

Identification of property outliers among ALS-associated SOD1 mutations

COMMON EFFECT ON SURFACE HYDROGEN BONDS

SUPPLEMENTARY MATERIAL

Table S1. Urea and thermal denaturation data used to plot $\Delta\Delta G^{\text{norm}}$ versus disease progression (ST) (Fig. 5). The stability data was normalized prior to comparison. ST is the mean survival time after first diagnosis and n is the number of patients in the data set.

Genotype	$\Delta\Delta G_{\text{D-N}}$ (kcal/mol) (1)	$\Delta\Delta G^{\text{norm}}$	ΔT_m (°K) (2)	ΔT_m (°K) (3)	ΔT_m (°K) (4)	ΔT_m (°K) (5)	ΔT_m (°K) (6)	ST (years)	n
A4V	-4.31	0.85	-12.01	-12.4	-8.9	-	-	1.2	205
V7E	-	0.52	-6.58	-	-	-	-	5.7	3
G37R	-	0.55	-7.13	-	-	-	-	17.0	27
L38V	-3.24	0.71	-9.57	-	-	-	-	2.4	22
G41D	-3.47	0.80	-	-	-	-	-	14.1	15
G41S	-4.47	0.96	-	-	-	-	-	1.0	16
H43R	-4.05	0.91	-	-	-	-	-	1.8	12
H46R	0.48	0.03	3.64	-	-	-	-	17.6	49
H48Q	-	0.45	-5.18	-	-	-	-	1.2	4
D76V	-0.06	0.15	-	-	-	-	-	18.8	4
D76Y	-0.09	0.16	-	-	-	-	-	9.0	2
L84V	-2.65	0.69	-10.73	-	-	-	-	3.2	10
G85R	-0.92	0.35	-3.63	-	-	-	-3.8	6.0	11
N86D	-0.94	0.32	-	-	-	-	-	-	0
N86K	-1.41	0.41	-	-	-	-	-	1.7	7
N86S	-0.45	0.28	-2.97	-	-	-	-	6.8	4
D90A	-0.65	0.26	-	-	-	-	-	8.0	15
D90V	-1.85	0.49	-	-	-	-	-	2.7	3
G93A	-2.97	0.70	-9.5	-10.5	-10.5	-	-	3.1	16
G93D	-	0.84	-	-	-	-12.8	-	8.8	7
G93R	-	0.60	-8.23	-	-3.3	-10.1	-10.1	5.3	4
G93S	-	0.61	-	-	-	-8.3	-	8.0	11
G93V	-	1.00	-	-	-	-15.9	-	6.0	12
E100G	-2.22	0.52	-12.56	-	-7.8	-	-7.7	4.7	50
E100K	-	0.30	-2.18	-	-	-	-	10.0	1
D101G	-1.39	0.40	-	-	-	-	-	1.9	3

D101N	0.75	0.10	-0.09	-	-	-	-	2.3	17
I104F	-1.24	0.37	-	-	-	-	-	21.3	3
S105L	-2.60	0.63	-	-	-	-	-	3.5	7
L106V	-3.62	0.82	-	-	-	-	-	1.9	6
I113T	-2.48	0.68	-9.79	-	-	-	-12.2	4.3	38
G114A	-3.27	0.76	-	-	-	-	-	2.7	2
D124V	-	0.01	3.42	-	-	-	-	-	0
D125H	-	0.21	-0.53	-	-	-	-	1.8	2
S134N	-	0.23	-0.9	-	-	-	-	1.2	3
N139D	0.36	0.07	-	-	-	-	-	-	-
N139K	-0.24	0.24	-2.12	-	-	-	-	-	-
L144F	-1.89	0.46	-4.29	-	-	-	-	11.8	15
L144S	-1.07	0.36	-3.65	-	-	-	-	12.3	2
V148G	-4.56	1.00	-	-	-	-	-	2.1	11

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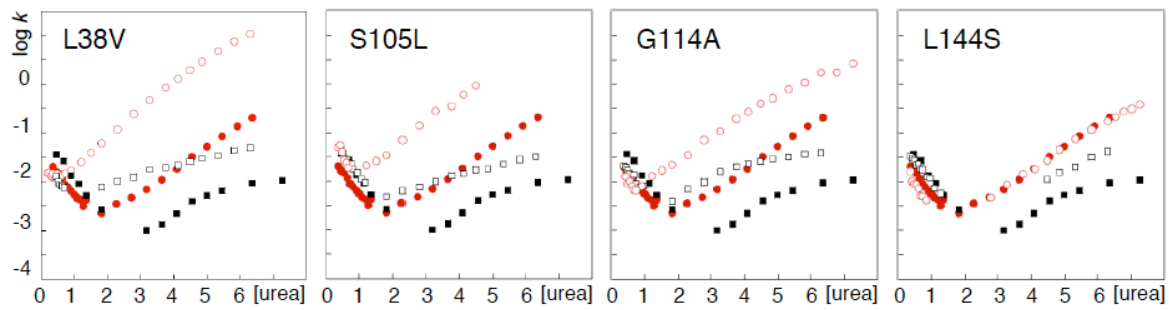
Table S2. The reference set of 75 confirmed ALS associated SOD1 mutations with fast and slow disease progression as listed in (1). *n* is the number of reported patients for each mutation. The mutants measured in this study are in bold letters.

Mutant	Fast <5 years	<i>n</i>	Slow >5years	<i>n</i>
A4S	>3	0		
A4T	1,5	21		
A4V	1,2	205		
C6F	1	1		
C6G	0,2	2		
V7E ¹			5,7	3
L8Q	1,6	5		
G10V	1,1	5		
G12A	>4	0		
G12R ²			5,5	2
V14G	1,7	1		
N19S	2,1	3		
F20C	2	7		
E21G ²			17,2	5
G37R ²			17	27
L38R ²	>2	0		
L38V	2,4	22		
G41D ¹			14,1	15
G41S	1	16		
H43R ²	1,8	12		
F45C			>6	0
H46R ²			17,6	49
H48Q	1,2	4		
N65S			>14	0
G72C	4,4	1		
G72S	3,3	2		
D76V ²			18,8	4
D76Y ²			11	2
L84F			5,8	18
L84V	3,2	10		
G85R ²			6	11
N86D ¹	>4	0*		
N86K ²	1,7	7		
N86S			6,8	4
A89V	>3,8	0		
D90A ²			8	15
D90V ²	2,7	3		
G93A	3,1	16		
G93C			12,1	27
G93D ¹			8,8	7
G93R ²			5,3	4
G93S			8	11
G93V			6	2
E100G ²	4,7	50		
E100K ²			10	1
D101G ²	1,9	3		
D101H ²	1,2	2		
D101N ²	2,3	17		
D101Y ²	0,9	1		

I104F			21,3	3
S105L	3,5	7		
L106V	1,9	6		
G108V	4	2		
I112M	3	9		
I112T	0,9	2		
I113F			>6	0
I113T	4,3	38		
G114A	2,7	2		
R115G ¹	2,5	2		
D124V ²	>2	0		
D125H ²	1,8	2		
L126S			8	5
L126X	3,8	14		
S134N	1,2	3		
N139H	3	6		
A140G			10	1
G141E ¹	3,5	2		
L144F			11,8	15
L144S			12,3	2
A145T	1,6	2		
C146R ²	2,8	2		
V148G	2,1	11		
V148I	1,7	5		
I149T	2,7	15		
I151T			20	1

¹Increase of the net repulsive charge (blue in plot). ²Decrease of the net repulsive charge (red in plot).
^{*}Patient still alive and displays a slow disease progression (P.M. Andersen, unpublished data).

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Supplementary Fig. 1. Chevron plots of L38V, S105L, G114A and L144S.

$\text{apoSOD1}_{\text{mono}}^{\text{pWT}}$ $\text{apoSOD1}_{\text{mono}}^{\text{pWT}}$ (●), $\text{apoSOD1}_{\text{mono}}^{\text{mut}}$ $\text{apoSOD1}_{\text{mono}}^{\text{mut}}$ (○), $\text{apoSOD1}_{\text{dimer}}^{\text{pWT}}$ $\text{apoSOD1}_{\text{dimer}}^{\text{pWT}}$ (■) and $\text{apoSOD1}_{\text{dimer}}^{\text{mut}}$ $\text{apoSOD1}_{\text{dimer}}^{\text{mut}}$ (□).