

Supporting Information.

Genotype-Property Patient-Phenotype Relations Suggest that Proteome Exhaustion Causes Amyotrophic Lateral Sclerosis

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TABLE S1. 150 ALS-associated SOD1 missense mutations (substitutions) and associated experimentally determined properties: Patient data collected from the ALSOD data base, Wang et al. 2008, with additional references in rightmost column. Data in columns are from left: Site position; type (beta-sheet, B; metal-region, M; disulfide/cystine region, D); wild-type and mutant residue, WT/MUT; free energy change for apomonomer and holodimer in kcal/mol, $\Delta\Delta G(m)$ and $\Delta\Delta G(d)$; number of patient data points, n; time of onset, t(o); survival time, t(s); age of death, t(d) = t(o)+t(s).

SITE	TYPE	WT	MUT	$\Delta\Delta G(m)$	$\Delta\Delta G(d)$	n	t(o)	t(s)	t(d)	Reference
3	B	K	E			8	54.2	8.4	63.0	1
4	B	A	S			1	34.0	3.0		2
		A	T			26	45.3	1.5	46.8	3
		A	V	4.31		212	47.7	1.2	48.9	4
		A	F			2	46.0			5
5	B	V	L			1	36	3.8	39.8	6
6	B	C	F			5	50.4	1.0	51.4	7
		C	G			6	49.0	0.2	49.2	8
		C	S			8	50.9	6.7	57.6	9
		C	W			4	67.0	1.9	68.9	7
7	B	V	G							
		V	E			4	48.5	5.7	54.2	10
8	B	L	Q			12	52.3	1.6	53.9	11
		L	V			1	28.0			12
10	B	G	V			5	31.2	1.1	32.3	13
		G	R			1	68.0			14
11	B	D	Y			1	40.0			15
		D	A							16
12	B	G	R			3	60.3	5.5	65.8	17,18
		G	A			1	63.0			
14	B	V	G			2	40.0	1.7	41.7	19
		V	M							20
16	B	G	S			1	18.0			21
		G	A							16
19	B	N	S			1	32.0			22

20	B	F	C			8	51.1	2.0	53.1	12
21	B	E	G			15	51.8	17.2	69.0	23
		E	K							24
22	B	Q	L							12
		Q	R			1	38.0			25
29	B	V	A							16
31	B	V	A			1	49	>11	>60	26
37	B	G	R			27	36.9	17.0	53.9	27
		G	V				62.0			28
38	B	L	R			3	42.0			29
		L	V	2.25	3.24	31	41.1	2.4	43.5	30
41	B	G	D		3.47	17	45.2	14.1	59.3	31
		G	S		4.47	25	48.4	1.0	49.4	32
43	B	H	R		4.05	14	49.3	1.8	51.1	33
45	B	F	C			3	58.0	6.0	64.0	34
46	M	H	R		-0.48	70	45.6	17.6	63.2	35
		H	D							16
47	B	V	F			1	36.0			36
		V	A							37
48	M	H	R							12
		H	Q			5	48.4	1.2	49.6	38
49	B	E	K							29
54	D	T	R							12
57	D	C	R							16
59	D	S	I							12
61	M	G	R							39
64	M	F	L							40
65	M	N	S			4	40.0			41

66	M	P	S							42
		P	A							16
		P	R							37
67	M	L	P			2	56.0			43
		L	R							29
72	M	G	S			4	37.7	3.3	41.0	44
		G	C			1	71.0	4.4		45
76	M	D	V	0.2	0.06	5	46.0	18.8	64.8	46
		D	Y	0.21	0.09	3	55.0	17.0	72.0	19
80	M	H	A							47
		H	R			1	24.0			16
83		D	G							16
84	M	L	F			26	43.3	5.8	49.1	48
		L	V		2.65	12	46.8	3.2	50.0	20
85	M	G	R	1.20	0.90	11	55.5	6.0	61.5	49
		G	S			2	37.5	1.5		50
86	B	N	D	-0.05	0.94					16
		N	S	-0.07	0.45	5	40.8	6.8	47.6	51
		N	K	0.66	1.41	7	58.2	1.7	59.9	52
		N	I							16
87	B	V	A							12
		V	M							16
89	B	A	T					>3.8		12
		A	V			5	55.6	3.8	59.4	53
90	B	D	A	0.66	0.65	28	48.6	8.0	56.6	54
		D	V	1.41	1.85	4	46.0	2.7	48.7	55
		D	N							56
93		G	A		2.98	15	46.0	3.1	49.1	57
		G	C			30	45.8	12.1	57.9	58
		G	D		4.5	10	39.3	8.8	48.1	59
		G	R		3	4	35.0	5.3	40.3	38
		G	S		3.1	15	51.6	8.0	59.6	60
		G	V		5.4	4	43.6	6.0	49.6	61
94		V	A							62

95	B	A	G							63
		A	T							41
		A	V							16
96	B	D	N							64
		D	V							
97	B	V	M							12
		V	L							
99	B	I	V			1	60.0			
100	B	E	G	2.40	2.22	54	47.3	4.7	52.0	31
		E	K			1	35.0	17.0		65
101	B	D	G	0.72	1.39	2	41.0	1.9		66
		D	H			2	52.0	1.2		67
		D	N	-0.80	-0.75	17	40.1	2.3	42.4	68
		D	Y			2	46.5	0.9		69
104	B	I	F		1.24	7	36.9	21.3	58.2	70
105	B	S	L	1.81	2.60	8	48.7	3.5	52.2	71
106	B	L	V		3.62	17	45.1	1.9	47.0	31
		L	F			6	48.8	1.9	50.7	72
108	B	G	V			5	53.6	4.0	57.6	73
109	B	D	Y			1	51.0	6.0		
111	B	C	Y							74
112	B	I	M			28	48.5	2.2	50.7	27
		I	T			3	45.3	0.9	46.2	38,59
113	B	I	F			3	58.7	6.0	64.7	75
		I	T		2.48	53	54.1	6.8	60.9	34
114	B	G	A	2.33	3.27	2	37.5	2.7		76
115	B	R	G			3	60.0	2.5	62.5	77
		R	C			1	74.0	0.9		78
116	B	T	R							
117	B	L	V							

118	B	V	L			1	38.0			12
		V	M							
120		H	L							62
124	M	D	G							12
		D	V			1	42.0	>2		61
125	M	D	H			5	60.2	1.8	62.0	38
126	B	L	S			8	52.3	8.0	60.3	79
127	B	G	R			1	60.0			80
134	M	S	N			5	53.8	1.2	55.0	81
		S	T							82
137	B	T	R			2	42.5			
		T	A			3	60.0			83
138	B	G	E			1	41.0			
139	B	N	H			9	57.9	3.0	60.9	84
		N	K	0.06	0.24			vitro		85
		N	D	0.01	-0.36					
		N	L							85
140	B	A	G			5	68.2	10.0	78.2	86
141	B	G	E			1	43.0	3.5		67
		G	A							62
144	B	L	F		1.89	26	52.4	11.8	64.2	87
		L	S	0.2	1.07	5	37.0	12.3	49.3	88
145	B	A	G			3	36.7			
		A	T			2	48.0	1.6		88
146	D	C	R			2	55.5	2.8		65
147	B	G	R							12
		G	S			1	64.0			
		G	D							
148	B	V	G		4.56	11	43.1	2.1	45.2	89
		V	I	-0.4		4	28.0	1.5	29.5	90

149	B	I	T			14	37.6	2.7	40.3	85,91
151	B	I	S							12
		I	T			2	48.5	20.0		

Stabilities ($\Delta\Delta G$) collected from:

Red numbers: Byström et al., J. Biol. Chem. 2010, 285, 19544.

Blue numbers: Vassall et al., Proc. Natl. Acad. Sci. USA 2011, 108, 2210.

Green numbers: Lindberg et al. Proc. Natl. Acad. Sci. USA 2005, 102, 9754.

Patient data collected from:

Black numbers: References in right column.

Red numbers: Wang et al. PLOS Biol. 2008, 6, e170.

Purple numbers: ALSOD data base. <http://alsod.iop.kcl.ac.uk/>

Blue numbers: Non-redundant combination of Wang et al. and ALSOD data base.

Table S2. Computed data for 150 SOD1-mutations in Table S1: SA: Solvent accessibility computed using PoPMuSiC; $\Delta\Delta G(\text{POP})$: stability change from PoPMuSiC2.1; $\Delta\Delta G(\text{Imut})$: stability change from IMutant2.0; dQ: Change in absolute net charge; dHydro: change in hydrophobicity (Rose, G.D. Science 229: 834, 1985); beta: ratio of beta propensities of mutant and WT residues; alpha: ratio of alpha propensities of mutant and WT residues; and corresponding natural logarithms of these ratios.

SITE	WT	MUT	SA	$\Delta\Delta G(\text{POP})$	$\Delta\Delta G(\text{Imut})$	dQ	dHydro	beta	alpha	LN(beta)	LN(alpha)
3	K	E	35.9	0.76	0.74	2	-0.14	0.87	1.17	-0.14	0.16
4	A	S	1.7	1.02	1.31	0	-1.63	1.14	0.51	0.14	-0.68
4	A	T	1.7	0.73	1.78	0	-1.39	1.57	0.53	0.45	-0.64
4	A	V	1.7	-0.43	1.08	0	0.91	2.47	0.63	0.91	-0.46
4	A	F	1.7	-0.14	1.16	0	1.88	1.93	0.66	0.66	-0.41
5	V	L	2.1	1.46	0.93	0	0.52	0.61	1.43	-0.49	0.36
6	C	F	1.0	0.15	1.43	0	2.02	1.20	1.32	0.18	0.28
6	C	G	1.0	2.42	3.19	0	-0.25	0.52	0.62	-0.65	-0.48
6	C	S	1.0	2.25	1.85	0	-1.49	0.71	1.01	-0.35	0.01
6	C	W	1.0	0.16	1.49	0	1.88	0.98	1.57	-0.02	0.45
7	V	G	17.6	2.09	3.70	0	-1.30	0.34	0.49	-1.08	-0.70
7	V	E	17.6	1.86	1.83	1	-4.21	0.38	1.48	-0.97	0.39
8	L	Q	0.3	3.36	2.18	0	-3.12	0.69	1.00	-0.38	0.00
8	L	V	0.3	1.33	1.27	0	-0.52	1.63	0.70	0.49	-0.36
10	G	V	33.5	0.01	0.39	0	1.30	2.94	2.02	1.08	0.70
10	G	R	33.5	0.88	0.80	-1	-3.95	1.45	2.61	0.37	0.96
11	D	Y	99.5	0.32	0.07	-1	5.28	2.94	1.06	1.08	0.06
11	D	A	99.5	-0.03	-0.10	-1	4.20	1.52	1.72	0.42	0.54
12	G	R	69.2	0.72	1.04	-1	-3.95	1.45	2.61	0.37	0.96
12	G	A	69.2	0.18	1.33	0	0.39	1.19	3.22	0.17	1.17
14	V	G	3.7	2.81	3.42	0	-1.30	0.34	0.49	-1.08	-0.70
14	V	M	3.7	0.97	1.11	0	-0.34	0.59	1.42	-0.54	0.35
16	G	S	12.5	0.67	0.95	0	-1.24	1.36	1.63	0.31	0.49
16	G	A	12.5	0.34	0.36	0	0.39	1.19	3.22	0.17	1.17
19	N	S	28.4	0.17	0.71	0	0.67	1.36	1.03	0.31	0.03
20	F	C	0.7	2.60	1.41	0	-2.02	0.84	0.76	-0.18	-0.28
21	E	G	25.8	1.73	1.51	-1	2.91	0.90	0.33	-0.10	-1.10
21	E	K	25.8	0.71	2.33	-2	0.14	1.15	0.86	0.14	-0.16
22	Q	L	3.4	-0.15	0.28	0	3.12	1.46	1.00	0.38	0.00
22	Q	R	3.4	0.74	1.76	-1	-2.65	1.18	0.90	0.16	-0.10
29	V	A	0.0	2.57	1.37	0	-0.91	0.40	1.59	-0.91	0.46
31	V	A	0.3	3.54	2.05	0	-0.91	0.40	1.59	-0.91	0.46
37	G	R	46.0	1.65	1.38	-1	-3.95	1.45	2.61	0.37	0.96
37	G	V	46.0	1.85	1.35	0	1.30	2.94	2.02	1.08	0.70
38	L	R	5.2	1.87	2.52	-1	-5.77	0.81	0.90	-0.21	-0.10

38	L	V	5.2	1.35	0.67	0	-0.52	1.63	0.70	0.49	-0.36
41	G	D	26.1	2.49	2.18	1	-3.81	0.78	1.87	-0.25	0.63
41	G	S	26.1	2.47	1.65	0	-1.24	1.36	1.63	0.31	0.49
43	H	R	0.7	1.42	1.33	-1	-3.31	0.94	1.35	-0.06	0.30
45	F	C	0.0	2.69	0.89	0	-2.02	0.84	0.76	-0.18	-0.28
46	H	R	0.0	1.04	0.74	-1	-3.31	0.94	1.35	-0.06	0.30
46	H	D	0.0	2.94	1.21	1	-3.17	0.51	0.97	-0.68	-0.03
47	V	F	0.0	0.65	1.22	0	0.97	0.78	1.05	-0.25	0.05
47	V	A	0.0	2.92	1.19	0	-0.91	0.40	1.59	-0.91	0.46
48	H	R	0.0	1.84	0.74	-1	-3.31	0.94	1.35	-0.06	0.30
48	H	Q	0.0	2.08	0.68	0	-0.66	0.80	1.49	-0.23	0.40
49	E	K	36.8	0.27	0.96	-2	0.14	1.15	0.86	0.14	-0.16
54	T	R	37.1	0.60	0.11	-1	-2.95	0.78	1.54	-0.25	0.43
57	C	R	11.6	2.48	1.11	-1	-4.20	0.76	1.62	-0.28	0.48
59	S	I	18.1	1.02	0.15	0	3.06	1.99	1.41	0.69	0.35
61	G	R	19.9	1.74	0.60	-1	-3.95	1.45	2.61	0.37	0.96
64	F	L	2.7	1.57	2.03	0	-0.45	0.78	1.36	-0.25	0.31
65	N	S	27.5	1.16	0.28	0	0.67	1.36	1.03	0.31	0.03
66	P	S	35.8	-0.15	1.36	0	-2.23	2.18	1.70	0.78	0.53
66	P	A	35.8	-0.08	1.72	0	-0.60	1.90	3.36	0.64	1.21
66	P	R	35.8	0.04	1.14	-1	-4.94	2.33	2.73	0.84	1.00
67	L	P	47.9	1.36	1.01	0	-0.83	0.35	0.33	-1.06	-1.11
67	L	R	47.9	0.18	0.71	-1	-5.77	0.81	0.90	-0.21	-0.10
72	G	S	1.7	0.70	0.57	0	-1.24	1.36	1.63	0.31	0.49
72	G	C	1.7	-0.18	1.32	0	0.25	1.92	1.61	0.65	0.48
76	D	V	35.0	0.43	0.31	-1	5.11	3.76	1.08	1.32	0.08
76	D	Y	35.0	0.70	-0.29	-1	5.28	2.94	1.06	1.08	0.06
80	H	A	6.4	2.86	0.53	0	1.03	0.77	1.66	-0.26	0.51
80	H	R	6.4	1.57	0.48	-1	-3.31	0.94	1.35	-0.06	0.30
83	D	G	0.0	1.49	1.19	-1	3.81	1.28	0.53	0.25	-0.63
84	L	F	1.8	1.14	0.81	0	0.45	1.28	0.74	0.25	-0.31
84	L	V	1.8	1.50	0.75	0	-0.52	1.63	0.70	0.49	-0.36
85	G	R	2.8	2.26	0.70	-1	-3.95	1.45	2.61	0.37	0.96
85	G	S	2.8	2.59	0.65	0	-1.24	1.36	1.63	0.31	0.49
86	N	D	22.7	1.19	1.70	1	-1.90	0.78	1.18	-0.25	0.16
86	N	S	22.7	0.81	0.38	0	0.67	1.36	1.03	0.31	0.03
86	N	K	22.7	0.89	0.87	-1	-0.86	1.28	1.62	0.25	0.48
86	N	I	22.7	-0.08	-0.58	0	3.73	2.70	1.45	0.99	0.37
87	V	A	4.6	2.38	1.82	0	-0.91	0.40	1.59	-0.91	0.46
87	V	M	4.6	1.34	1.13	0	-0.34	0.59	1.42	-0.54	0.35
89	A	T	1.7	0.38	1.66	0	-1.39	1.57	0.53	0.45	-0.64
89	A	V	1.7	-0.44	0.40	0	0.91	2.47	0.63	0.91	-0.46
90	D	A	46.9	0.86	0.58	-1	4.20	0.66	0.58	-0.42	-0.54
90	D	V	46.9	0.72	0.47	-1	5.11	3.76	1.08	1.32	0.08
90	D	N	46.9	0.24	0.22	-1	1.90	1.28	0.85	0.25	-0.16
93	G	A	5.7	2.80	0.48	0	0.39	1.19	3.22	0.17	1.17

93	G	C	5.7	1.56	1.25	0	0.25	1.92	1.61	0.65	0.48
93	G	D	5.7	2.27	1.92	1	-3.81	0.78	1.87	-0.25	0.63
93	G	R	5.7	1.94	1.27	-1	-3.95	1.45	2.61	0.37	0.96
93	G	S	5.7	2.20	1.62	0	-1.24	1.36	1.63	0.31	0.49
93	G	V	5.7	2.78	0.93	0	1.30	2.94	2.02	1.08	0.70
94	V	A	25.8	1.56	0.34	0	-0.91	0.40	1.59	-0.91	0.46
95	A	G	0.0	1.89	2.31	0	-0.39	0.84	0.31	-0.17	-1.17
95	A	T	0.0	1.18	1.75	0	-1.39	1.57	0.53	0.45	-0.64
95	A	V	0.0	0.60	0.42	0	0.91	2.47	0.63	0.91	-0.46
96	D	N	83.5	-0.21	1.02	-1	1.90	1.28	0.85	0.25	-0.16
96	D	V	83.5	-0.61	0.92	-1	5.11	3.76	1.08	1.32	0.08
97	V	M	4.9	1.36	1.32	0	-0.34	0.59	1.42	-0.54	0.35
97	V	L	4.9	1.14	1.27	0	0.52	0.61	1.43	-0.49	0.36
99	I	V	18.0	1.10	-0.08	0	-0.52	1.09	0.88	0.08	-0.13
100	E	G	72.2	0.73	1.26	-1	2.91	0.90	0.33	-0.10	-1.10
100	E	K	72.2	0.02	1.82	-2	0.14	1.15	0.86	0.14	-0.16
101	D	G	6.9	1.53	2.79	-1	3.81	1.28	0.53	0.25	-0.63
101	D	H	6.9	0.54	1.77	-1	3.17	1.98	1.03	0.68	0.03
101	D	N	6.9	0.63	1.86	-1	1.90	1.28	0.85	0.25	-0.16
101	D	Y	6.9	0.12	0.60	-1	5.28	2.94	1.06	1.08	0.06
104	I	F	0.8	0.79	1.01	0	0.45	0.85	0.92	-0.16	-0.08
105	S	L	8.1	1.00	0.98	0	3.06	1.32	1.77	0.28	0.57
106	L	V	6.0	1.00	1.19	0	-0.52	1.63	0.70	0.49	-0.36
106	L	F	6.0	0.69	1.24	0	0.45	1.28	0.74	0.25	-0.31
108	G	V	71.5	1.34	1.32	0	1.30	2.94	2.02	1.08	0.70
109	D	Y	81.9	0.68	0.89	-1	5.28	2.94	1.06	1.08	0.06
111	C	Y	17.5	1.27	0.60	0	1.22	1.20	1.23	0.18	0.21
112	I	M	0.0	1.08	1.08	0	-0.86	0.64	1.25	-0.45	0.22
112	I	T	0.0	1.31	2.34	0	-2.82	0.69	0.74	-0.37	-0.31
113	I	F	11.1	0.93	1.12	0	0.45	0.85	0.92	-0.16	-0.08
113	I	T	11.1	1.53	2.23	0	-2.82	0.69	0.74	-0.37	-0.31
114	G	A	0.0	2.22	0.34	0	0.39	1.19	3.22	0.17	1.17
115	R	G	15.0	1.98	1.59	1	3.95	0.69	0.38	-0.37	-0.96
115	R	C	15.0	0.54	0.75	1	4.20	1.32	0.62	0.28	-0.48
116	T	R	1.0	1.60	1.52	-1	-2.95	0.78	1.54	-0.25	0.43
117	L	V	0.0	1.54	1.12	0	-0.52	1.63	0.70	0.49	-0.36
118	V	L	0.0	1.19	0.15	0	0.52	0.61	1.43	-0.49	0.36
118	V	M	0.0	1.11	0.85	0	-0.34	0.59	1.42	-0.54	0.35
120	H	L	3.2	0.98	-0.60	0	2.46	1.16	1.49	0.15	0.40
124	D	G	3.5	1.10	0.74	-1	3.81	1.28	0.53	0.25	-0.63
124	D	V	3.5	0.32	0.07	-1	5.11	3.76	1.08	1.32	0.08
125	D	H	28.7	0.42	-0.16	-1	3.17	1.98	1.03	0.68	0.03
126	L	S	30.8	0.27	0.71	0	-3.06	0.76	0.56	-0.28	-0.57
127	G	R	11.9	2.13	0.90	-1	-3.95	1.45	2.61	0.37	0.96
134	S	N	0.4	1.51	-0.10	0	-0.67	0.74	0.97	-0.31	-0.03
134	S	T	0.4	1.00	0.22	0	0.24	1.37	1.04	0.31	0.04

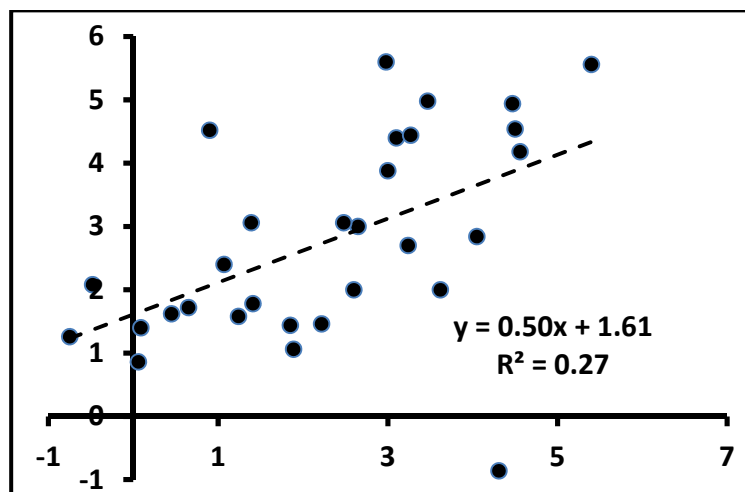
137	T	R	41.0	1.15	-0.06	-1	-2.95	0.78	1.54	-0.25	0.43
137	T	A	41.0	0.87	0.22	0	1.39	0.64	1.90	-0.45	0.64
138	G	E	0.0	3.50	1.00	1	-2.91	1.11	3.00	0.10	1.10
139	N	H	30.8	0.73	0.50	0	1.27	1.55	1.22	0.44	0.20
139	N	K	30.8	1.42	0.26	-1	-0.86	1.28	1.62	0.25	0.48
139	N	D	30.8	1.00	0.75	1	-1.90	0.78	1.18	-0.25	0.16
139	N	L	30.8	0.96	-0.93	0	3.73	1.80	1.82	0.59	0.60
140	A	G	0.4	1.51	1.68	0	-0.39	0.84	0.31	-0.17	-1.17
141	G	E	40.9	2.02	0.84	1	-2.91	1.11	3.00	0.10	1.10
141	G	A	40.9	1.76	1.19	0	0.39	1.19	3.22	0.17	1.17
144	L	F	24.1	0.53	0.75	0	0.45	1.28	0.74	0.25	-0.31
144	L	S	24.1	1.20	1.15	0	-3.06	0.76	0.56	-0.28	-0.57
145	A	G	0.0	0.87	2.25	0	-0.39	0.84	0.31	-0.17	-1.17
145	A	T	0.0	0.62	1.04	0	-1.39	0.80	0.53	-0.22	-0.64
146	C	R	3.8	2.54	1.59	-1	-4.20	0.76	1.62	-0.28	0.48
147	G	R	11.9	0.76	1.05	-1	-3.95	1.45	2.61	0.37	0.96
147	G	S	11.9	0.52	0.65	0	-1.24	1.36	1.63	0.31	0.49
147	G	D	11.9	1.34	1.72	1	-3.81	0.78	1.87	-0.25	0.63
148	V	G	13.7	2.09	3.15	0	-1.30	0.34	0.49	-1.08	-0.70
148	V	I	13.7	0.56	0.98	0	0.52	0.92	1.14	-0.08	0.13
149	I	T	0.0	2.60	2.60	0	-2.82	0.69	0.74	-0.37	-0.31
151	I	S	21.6	1.37	1.92	0	-3.06	0.50	0.71	-0.69	-0.35
151	I	T	21.6	0.99	2.10	0	-2.82	0.69	0.74	-0.37	-0.31

Table S3. 30 variants with experimentally known dimer stabilities (kcal/mol) correlated against t(o), t(s), and t(d) (years). Change in net charge is given in the last column. These data are shown in the main paper, Figure 2. Color codes follow literature collections from Table S1.

SITE	TYPE	WT	MUT	$\Delta\Delta G(d)$	n	t(o)	t(s)	t(d)	ΔQ
4		A	V	4.31	212	47.7	1.2	48.9	0
38		L	V	3.24	31	41.1	2.4	43.5	0
41	B	G	D	3.47	17	45.2	14.1	59.3	-1
41		G	S	4.47	25	48.4	1.0	49.4	0
43	B	H	R	4.05	14	49.3	1.8	51.1	1
46	M	H	R	-0.48	70	45.6	17.6	63.2	1
76	M	D	V	0.06	5	46.0	18.8	64.8	1
76		D	Y	0.09	3	55.0	17	72.0	1
84		L	V	2.65	12	46.8	3.2	50.0	0
85	M	G	R	0.9	11	55.5	6.0	61.5	1
86		N	S	0.45	5	40.8	6.8	47.6	0
86		N	K	1.41	7	58.2	1.7	59.9	1
90	B	D	A	0.65	28	48.6	8.0	56.6	1
90		D	V	1.85	4	46.0	2.7	48.7	1
93		G	A	2.98	15	46.0	3.1	49.1	0
93		G	D	4.5	10	39.3	8.8	48.1	-1
93		G	R	3	4	35.0	5.3	40.3	1
93		G	S	3.1	15	51.6	8.0	59.6	0
93		G	V	5.4	4	43.6	6.0	49.6	0
100	B	E	G	2.22	54	47.3	4.7	52	1
101	B	D	G	1.39	2	41.0	1.9	42.9	1
101		D	N	-0.75	17	40.1	2.3	42.4	1
104	B	I	F	1.24	7	36.9	21.3	58.2	0
105	B	S	L	2.6	8	48.7	3.5	52.2	0
106	B	L	V	3.62	17	45.1	1.9	47	0
113		I	T	2.48	53	54.1	6.8	60.9	0
114	B	G	A	3.27	2	37.5	2.7	40.2	0
144	B	L	F	1.89	26	52.4	11.8	64.2	0
144		L	S	1.07	5	37.0	12.3	49.3	0
148	B	V	G	4.56	11	43.1	2.1	45.2	0

Figure S1. Correlation between $\Delta\Delta G$ computed with POPMUSIC (multiplied by 2 to reflect the dimer estimates) and IMUTANT vs. the experimental holodimer data (all values in kcal/mol) (numerical data in Table S1 (dimer experimental data) and Table S2 (POPMUSIC numbers)).

POPMUSIC2.1



IMUTANT2.0

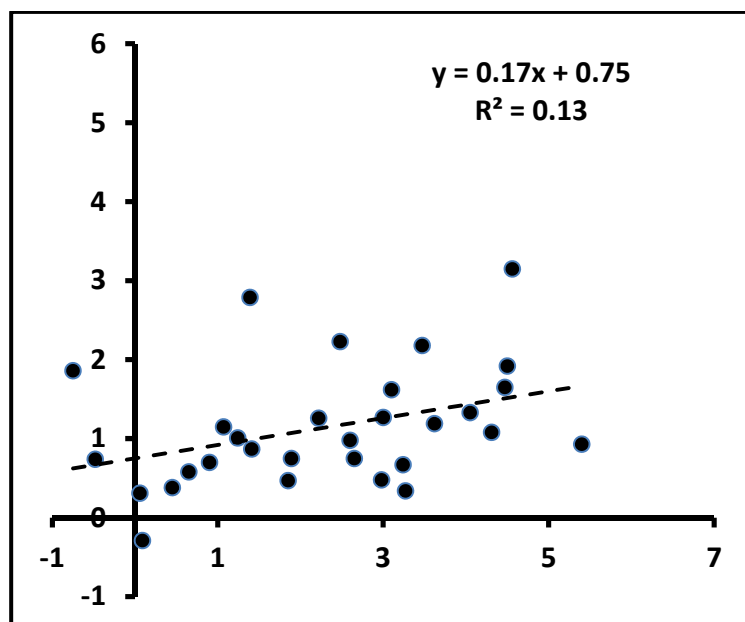


Table S4. Computed steady-state copy numbers from Equation (2) using the experimental ΔG s, as shown in Figure 6 in the main paper.

SITE	WT	MUT	Ubefore	Uafter	dU	dE _m /dt	t(s)	Ln($\Delta dE_m/dt$)
4	A	V	2.06E-04	2.80E-01	2.80E-01	2.80E-08	1.2	-17.39
38	L	V	2.06E-04	4.67E-02	4.65E-02	4.65E-09	2.4	-19.19
41	G	D	2.06E-04	6.86E-02	6.84E-02	6.84E-09	14.1	-18.80
41	G	S	2.06E-04	3.66E-01	3.65E-01	3.65E-08	1	-17.12
43	H	R	2.06E-04	1.81E-01	1.81E-01	1.81E-08	1.8	-17.83
76	D	V	2.06E-04	2.28E-04	2.18E-05	2.18E-12	18.8	-26.85
76	D	Y	2.06E-04	2.40E-04	3.35E-05	3.35E-12	17	-26.42
84	L	V	2.06E-04	1.74E-02	1.72E-02	1.72E-09	3.2	-20.18
85	G	R	2.06E-04	9.30E-04	7.23E-04	7.23E-11	6	-23.35
86	N	S	2.06E-04	4.38E-04	2.32E-04	2.32E-11	6.8	-24.49
86	N	K	2.06E-04	2.18E-03	1.98E-03	1.98E-10	1.7	-22.34
90	D	A	2.06E-04	6.12E-04	4.06E-04	4.06E-11	8	-23.93
90	D	V	2.06E-04	4.56E-03	4.35E-03	4.35E-10	2.7	-21.56
93	G	A	2.06E-04	3.02E-02	3.00E-02	3.00E-09	3.1	-19.62
93	G	D	2.06E-04	3.84E-01	3.84E-01	3.84E-08	8.8	-17.07
93	G	R	2.06E-04	3.12E-02	3.10E-02	3.10E-09	5.3	-19.59
93	G	S	2.06E-04	3.69E-02	3.67E-02	3.67E-09	8	-19.42
93	G	V	2.06E-04	1.73E+00	1.73E+00	1.73E-07	6	-15.57
100	E	G	2.06E-04	8.47E-03	8.26E-03	8.26E-10	4.7	-20.91
101	D	G	2.06E-04	2.11E-03	1.90E-03	1.90E-10	1.9	-22.38
104	I	F	2.06E-04	1.64E-03	1.44E-03	1.44E-10	21.3	-22.66
105	S	L	2.06E-04	1.60E-02	1.58E-02	1.58E-09	3.5	-20.27

106	L	V	2.06E-04	8.82E-02	8.80E-02	8.80E-09	1.9	-18.55
113	I	T	2.06E-04	1.31E-02	1.29E-02	1.29E-09	6.8	-20.47
114	G	A	2.06E-04	4.91E-02	4.89E-02	4.89E-09	2.7	-19.14
144	L	F	2.06E-04	4.87E-03	4.67E-03	4.67E-10	11.8	-21.49
144	L	S	2.06E-04	1.24E-03	1.03E-03	1.03E-10	12.3	-23.00
148	V	G	2.06E-04	4.25E-01	4.25E-01	4.25E-08	2.1	-16.97

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