

## Supplementary Results

### **Supplementary Figure S1. Interaction between HDAC6 and mutant SOD1.** (A).

FLAG-HDAC6 and the respective SOD1-3xHA (WT, A4V, G85R and G93A) were co-transfected into HEK293 cells. FLAG-HDAC6 immunoprecipitations were performed followed by western blot using the indicated antibodies. (B). Endogenous HDAC6 interacted with the A4V SOD1 mutant but not WT SOD1. The respective SOD1-3xFLAG constructs were transfected into HEK293 cells. FLAG immunoprecipitations were performed followed by western blot using the indicated antibodies.

### **Supplementary Figure S2. The MBP-tagged HDAC6 C-SMIR is able to pull down mutant SOD1.** (A).

The MBP-tagged HDAC6 L816-S859 segment and WT or A4V mutant SOD1 were co-expressed in HEK293 cells. MBP pulldowns were performed followed by SDS-PAGE and Sypro Ruby staining. The band indicated by the asterisk in the A4V SOD1 lane represented the only apparent difference between the WT and A4V SOD1 lanes. (B) The band indicated by the asterisk was identified as SOD1 using proteomics and the three SOD1 peptides identified by mass spectrometry are shown.

Analysis of the corresponding area in the WT lane did not identify any SOD1 fragment.

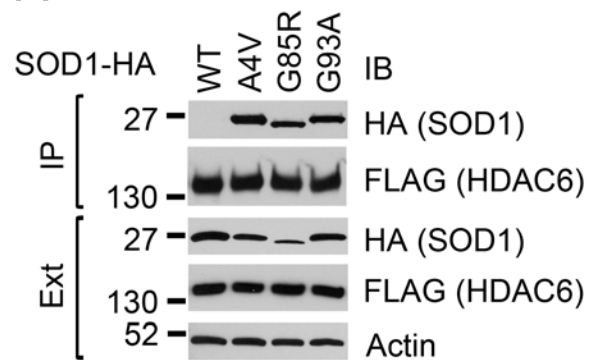
### **Supplementary Figure S3. The homology model of the first deacetylase domain of**

**HDAC6.** The SMIR-like motif (H279-K287) is highlighted in green. The active center H215 residue is highlighted in red. The structure was displayed with Geneious Pro 5.5.7.

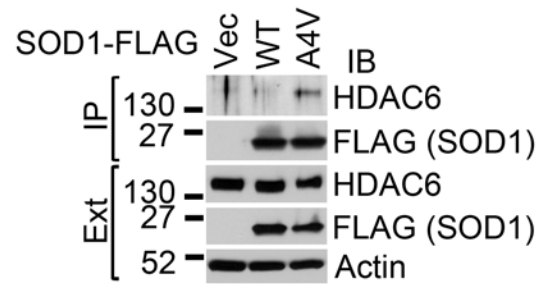
**Supplementary Figure S4. Confocal microscopy of cortactin, F-actin and mutant SOD1 inclusions.** NSC34 cells were transfected with GFP-tagged A4V SOD1, fixed and either immunostained with anti-cortactin antibody to visualize cortactin (top two panels) or stained with phalloidin to visualize F-actin (bottom two panels). Neither cortactin nor F-actin showed appreciable accumulation in the A4V SOD1 inclusions. All scale bars stand for 10 $\mu$ m.

# Supplementary figure 1

## A

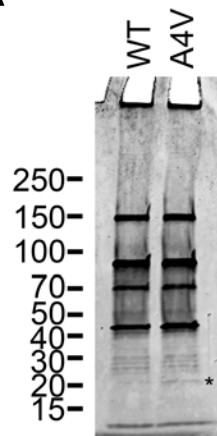


## B



## Supplementary figure 2

A

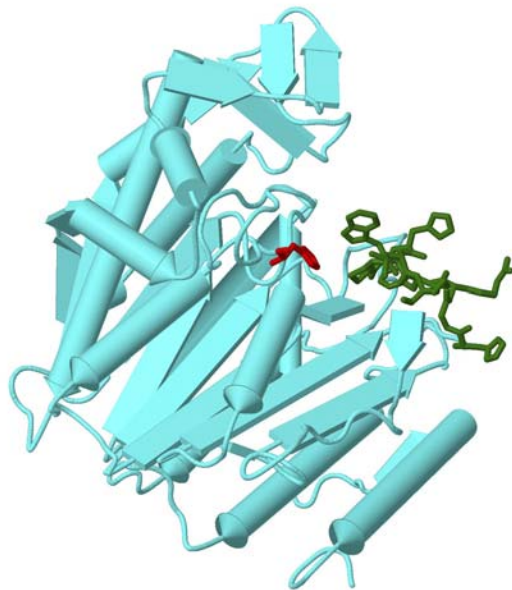


B

SODC\_HUMAN: 54% coverage, Mascot score: 219.82

Identified peptide		Ion score
80 HVGDLGNVTADKDGADVSIEDSVISLSGDHCIIGR	115	103
10 GDGPVQGIINFEQK	23	56
37 GLTEGLHGFHVHEFGDNTAGCTSAGPHNPLSR	69	17

Supplementary figure 3



Supplementary figure 4

