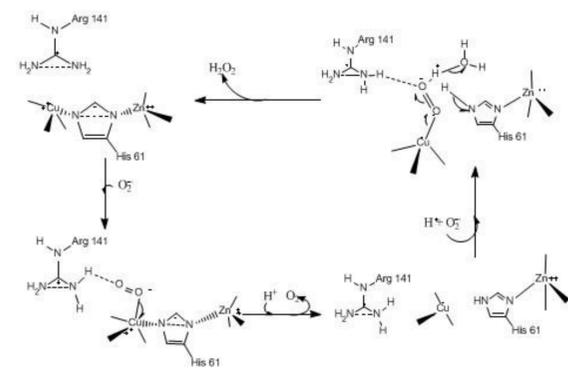
**Cofactor:** Binds 1 copper ion per subunit

**Cofactor:** Binds 1 zinc ion per subunit

**Subunit:** Homodimer. The pathogenic variants ALS1 Arg-38, Arg-47, Arg-86 and Ala-94 interact with RNF19A, whereas wild-type protein does not

**Subcellular location:** Cytoplasm

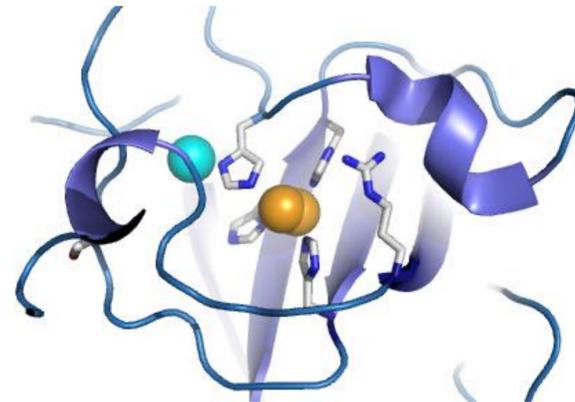
**Miscellaneous:** The protein (both wild-type and ALS1 variants) has a tendency to form fibrillar aggregates in the absence of the intramolecular disulfide bond or of bound zinc ions. These aggregates may have cytotoxic effects. Zinc binding promotes dimerization and stabilizes the native form



► Schematic dismutation of superoxide in SOD1

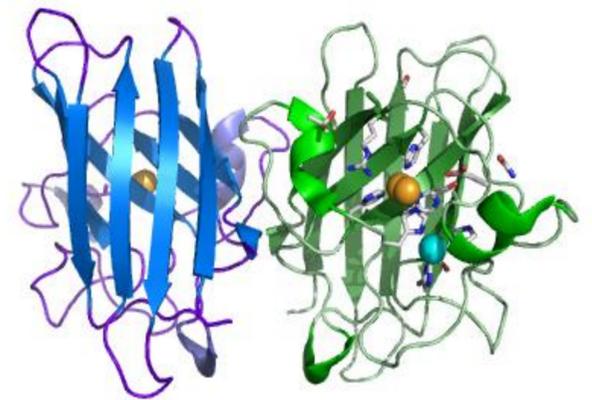
## Function

The SOD1 gene provides instructions for making an enzyme called superoxide dismutase that is abundant in cells throughout the body. This enzyme neutralizes supercharged oxygen molecules (superoxide radicals), which can damage cells if their levels are not controlled. Superoxide radicals are byproducts of normal cell processes, particularly energy-producing reactions that occur in specialized structures called mitochondria. To function properly, the superoxide dismutase enzyme must bind to copper and zinc.



► SOD1 active site. The human SOD1 active site channel includes four critical histidine sidechains and one arginine. The zinc (blue) and copper (orange) ions are shown as spheres.

## Structure



► Dimer of human SOD1. Human SOD1 is a homodimeric metalloenzyme. The copper ions (orange) and zinc ions (blue) are shown as spheres. The active channel sidechains are shown in stick form in the green-colored side of the dimer.

### Amino acid composition :

|         |    |      |         |    |       |         |    |      |
|---------|----|------|---------|----|-------|---------|----|------|
| Ala (A) | 10 | 6.5% | Arg (R) | 4  | 2.6%  | Asn (N) | 7  | 4.5% |
| Asp (D) | 11 | 7.1% | Cys (C) | 4  | 2.6%  | Gln (Q) | 3  | 1.9% |
| Glu (E) | 10 | 6.5% | Gly (G) | 25 | 16.2% | His (H) | 8  | 5.2% |
| Ile (I) | 9  | 5.8% | Leu (L) | 9  | 5.8%  | Lys (K) | 11 | 7.1% |
| Met (M) | 1  | 0.6% | Phe (F) | 4  | 2.6%  | Pro (P) | 5  | 3.2% |
| Ser (S) | 10 | 6.5% | Thr (T) | 8  | 5.2%  | Trp (W) | 1  | 0.6% |
| Tyr (Y) | 0  | 0.0% | Val (V) | 14 | 9.1%  | Pyl (O) | 0  | 0.0% |
| Sec (U) | 0  | 0.0% | (B)     | 0  | 0.0%  | (Z)     | 0  | 0.0% |
| (X)     | 0  | 0.0% |         |    |       |         |    |      |

### SOD1 gene located

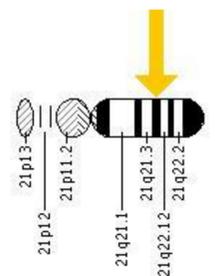
Cytogenetic Location: 21q22.1

Molecular Location on chromosome 21:

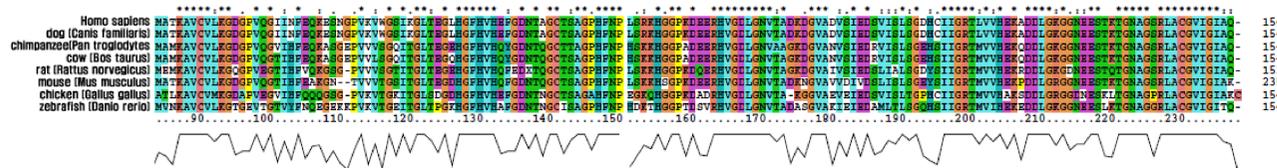
base pairs 33,031,934 to 33,041,243

The SOD1 gene is located on the long (q) arm of chromosome 21 at position 22.1.

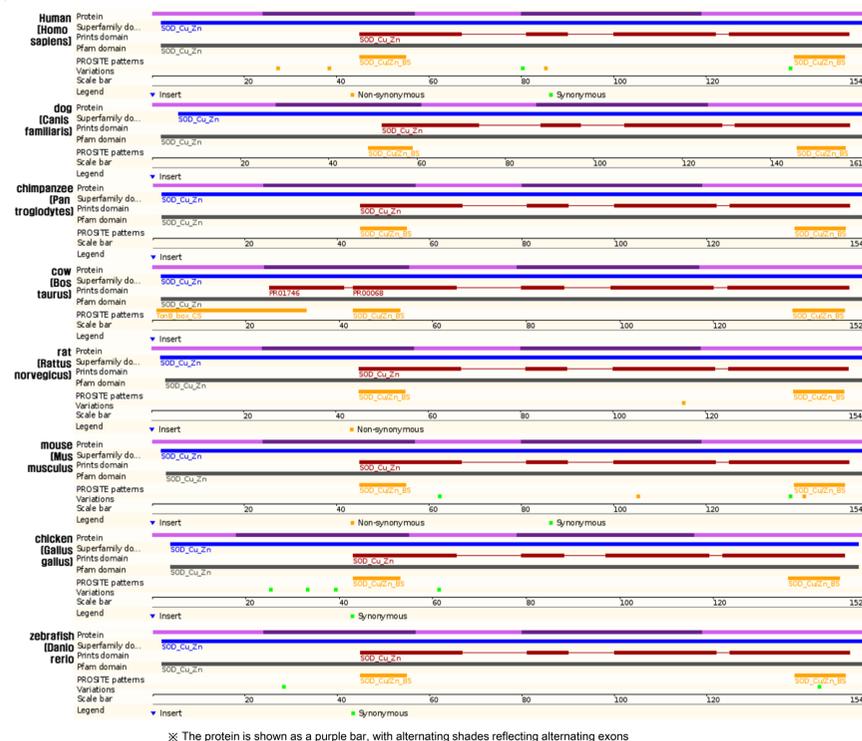
More precisely, the SOD1 gene is located from base pair 33,031,934 to base pair 33,041,243 on chromosome 21.



## Multiple protein sequence alignment



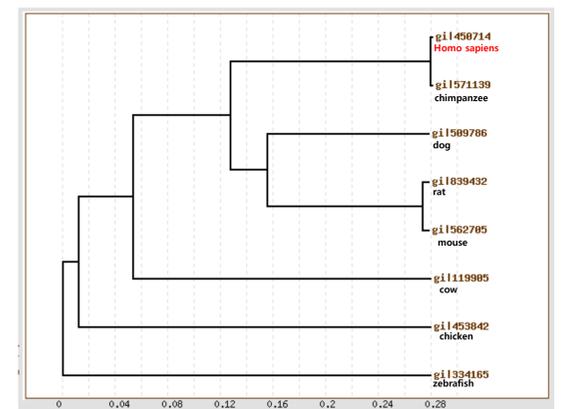
## Protein homology comparison



| Organism                                     | Human Similarity                              | Gene  |
|--|---|---|
| dog (Canis familiaris)                       | 86.49(n) / 81.58(a)                           | SOD1 <sup>1</sup>                               |
| chimpanzee (Pan troglodytes)                 | 99.78(n) / 100(a)                             | SOD1 <sup>1</sup>                               |
| cow (Bos taurus)                             | 86.4(n) / 82.89(a)                            | SOD1 <sup>1</sup>                               |
| rat (Rattus norvegicus)                      | 84.42(n) / 83.12(a)                           | Sod1 <sup>1</sup>                               |
| mouse (Mus musculus)                         | 83.77(n) <sup>1</sup> / 83.77(a) <sup>1</sup> | Sod1 <sup>1-5</sup>                             |
| chicken (Gallus gallus)                      | 75.66(n) / 75.66(a)                           | SOD1 <sup>1</sup>                               |
| zebrafish (Danio rerio)                      | 73.04(n)                                      | sod1 <sup>2</sup>                               |
| baker's yeast (Saccharomyces cerevisiae)     | 56.82(n)/56.38(a)                             | SOD1(YJR104C) <sup>3</sup><br>SOD1 <sup>1</sup> |
| African clawed frog (Xenopus laevis)         | 80.41(n)                                      | sod1-A-prov <sup>2</sup>                        |
| tropical clawed frog (Silurana tropicalis)   | 74.16(n)                                      | Str.1999 <sup>2</sup>                           |
| rainbow trout (Oncorhynchus mykiss)          | 73.24(n)                                      | Omy.9641 <sup>2</sup>                           |
| African malaria mosquito (Anopheles gambiae) | 59.65(n) / 59.21(a)                           | SOD3 <sup>1</sup>                               |
| thale cress (Arabidopsis thaliana)           | 56.31(n) / 54.73(a)                           | CSD1 <sup>1</sup>                               |
| rice blast fungus (Magnaporthe grisea)       | 54.22(n) / 57.33(a)                           | MGG_02625 <sup>1</sup>                          |
| rice (Oryza sativa)                          | 59.46(n) / 60.81(a)                           | Os07g0665200 <sup>1</sup>                       |
| corn (Zea mays)                              | 73.33(n)                                      | M15175.1 <sup>2</sup>                           |
| Alicante grape (Vitis vinifera)              | 76.1(n)                                       | Vvi.3600 <sup>2</sup>                           |
| bread mold (Neurospora crassa)               | 51.21(n) / 54.3(a)                            | NCU02133.1 <sup>1</sup>                         |
| fission yeast (Schizosaccharomyces pombe)    | 55.56(n) / 56.67(a)                           | sod1 <sup>1</sup>                               |

• **Orthologs**  
Human Similarity - The percent similarity to the human gene, followed either by (n) where the comparison was based on nucleic acids or (a) for amino acid based comparisons.

## Phylogram



## Conclusion

This report reviews the difference between human and other species of Cu,Zn-SOD (SOD1) and structure and function of the human SOD1. As an important antioxidant enzyme in vivo in several species of SOD1 showed high similarity with human.

Much more research remains to be done on SOD1, on the mechanism of SOD1 multimer formation, as well as on the cellular response to SOD1 mutant multimers.

This future research may lead to therapies that could help to prevent the neural cell degeneration that is at the root of FALS.

Applying a variety of information technology (IT), the efficient analysis of biological information seems to be possible.

## References

- <http://en.wikipedia.org>
- <http://www.phosphosite.org/proteinAction.do?id=15569&showAllSites=true>
- <http://www.pnas.org/>
- <http://ghr.nlm.nih.gov/gene/SOD1>
- Laura Goodman, Biochemistry and Molecular Biophysics University of Arizona, Human Cu,Zn-Superoxide Dismutase structure, function and the effects of its mutation in familial amyotrophic lateral sclerosis

## Genetrees



◀ Genetrees aim to represent the evolutionary history of gene families, genes that diverged from a common ancestor.

Gene trees are constructed using the longest protein for every gene in every species

Red squares represent duplications nodes, blue squares represent speciation nodes, giving rise to paralogues, orthologues, or between-species paralogues. Another class of node, ambiguous, is shown as a lighter blue square.

The gene of interest is highlighted in red and within-species paralogues (within-Sp) are shown in blue.

Multiple alignment of the peptides (green bars) was made using MUSCLE.

Green shows areas of amino acid alignment, white areas are gaps in the alignment.