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online data

Original Paper

## SUPPLEMENTARY ONLINE DATA

# Structural switching of Cu,Zn-superoxide dismutases at loop VI: insights from the crystal structure of 2-mercaptoethanol-modified enzyme

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See the following pages for Supplementary Figure S1 and Supplementary Tables S1–S6



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The structural co-ordinates reported will appear in the Protein Data Bank under accession number 3T5W.

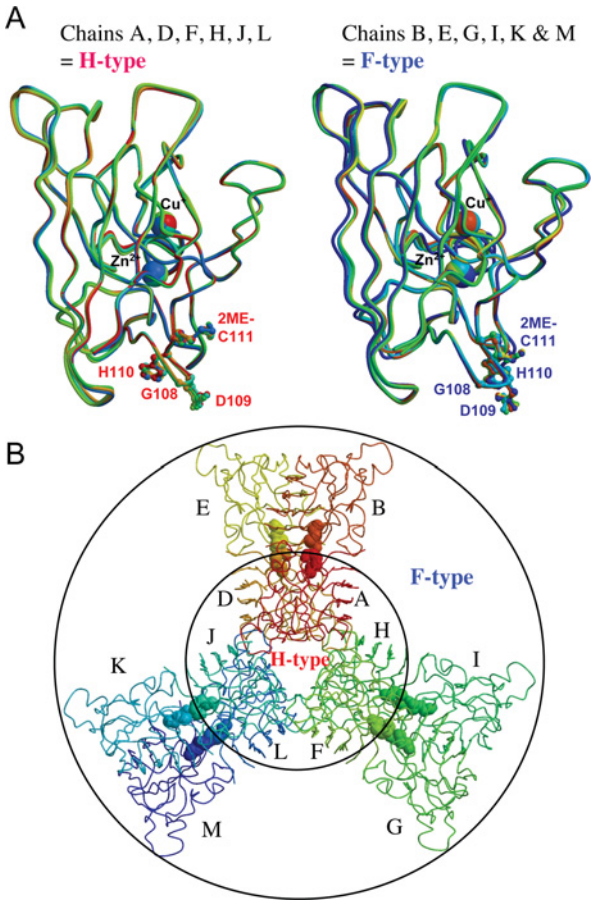


**Figure S1 H/F types of six dimers in the crystallographic asymmetric unit**

(**A**) Chains A (red), D (orange yellow), F (yellow green), H (green), J (green cyan) and L (blue) are superimposed using all 153 C$\alpha$ atoms as H-type. Similarly, chains B (orange), E (yellow), G (light green), I (dark green), K (cyan) and M (purple) are superimposed as F-type. C$\alpha$ atoms and side-chains of $Gly^{108}$, $Asp^{109}$, $His^{110}$ and 2-ME-$Cys^{111}$ are indicated as ball-and-sticks. Even the side-chains superimpose well in each type. (**B**) All six dimers (A/B, D/E, F/G, H/I, J/K and L/M) in the crystallographic asymmetric unit are shown and colored as in (**A**). H-type chains (A, D, F, H, J and L) locate inside and F-type chains (B, E, G, I, K and M) locate outside of the asymmetric group.

**Table S1 H/F typing of loop VI by comparing with chains A and B**
Rmsd of 153 Cα atoms, distances of corresponding Cα atom from $Gly^{108}$ to $Cys^{111}$ compared with chain A or B (Å), distances (Å) and existence of water molecule between $Ser^{105}$-N and $His^{110}$-O, and designated chain type.

| | Compared with chain A | | | | | Compared with chain B | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Distances of corresponding Cα (Å) | | | | | Distances of corresponding Cα (Å) | | | | | | | |
| Chain | Rmsd of 153 Cα atoms (Å) | $Gly^{108}$ | $Asp^{109}$ | $His^{110}$ | $Cys^{111}$ | Rmsd of 153 Cα atoms (Å) | $Gly^{108}$ | $Asp^{109}$ | $His^{110}$ | $Cys^{111}$ | A- like or B- like | Distance between $S^{105}$-N and $H^{110}$-O (Å) | $H_2O$ | Type of loop VI |
| A | – | – | – | – | – | 0.37 | 0.97 | 2.57 | 2.61 | 0.48 | A | 3.24 | – | H |
| B | 0.37 | 0.97 | 2.57 | 2.61 | 0.48 | – | – | – | – | – | B | 4.94 | + | F |
| D | 0.20 | **0.15** | **0.20** | **0.15** | **0.05** | 0.37 | 0.88 | 2.57 | 2.49 | 0.51 | A | 3.17 | – | H |
| E | 0.37 | 0.89 | 2.58 | 2.64 | 0.50 | 0.15 | **0.08** | **0.17** | **0.13** | **0.07** | B | 5.06 | + | F |
| F | 0.28 | **0.09** | **0.29** | **0.07** | **0.10** | 0.42 | 0.92 | 2.69 | 2.58 | 0.46 | A | 3.16 | – | H |
| G | 0.39 | 0.76 | 2.44 | 2.52 | 0.50 | 0.22 | **0.43** | **0.17** | **0.21** | **0.21** | B | 4.93 | + | F |
| H | 0.18 | **0.13** | **0.16** | **0.13** | **0.12** | 0.39 | 0.87 | 2.53 | 2.49 | 0.41 | A | 3.22 | – | H |
| I | 0.41 | 0.79 | 2.42 | 2.48 | 0.35 | 0.23 | **0.35** | **0.16** | **0.16** | **0.19** | B | 4.89 | + | F |
| J | 0.18 | **0.08** | **0.10** | **0.15** | **0.08** | 0.36 | 0.96 | 2.49 | 2.48 | 0.45 | A | 3.40 | – | H |
| K | 0.43 | 0.94 | 2.72 | 2.78 | 0.47 | 0.24 | **0.19** | **0.30** | **0.28** | **0.10** | B | 5.18 | + | F |
| L | 0.19 | **0.10** | **0.19** | **0.18** | **0.16** | 0.39 | 1.05 | 2.63 | 2.50 | 0.38 | A | 3.17 | – | H |
| M | 0.59 | 0.91 | 2.53 | 2.55 | 0.44 | 0.48 | **0.14** | **0.20** | **0.14** | **0.05** | B | 4.64 | + | F |

**Table S2 H/F typing of loop VI in human SOD1**

| PDB | Mutation | Type | ALS? | Monomer? |
|---|---|---|---|---|
| 3T5W C111-2-ME (present study) | | H**F** | | |
| 1N18 | C6A C111S | H**F**, HH | | |
| 1PU0 | | HH, H**F** | | |
| 1SPD | | H**F** | | |
| 2GBT | C6A C111A | H**F** | | |
| 2GBU | C6A C111A C57A C146A | H**F** | | |
| 2GBV | C6A C111A C57A C146A | H**F**, **FF** | | |
| 2ZKY | G93A | HH, H**F** | ALS | |
| 3CQP | G85R | HH, H**F** | ALS | |
| 1UXL | I113T | HH, H**F** | ALS | |
| 2C9V | | HH | | |
| 3GZO | G93A | HH, H**F** | ALS | |
| 1AZV | G37R | HH | ALS | |
| 1FUN | C6A C111S K136E | HH | | |
| 1HL4 | | HH | | |
| 1HL5 | | HH | | |
| 1N19 | A4V C6A C111S | HH | ALS | |
| 1OEZ | H46R | HH | ALS | |
| 1OZT | H46R | HH | ALS | |
| 1OZU | C111s-oxyC S134N | HH | ALS | |
| 1P1V | C111s-oxyC D125H | HH | ALS | |
| 1PTZ | C6A C111S H43R | HH | ALS | |
| 1SOS | C6A C111S | HH | | |
| 1UXM | A4V | HH, H**F** | ALS | |
| 2C9S | C111s-hydroxyC | HH | | |
| 2C9U | | HH | | |
| 2NNX | H46R H48Q | HH | ALS | |
| 2R27 | C6A H80S D83S C111S | HH | | |
| 2V0A | | HH | | |
| 2VR6 | G85R | HH | ALS | |
| 2VR7 | G85R | HH | ALS | |
| 2VR8 | C111s-hydroxyC G85R | HH | ALS | |
| 2WKO | G93A (C111s-hydroxyC) | HH | ALS | |
| 2WZ0 | L38V | HH | ALS | |
| 2WZ5 | L38V | HH | ALS | |
| 2WZ6 | G93A | HH | ALS | |
| 2WYT | L38V | HH | ALS | |
| 2WYZ | L38V(C111s-hydroxyC) | HH | ALS | |
| 2ZKW | G85R | HH | ALS | |
| 2ZKX | G85R | HH | ALS | |
| 3CQQ | C111s-oxyC G85R | HH | ALS | |
| 3ECU | | HH | | |
| 3ECV | I113T | HH | ALS | |
| 3ECW | T54R | HH | ALS | |
| 3H2P | D124V | HH | ALS | |
| 3H2Q | H80R | HH | ALS | |
| 3KH3 | | HH, **F**H | | |
| 3KH4 | | HH | | |
| 3GQF | H46R H48Q | HH | ALS | |
| 3GZP | G93A | HH | ALS | |
| 3GZQ | A4V | HH | ALS | |

**Table S2 Continued**

| PDB | Mutation | Type | ALS? | Monomer? |
|---|---|---|---|---|
| 3K91 | H46R H48Q C111 pentaS-bridged | HH | ALS | |
| 3QQD | H80R C111 cysteinesulfonate | HH | ALS | |
| 1MFM | C6A C111S F50E G51E E133Q | **F** | | Monomer |
| 2XJK | C6A C111A F50E G51E | **F** | | Monomer |
| 2XJL | C6A C111A F50E G51E | | | |
| H46S H48S D120S | | **F** | | Monomer |
| 3HFF | C6A C111A F50E G51E | | | |
| | H63S H71S H80S D83S | **F** | | Monomer |

**Table S3 Determination of loop VI type in each chain (human SOD1)**
Each two chains from the first row form a dimer.

| PDB | Mutation / resolution / year | ALS / monomer | Chain | Distance between S105-N and H110-O (Å) | A like or B like | $H_2O$ | Type of loop VI |
|---|---|---|---|---|---|---|---|
| 3T5W (present study) | 2-ME at C111 / 1.8 / 2011 | | A | 3.2 | A | – | H |
| | | | B | 4.9 | B | + | F |
| | | | D | 3.2 | A | – | H |
| | | | E | 5.1 | B | + | F |
| | | | F | 3.2 | A | – | H |
| | | | G | 4.9 | B | + | F |
| | | | H | 3.2 | A | – | H |
| | | | I | 4.9 | B | + | F |
| | | | J | 3.4 | A | – | H |
| | | | K | 5.2 | B | + | F |
| | | | L | 3.2 | A | – | H |
| | | | M | 4.6 | B | + | F |
| 1N18 | C6A C111S / 2.0 / 2002 | | A | 4.9 | B | + | F |
| | | | B | 3.2 | A | – | H |
| | | | C | 4.7 | B | + | F |
| | | | D | 3.3 | A | – | H |
| | | | E | 4.6 | B | + | F |
| | | | F | 3.3 | A | – | H |
| | | | G | 3.3 | A | – | H |
| | | | H | 3.3 | A | – | H |
| | | | I | 3.5 | A | – | H |
| | | | J | 3.4 | A | – | H |
| 1PU0 | / 1.7 / 2003 | | A | 4.8 | B | + | F |
| | | | B | 3.2 | A | – | H |
| | | | C | 4.8 | B | + | F |
| | | | D | 3.2 | A | – | H |
| | | | E | 3.2 | A | – | H |
| | | | F | 3.1 | A | – | H |
| | | | G | 3.3 | A | – | H |
| | | | H | 3.3 | A | – | H |
| | | | I | 3.3 | A | – | H |
| | | | J | 3.1 | A | – | H |
| 1SPD | /2.4 / 1993 | | A | 2.9 | A | – | H |
| | | | B | 5.5 | B | – | F |
| 2GBT | C6A C111A / 1.7 / 2006 | | A | 3.5 | A | – | H |
| | | | B | 4.9 | B | + | F |
| | | | C | 5.2 | B | – | F |

**Table S3 Continued**

| PDB | Mutation / resolution / year | ALS / monomer | Chain | Distance between S105-N and H110-O (Å) | A like or B like | $H_2O$ | Type of loop VI |
|---|---|---|---|---|---|---|---|
| | | | D | 3.3 | A | – | H |
| 2GBU | C6A C111A C57A C146A / 2.0 / 2006 | | A | 3.6 | A | – | H |
| | | | B | 4.7 | B | + | F |
| | | | C | 5.1 | B | + | F |
| | | | D | 3.4 | A | – | H |
| 2GBV | C6A C111A C57A C146A / 2.0 / 2006 | | A | 5.1 | B | + | F |
| | | | F | 4.8 | B | – | F |
| | | | B | 5.0 | B | + | F |
| | | | G | 3.6 | A | – | H |
| | | | C | 5.0 | B | + | F |
| | | | H | 3.4 | A | – | H |
| | | | D | 3.5 | A | – | H |
| | | | I | 4.8 | B | – | F |
| | | | E | 5.1 | B | + | F |
| | | | J | 5.1 | B | + | F |
| 2ZKY | G93A / 2.4 / 2008 | ALS | A | 3.2 | A | – | H |
| | | | B | 3.3 | A | – | H |
| | | | C | 4.0 | B | – | F |
| | | | D | 3.2 | A | – | H |
| | | | E | 3.3 | A | – | H |
| | | | F | 3.2 | A | – | H |
| | | | G | 3.3 | A | – | H |
| | | | H | 3.5 | A | – | H |
| | | | I | 3.4 | A | – | H |
| | | | J | 3.0 | A | – | H |
| 3CQP | G85R / 2.0 / 2008 | ALS | A | 3.3 | A | – | H |
| | | | B | 3.1 | A | – | H |
| | | | C | 3.1 | A | – | H |
| | | | D | 4.6 | B | + | F |
| 1UXL | I113T / 1.6 / 2004 | ALS | A | 5.1 &3.3 | B & A | + & – | F & H |
| | | | F | 3.3 | A | – | H |
| | | | B | 5.2 &3.9 | B & A | + & – | F & H |
| | | | G | 3.2 | A | – | H |
| | | | C | 3.2 | A | – | H |
| | | | H | 3.2 | A | – | H |
| | | | D | 3.4 | A | – | H |
| | | | I | 5.3 & 3.5 | B & A | – | F & H |
| | | | E | 3.2 | A | – | H |
| | | | J | 3.3 | A | – | H |
| 2C9V | / 1.1 / 2005 | | A | 3.3 | A | – | H |
| | | | F | 3.2 | X† | – | H |
| 3GZO | G93A / 2.1 / 2009 | ALS | A | 3.2 | A | – | H |
| | | | B | 3.2 | A | – | H |
| | | | C | 3.1 | A | – | H |
| | | | D | 3.1 | A | – | H |
| | | | E | 3.2 | A | – | H |
| | | | F | 3.1 | A | – | H |
| | | | G | 3.2 | A | – | H |

**Table S3 Continued**

| PDB | Mutation / resolution / year | ALS / monomer | Chain | Distance between S105-N and H110-O (Å) | A like or B like | $H_2O$ | Type of loop VI |
|---|---|---|---|---|---|---|---|
| | | | H | 8.5 | Y† | – | F |
| | | | I | 3.3 | A | – | H |
| | | | J | 3.2 | A | – | H |
| 1AZV | G37R / 1.9 / 1997 | ALS | A | 3.3 | A | – | H |
| | | | B | 3.1 | A | – | H |
| 1FUN | C6A C111S K136E / 2.9 / 1998 | | A | 3.4 | A | – | H |
| | | | F | 3.3 | A | – | H |
| | | | B | 3.0 | A | – | H |
| | | | G | 2.9 | A | – | H |
| | | | C | 3.0 | A | – | H |
| | | | H | 3.3 | A | – | H |
| | | | D | 3.4 | A | – | H |
| | | | I | 3.3 | A | – | H |
| | | | E | 3.6 | A | – | H |
| | | | J | 3.1 | A | – | H |
| 1HL4 | / 1.8 / 2003 | | A | 3.5 | A | – | H |
| | | | B | 3.2 | A | – | H |
| | | | C | 3.2 | A | – | H |
| | | | D | 3.4 | A | – | H |
| 1HL5 | / 1.8 / 2003 | | A | 3.2 | A | – | H |
| | | | H | 3.2 | A | – | H |
| | | | B | 3.3 | A | – | H |
| | | | I | 3.4 | A | – | H |
| | | | C | 3.1 | A | – | H |
| | | | J | 3.3 | A | – | H |
| | | | D | 3.2 | A | – | H |
| | | | K | 3.2 | A | – | H |
| | | | E | 3.2 | A | – | H |
| | | | L | 3.2 | A | – | H |
| | | | F | 3.1 | A | – | H |
| | | | M | 3.3 | A | – | H |
| | | | G | 3.0 | A | – | H |
| | | | N | 3.2 | A | – | H |
| | | | O | 3.0 | A | – | H |
| | | | Q | 3.2 | A | – | H |
| | | | P | 3.3 | A | – | H |
| | | | S | 3.2 | A | – | H |
| 1N19 | A4V C6A C111S / 1.8 / 2002 | ALS | A | 3.3 | A | – | H |
| | | | B | 3.2 | A | – | H |
| 1OEZ | H46R / 2.2 / 2003 | ALS | W | 3.3 | A | – | H |
| | | | X | 3.3 | A | – | H |
| | | | Y | 3.1 | A | – | H |
| | | | Z | 3.1 | A | – | H |
| 1OZT | H46R / 2.5 / 2003 | ALS | G | 3.1 | A | – | H |
| | | | H | 3.2 | A | – | H |
| | | | I | 3.2 | A | – | H |
| | | | J | 3.1 | A | – | H |

**Table S3 Continued**

| PDB | Mutation / resolution / year | ALS / monomer | Chain | Distance between S105-N and H110-O (Å) | A like or B like | $H_2O$ | Type of loop VI |
|---|---|---|---|---|---|---|---|
| | | | K | 3.2 | A | – | H |
| | | | L | 3.2 | A | – | H |
| | | | M | 3.2 | A | – | H |
| | | | N | 3.2 | A | – | H |
| 1OZU | C111s – oxyC S134N / 1.3 / 2003 | ALS | A | 3.2 | A | – | H |
| | | | B | 3.2 | A | – | H |
| 1P1V | C111s – oxyC D125H / 1.4 / 2003 | ALS | A | 3.3 | A | – | H |
| | | | B | 3.4 | A | – | H |
| | | | C* | 3.3 | A | – | H |
| 1PTZ | C6A C111S H43R / 1.8 / 2003 | ALS | A | 3.4 | A | – | H |
| | | | B | 3.3 | A | – | H |
| 1SOS | C6A C111S / 2.5 / 1992 | | A | 3.2 | A | – | H |
| | | | F | 3.1 | A | – | H |
| | | | B | 3.1 | A | – | H |
| | | | G | 3.1 | A | – | H |
| | | | C | 3.2 | A | – | H |
| | | | H | 3.1 | A | – | H |
| | | | D | 3.7 | A | – | H |
| | | | I | 3.4 | A | – | H |
| | | | E | 3.0 | A | – | H |
| | | | J | 3.1 | A | – | H |
| 1UXM | A4V / 1.9 / 2004 | ALS | A | 3.2 | A | – | H |
| | | | B | 3.2 | A | – | H |
| | | | C | 3.3 | A | – | H |
| | | | D | 3.3 | A | – | H |
| | | | E | 3.3 | A | – | H |
| | | | F | 3.0 | A | – | H |
| | | | G | 3.3 | A | – | H |
| | | | H | 4.3 | A | – | F |
| | | | I | 3.4 | A | – | H |
| | | | J | 3.3 | A | – | H |
| | | | K | 3.2 | A | – | H |
| | | | L | 3.1 | A | – | H |
| 2C9S | C111s – hydroxyC / 1.2 / 2005 | | A | 3.2 | A | – | H |
| | | | F | 3.3 | A | – | H |
| 2C9U | / 1.2 / 2005 | | A | 3.2 | A | – | H |
| | | | F | 3.2 | A | – | H |
| 2NNX | H46R H48Q / 2.3 / 2006 | ALS | A | 3.1 | A | – | H |
| | | | B | 3.0 | A | – | H |
| | | | C | 3.2 | A | – | H |
| | | | D | 3.3 | A | – | H |
| 2R27 | C6A H80S D83S C111S / 2.0 / 2007 | | A | 3.0 | A | – | H |
| | | | B | 3.0 | A | – | H |
| 2V0A | / 1.2 / 2007 | | A | 3.2 | A | – | H |

**Table S3 Continued**

| PDB | Mutation / resolution / year | ALS / monomer | Chain | Distance between S105-N and H110-O (Å) | A like or B like | $H_2O$ | Type of loop VI |
|---|---|---|---|---|---|---|---|
| | | | F | 3.2 | A | – | H |
| 2VR6 | G85R / 1.3 / 2008 | ALS | A | 3.3 | A | – | H |
| | | | F | 3.3 | A | – | H |
| 2VR7 | G85R / 1.6 / 2008 | ALS | A | 3.2 | A | – | H |
| | | | F | 3.2 | A | – | H |
| 2VR8 | C111S – hydroxyC G85R / 1.4 / 2008 | ALS | A | 3.2 | A | – | H |
| | | | F | 3.2 | A | – | H |
| 2WKO | G93A (C111s – hydroxyC: F) / 2.1 / 2009 | ALS | A | 3.3 | A | – | H |
| | | | F | 3.1 | A | – | H |
| 2ZKW | G85R / 1.9 / 2008 | ALS | A | 3.4 | A | – | H |
| | | | B | 3.4 | A | – | H |
| 2ZKX | G85R / 2.7 / 2008 | ALS | A | 3.5 | A | – | H |
| | | | B | 2.9 | A | – | H |
| | | | C | 3.4 | A | – | H |
| | | | D | 3.3 | A | – | H |
| 2WZ0 | L38V / 1.7 / 2009 | ALS | A | 3.3 | A | – | H |
| | | | F | 3.2 | A | – | H |
| 2WZ5 | L38V / 1.5 / 2009 | ALS | A | 3.2 | A | – | H |
| | | | F | 3.2 | A | – | H |
| 2WZ6 | G93A / 1.6 / 2009 | ALS | A | 3.3 | A | – | H |
| | | | F | 3.2 | A | – | H |
| 2WYT | L38V / 1.0 / 2009 | ALS | A | 3.3 | A | – | H |
| | | | F | 3.2 | A | – | H |
| 2WYZ | L38V C111s – hydroxyC / 1.7 / 2009 | ALS | A | 3.2 | A | – | H |
| | | | F | 3.2 | A | – | H |
| 3CQQ | C111S – oxyC G85R / 1.9 / 2008 | ALS | A | 3.1 | A | – | H |
| | | | B | 3.2 | A | – | H |
| 3ECU | / 1.9 / 2008 | | A | 3.0 | A | – | H |
| | | | B | 2.8 | A | – | H |
| | | | C | 3.0 | A | – | H |
| | | | D | 2.8 | A | – | H |
| 3ECV | I113T / 1.9 / 2008 | ALS | A | 3.2 | A | – | H |
| | | | B | 2.8 | A | – | H |
| | | | C | 2.9 | A | – | H |
| | | | D | 3.0 | A | – | H |
| 3ECW | T54R / 2.2 / 2008 | ALS | A | 3.1 | A | – | H |
| | | | B | 3.1 | A | – | H |
| | | | C | 3.0 | A | – | H |
| | | | D | 3.4 | A | – | H |
| 3GQF | H46R H48Q / 2.2 / 2009 | ALS | A | 3.2 | A | – | H |
| | | | B | 3.1 | A | – | H |
| | | | C | 3.2 | A | – | H |
| | | | D | 3.0 | A | – | H |
| | | | E | 3.1 | A | – | H |
| | | | F | 3.1 | A | – | H |

**Table S3 Continued**

| PDB | Mutation / resolution / year | ALS / monomer | Chain | Distance between S105-N and H110-O (Å) | A like or B like | $H_2O$ | Type of loop VI |
|---|---|---|---|---|---|---|---|
| 3GZP | G93A / 3.1 / 2009 | ALS | A | 3.1 | A | – | H |
| | | | B | 3.1 | A | – | H |
| | | | C | 3.1 | A | – | H |
| | | | D | 3.1 | A | – | H |
| 3GZQ | A4V / 1.4 / 2009 | ALS | A | 3.1 | A | – | H |
| | | | B | 3.2 | A | – | H |
| 3H2P | D124V / 1.6 / 2009 | ALS | A | 3.2 | A | – | H |
| | | | B | 3.3 | A | – | H |
| 3H2Q | H80R / 1.9 / 2009 | ALS | A | 3.1 | A | – | H |
| | | | B | 3.2 | A | – | H |
| | | | C | 3.1 | A | – | H |
| | | | D | 3.1 | A | – | H |
| 3KH3 | / 3.5 /2009 | | A | 3.2 | A | – | H |
| | | | B | 3.6 | A | – | H |
| | | | C | 3.5 | A | – | H |
| | | | D | 3.5 | A | – | H |
| | | | E | 4.6 | B | – | F |
| | | | F | 3.5 | A | – | H |
| | | | G | 3.5 | A | – | H |
| | | | H | 3.6 | A | – | H |
| | | | I | 3.5 | A | – | H |
| | | | J | 3.6 | A | – | H |
| | | | K | 3.6 | A | – | H |
| | | | L | 3.6 | A | – | H |
| 3KH4 | / 3.5 / 2009 | | A | 3.5 | A | – | H |
| | | | B | 3.6 | A | – | H |
| | | | C | 3.5 | A | – | H |
| | | | D | 3.6 | A | – | H |
| | | | E | 3.5 | A | – | H |
| | | | F | 3.5 | A | – | H |
| 3K91 | H46R H48Q C111pentaS – bridged / 1.8 /2009 | ALS | A | 3.1 | A | – | H |
| | | | B | 3.2 | A | – | H |
| 3QQD | H80R C111cysteinesulfonate (C111s – oxyC: B) / 1.7 / 2011 | ALS | A | 3.1 | A | – | H |
| | | | B | 3.2 | A | – | H |
| 1MFM | C6A C111S F50E G51E E133Q / 1.0 / 1999 | Monomer | A | 5.1 | B | + | F |
| 2XJK | C6A C111A F50E G51E / 1.5 / 2010 | Monomer | A | 5.2 | B | + | F |
| 2XJL | C6A C111A F50E G51E H46S H48S D120S / 1.6 / 2010 | Monomer | A | 5.2 | B | + | F |
| 3HFF | C6A C111A F50E G51E H63S H71S H80S D83S / 2.2 / 2009 | Monomer | A | 4.6 | B | + | F |

*C makes a dimer with a crystallographic mate
†X and Y are neither A nor B

**Table S4 H/F typing of loop VI in eukaryotic SOD1**

| PDB | Species/mutation | Type | Amino acids 109–111 |
|---|---|---|---|
| 1CB4 | Bovine | HH | EYS |
| 1CBJ | Bovine | HH | EYS |
| 1COB | Bovine | HH | EYS |
| 1E9O | Bovine | HH | EYS |
| 1E9P | Bovine | HH | EYS |
| 1E9Q | Bovine | HH | EYS |
| 1Q0E | Bovine | HH | EYS |
| 1SDA | Bovine | HH | EYS |
| 1SXA | Bovine | HH | EYS |
| 1SXB | Bovine | HH | EYS |
| 1SXC | Bovine | HH | EYS |
| 1SXN | Bovine | HH | EYS |
| 1SXS | Bovine | HH | EYS |
| 1SXZ | Bovine | HH | EYS |
| 2AEO | Bovine | HH | EYS |
| 2ZOW | Bovine | HH | EYS |
| 2SOD | Bovine | HH | EYS |
| 3SOD | Bovine | HH | EYS |
| 3HW7 | Bovine | HH | EYS |
| 2Z7U | Bovine/$H_2O_2$ | FH | EYS |
| 2Z7W | Bovine/$H_2O_2$ | FH | EYS |
| 2Z7Y | Bovine/$H_2O_2$ | FH | EYS |
| 2Z7Z | Bovine/$H_2O_2$ | FH | EYS |
| 1B4L | Yeast | FF | PTS |
| 1B4T | Yeast/H48C | FF | PTS |
| 1F18 | Yeast/G85R | FF | PTS |
| 1F1A | Yeast/H48Q | FF | PTS |
| 1F1D | Yeast/H46C | FF | PTS |
| 1F1G | Yeast | FF | PTS |
| 1JCV | Yeast | FF | PTS |
| 1SDY | Yeast | FF | PTS |
| 1YAZ | Yeast | FF | PTS |
| 1YSO | Yeast | FF | PTS |
| 2JCW | Yeast | FF | PTS |
| 1TO4 | Schistosome | HH | SHS |
| 1TO5 | Schistosome | HH | SHS |
| 3CE1 | Deep-sea yeast | FF | PHS |
| 2Q2L | Rosaceae | FF | PHS |
| 3F7L | Tubeworm | FF | PDS |
| 3F7K | Tubeworm | FF | PDS |
| 1XSO | Frog | HH | PNS |
| 1SRD | Spinach | FF | PNS |
| 3L9E | Silkworm | HH | PNS |
| 3L9Y | Silkworm | HH | PNS |
| 3KBE | Nematode | FF | PNT |
| 3KBF | Nematode | FF | PNT |
| 3GTT | Mouse | HH | EHS |
| 3MND | Pig tapeworm | HH | EHS |

**Table S5 Determination of loop VI type in each chain (eukaryotic SOD1)**
Each two chains from the first row form a dimer. *Equivalent to the distance between S105-N and H110-O in human SOD1 residue

(a) Bovine

| PDB | Mutation /resolution /year | Chain | Distance between S103-N and Y108-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 1CB4 | *Bos taurus* / – / 2.3 / 1999 | A | 3.3 | A | – | H | EYS |
| | | B | 3.5 | A | – | H | EYS |
| 1CBJ | *Bos taurus* / – / 1.7 / 1999 | A | 3.4 | A | – | H | EYS |
| | | B | 3.2 | A | – | H | EYS |
| 1COB | *Bos taurus* / – / 2.0 / 1992 | A | 3.1 | A | – | H | EYS |
| | | B | 3.1 | A | – | H | EYS |
| 1E9O | *Bos taurus* / – / 1.9 / 2000 | A | 3.4 | A | – | H | EYS |
| | | B | 3.2 | A | – | H | EYS |
| 1E9P | *Bos taurus* / – / 1.7 / 2000 | A | 3.4 | A | – | H | EYS |
| | | B | 3.2 | A | – | H | EYS |
| 1E9Q | *Bos taurus* / – / 1.8 / 2000 | A | 3.5 | A | – | H | EYS |
| | | B | 3.2 | A | – | H | EYS |
| 1Q0E | *Bos taurus* / – / 1.2 / 2003 | A | 3.2 | A | – | H | EYS |
| | | B | 3.2 | A | – | H | EYS |
| 1SDA | *Bos taurus* / – / 2.5 / 1993 | B | 2.8 | A | – | H | EYS |
| | | G | 3.2 | A | – | H | EYS |
| | | O | 3.3 | A | – | H | EYS |
| | | Y | 3.2 | A | – | H | EYS |
| 1SXA | *Bos taurus* / – / 1.9 / 1995 | A | 3.3 | A | – | H | EYS |
| | | B | 3.1 | A | – | H | EYS |
| 1SXB | *Bos taurus* / – / 2.0 / 1995 | A | 3.3 | A | – | H | EYS |
| | | B | 3.1 | A | – | H | EYS |
| 1SXC | *Bos taurus* / – / 1.9 / 1995 | A | 3.3 | A | – | H | EYS |
| | | B | 3.1 | A | – | H | EYS |
| 1SXN | *Bos taurus* / – / 1.9 / 1997 | A | 3.2 | A | – | H | EYS |
| | | B | 3.4 | A | – | H | EYS |
| 1SXS | *Bos taurus* / – / 2.0 / 1998 | A | 3.2 | A | – | H | EYS |
| | | B | 3.3 | A | – | H | EYS |
| 1SXZ | *Bos taurus* / – / 2.1 / 1998 | A | 3.2 | A | – | H | EYS |
| | | B | 3.2 | A | – | H | EYS |
| 2AEO | *Bos taurus* / – / 1.8 / 2005 | A | 3.1 | A | – | H | EYS |
| | | B | 3.3 | A | – | H | EYS |
| 2ZOW | *Bos taurus* / – / 1.5 / 2008 | A | 3.3 | A | – | H | EYS |
| | | B | 3.2 | A | – | H | EYS |
| 2SOD | *Bos taurus* / – / 2.0 / 1980 | B | 3.2 | A | – | H | EYS |
| | | G | 3.5 | X† | – | H | EYS |
| | | O | 3.0 | A | – | H | EYS |
| | | Y | 3.8 | A | – | H | EYS |
| 3HW7 | *Bos taurus* / – / 2.0 / 2009 | A | 3.3 | A | – | H | EYS |
| | | B | 3.1 | A | – | H | EYS |
| 3SOD | *Bos taurus* / C6A / 2.1 / 1990 | B | 3.5 | A | – | H | EYS |
| | | G | 3.5 | A | – | H | EYS |
| | | O | 3.5 | A | – | H | EYS |
| | | Y | 3.5 | A | – | H | EYS |
| 2Z7U | *Bos taurus* / – / 2.1 / 2007/ $H_2O_2$ | A | 3.9 | B | + | F | EYS |
| | | B | 3.0 | A | – | H | EYS |

**Table S5 Continued**

| PDB | Mutation /resolution /year | Chain | Distance between S103-N and Y108-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 2Z7W | *Bos taurus* / – / 1.8 / 2007/ $H_2O_2$ | A | 4.2 | B | – | F | EYS |
| | | B | 3.2 | A | – | H | EYS |
| 2Z7Y | *Bos taurus* / – / 1.6 / 2007/ $H_2O_2$ | A | 3.8 | B | + | F | EYS |
| | | B | 3.1 | A | – | H | EYS |
| 2Z7Z | *Bos taurus* / – / 1.9 / 2007/ $H_2O_2$ | A | 4.1 | B | + | F | EYS |
| | | B | 3.1 | A | – | H | EYS |

(b) Yeast

| PDB | Mutation /resolution /year | Chain | Distance between K105-N and T110-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 1B4L | *Saccharomyces cerevisiae* / – / 1.8 / 1998 | A# | 4.7 | B | + | F | PTS |
| 1B4T | *Saccharomyces cerevisiae* / H48C / 1.8 / 1998 | A# | 4.8 | B | + | F | PTS |
| 1F18 | *Saccharomyces cerevisiae* / G85R / 1.7 / 2000 | A# | 4.7 | B | + | F | PTS |
| 1F1A | *Saccharomyces cerevisiae* / H48Q / 1.8 / 2000 | A# | 4.7 | B | + | F | PTS |
| 1F1D | *Saccharomyces cerevisiae* / H46C / 2.1 / 2000 | A# | 4.8 | B | – | F | PTS |
| 1F1G | *Saccharomyces cerevisiae* / – / 1.4 / 2000 | A | 4.8 | B | + | F | PTS |
| | | B | 4.8 | B | + | F | PTS |
| | | C | 4.8 | B | + | F | PTS |
| | | D | 4.8 | B | + | F | PTS |
| | | E | 4.8 | B | + | F | PTS |
| | | F | 4.8 | B | + | F | PTS |
| 1JCV | *Saccharomyces cerevisiae* / – / 1.6 / 1995 | A# | 4.7 | B | + | F | PTS |
| 1SDY | *Saccharomyces cerevisiae* / – / 2.5 / 1991 | A | 4.5 | B | + | F | PTS |
| | | B | 4.8 | B | + | F | PTS |
| | | C | 4.5 | B | + | F | PTS |
| | | D | 4.8 | B | – | F | PTS |
| 1YAZ | *Saccharomyces cerevisiae* / – / 1.7 / 1998 | A# | 4.7 | B | + | F | PTS |
| 1YSO | *Saccharomyces cerevisiae* / – / 1.7 / 1995 | A# | 4.7 | B | + | F | PTS |
| 2JCW | *Saccharomyces cerevisiae* / – / 1.7 / 1998 | A# | 4.7 | B | + | F | PTS |

(c) Schistosome

| PDB | Mutation /resolution /year | Chain | Distance between S104-N and H109-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 1TO4 | *Schistosoma mansoni* / – / 1.6 / 2004 | A | 3.3 | A | – | H | SHS |

**Table S5 Continued**

| PDB | Mutation /resolution /year | Chain | Distance between S104-N and H109-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| | | B | 3.3 | A | – | H | SHS |
| | | C | 3.3 | A | – | H | SHS |
| | | D | 3.3 | A | – | H | SHS |
| 1TO5 | *Schistosoma mansoni* / – / 2.2 / 2004 | A | 3.3 | A | – | H | SHS |
| | | B | 3.2 | A | – | H | SHS |
| | | C | 3.3 | A | – | H | SHS |
| | | D | 3.1 | A | – | H | SHS |

(d) Deep – sea yeast

| PDB | Mutation /resolution /year | Chain | Distance between S109-N and H114-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 3CE1 | *Cryptococcus liquefaciens* / – / 1.2 / 2008 | A# | 3.9 | Y† | – | F | PHS |

(e) Rosaceae

| PDB | Mutation /resolution /year | Chain | Distance between P104-N and N109-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 2Q2L | *Potentilla atrosanguinea* / – / 2.4 / 2007 | A | 4.2 | B | – | F | PHS |
| | | B | 4.6 | B | – | F | PHS |

(f) Tubeworm

| PDB | Mutation /resolution /year | Chain | Distance between K103-N and T108-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 3F7L | *Alvinella pompejana* / – / 1.0 / 2008 | A# | 4.1 | B | + | F | PDS |
| 3F7K | *Alvinella pompejana* / – / 1.4 / 2008 | A# | 4.09 (4.37) | B | + | F | PDS |

(g) Frog

| PDB | Mutation /resolution /year | Chain | Distance between S103-N and N108-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 1XSO | *Xenopus laevis* / – / 1.5 / 1995 | A | 3.4 | A | – | H | PNS |
| | | B | 3.4 | A | – | H | PNS |

**Table S5 Continued**

(h) Spinach

| PDB | Mutation /resolution /year | Chain | Distance between P103-N and N108-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 1SRD | *Spinacea oleracea* / – / 2.0 / 1993 | A | 4.4 | B | – | F | PNS |
| | | B | 4.6 | B | – | F | PNS |
| | | C | 4.4 | B | – | F | PNS |
| | | D | 4.5 | B | – | F | PNS |

(i) Silkworm

| PDB | Mutation /resolution /year | Chain | Distance between S105-N and N110-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 3L9E | *Bombyx mori* / – / 2.1 / 2010 | A | 3.2 | A | – | H | PNS |
| | | B | 3.1 | A | – | H | PNS |
| | | C | 3.2 | A | – | H | PNS |
| | | D | 3.1 | A | – | H | PNS |
| 3L9Y | *Bombyx mori* / S92A H131N / 1.8 / 2010 | A | 3.2 | A | – | H | PNS |
| | | B | 3.3 | A | – | H | PNS |

(j) Nematode

| PDB | Mutation /resolution /year | Chain | Distance between T104-N and N109-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 3KBE | *Caenorhabditis elegans* / – / 1.1 / 2009 | A# | 4.8 | B | + | F | PNT |
| 3KBF | *Caenorhabditis elegans* / – / 1.3 / 2009 | A# | 5.0 | B | + | F | PNT |

(k) Mouse

| PDB | Mutation /resolution /year | Chain | Distance between S105-N and H110-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 3GTT | *Mus musculus* / – / 2.4 / 2009 | A | 3.1 | A | – | H | EHF |
| | | B | 3.7 | A | – | H | EHF |
| | | C | 3.0 | A | – | H | EHF |
| | | D | 3.2 | A | – | H | EHF |
| | | E | 3.2 | A | – | H | EHF |
| | | F | 3.0 | A | – | H | EHF |

**Table S5 Continued**

(I) Pig tapeworm

| PDB | Mutation /resolution /year | Chain | Distance between S102-N and H107-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 109–111 |
|---|---|---|---|---|---|---|---|
| 3MND | *Taenia solium* / – / 2.2 / 2010 | A | 3.2 | A | – | H | EHS |
| | | B | 3.1 | A | – | H | EHS |

#A makes a dimer with a crystallographic mate.
†X and Y are neither A nor B.

**Table S6 Determination of loop VI type in each chain (prokaryotic SOD1)**

(a)

| PDB | Mutation / resolution / year | Chain | Distance between S146-N and L153-O (Å)* | A-like or B-like | $H_2O$ | Type of loop VI | Amino acids 108 – 111 |
|---|---|---|---|---|---|---|---|
| 1S4I | *Bacillus subtilis* / – / 1.8 / 2004 (monomer) | A | 2.9 | A | – | H | KGSKLN (KG: insertion) |
| | | B | 2.8 | A | – | H | |
| | | C | 2.8 | A | – | H | |
| | | D | 2.9 | A | – | H | |
| 1XTL | *Bacillus subtilis* / P104H / 2.0 / 2004 (monomer) | A | 2.8 | A | – | H | KGSKLN (KG: insertion) |
| | | B | 2.9 | A | – | H | |
| | | C | 2.8 | A | – | H | |
| | | D | 3.0 | A | – | H | |
| 1XTM | *Bacillus subtilis* / Y88H P104H / 1.6 / 2004 (monomer) | A | 3.1 | A | – | H | KGSKLN (KG: insertion) |
| | | B | 2.9 | A | – | H | |

(b)

| PDB | Mutation / resolution / year | Chain | Amino acids |
|---|---|---|---|
| 2APS | *Actinobacillus pleuropneumoniae* / – / 1.9 / 1999 | AB (type 2 dimer) | Δ108–110 |
| 2AQM | *Brucella abortus* / – / 1.1 / 2005 | A (monomer) | Δ108–110 |
| 1ESO | *Escherichia coli* / – / 2.0 / 1997 | A (monomer) | Δ108–110 |
| 1Z9N | *Haemophilus ducreyi* / – / 1.5 / 2005 | ABCD (type 2 dimer) | Δ108–110 |
| 1Z9P | *Haemophilus ducreyi* / – / 1.5 / 2005 | AB (type 2 dimer) | Δ108–110 |
| 1PZS | *Mycobacterium tuberculosis* / – / 1.6 / 2003 | A (type 3 dimer) | Δ108–110 |

**Table S6 Continued**

| PDB | Mutation / resolution / year | Chain | Amino acids |
|---|---|---|---|
| 2AQN | *Neisseria meningitidis* / – / 1.4 / 2005 | ABC* (type 2 dimer) | Δ108–110 |
| 2AQP | *Neisseria meningitidis* / E73A / 1.3 / 2005 | AB (type 2 dimer) | Δ108–110 |
| 2AQQ | *Neisseria meningitidis* / K91E / 1.7 / 2005 | ABC* (type 2 dimer) | Δ108–110 |
| 2AQR | *Neisseria meningitidis* / K91Q / 1.8 / 2005 | ABC* (type 2 dimer) | Δ108–110 |
| 2AQS | *Neisseria meningitidis* / K91E K94E / 1.7 / 2005 | AB (type 2 dimer) | Δ108–110 |
| 2AQT | *Neisseria meningitidis* / K91Q K94Q / 1.8 / 2005 | ABC* (type 2 dimer) | Δ108–110 |
| 1BZO | *Photobacterium leiognathi* / – / 2.1 / 1998 | A# (type 1 dimer) | Δ108–110 |
| 1IB5 | *Photobacterium leiognathi* / W83Y / 2.5 / 2001 | A# (type 1 dimer) | Δ108–110 |
| 1YAI | *Photobacterium leiognathi* / – / 1.9 / 1996 | ABC* (type 1 dimer) | Δ108–110 |
| 1EQW | *Salmonella typhimurium* / – / 2.3 / 2000 | ABCD (type 2 dimer) | Δ108–110 |
| 2WWN | *Yersinia pseudotuberculosis* / – / 2.6 / 2009 | AB (type 2 dimer) | Δ108–110 |
| 2WWO | *Yersinia pseudotuberculosis* / – / 2.4 / 2009 | AB (type 2 dimer) | Δ108–110 |

*C makes a dimer with a crystallographic mate.
#A makes a dimer with a crystallographic mate.

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