

Supporting Information

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Table S1. Parameters obtained from global fitting of all kinetic folding data on pseudo-wild-type and mutant PSD-95 PDZ3 using shared *m* values

Protein region	Mutant	k_f, s^{-1} D→TS1	k_{u1}, s^{-1} N→TS1	$k_{u2},^* \text{s}^{-1}$ N→TS2
	Pseudo-WT	20 ± 0.9	0.032 ± 0.002	6.2 ± 0.9
$\beta 1$	I314V	17 ± 0.8	0.013 ± 0.001	2.4 ± 0.4
$\beta 1$	I316A	3.8 ± 1.2	2.3 ± 0.1	110 ± 15
Loop	L323A	37 ± 3	1.4 ± 0.1	44 ± 7
$\beta 2$	F325A	1.0 ± 1.7	6.6 ± 0.4	98 ± 15
$\beta 2$	I327V	13 ± 0.6	0.11 ± 0.008	14 ± 2
$\beta 2$	V328A	17 ± 0.9	0.046 ± 0.004	4.6 ± 0.7
$\beta 3$	I336V	20 ± 0.9	0.068 ± 0.005	6.6 ± 1.0
$\beta 3$	I336A	20 ± 1	0.31 ± 0.02	18 ± 3
$\beta 3$	I338A	12 ± 1	0.76 ± 0.05	36 ± 5
$\beta 3$	F340A	11 ± 0.5	0.021 ± 0.002	3.3 ± 0.6
$\beta 3$	I341V	23 ± 1	0.028 ± 0.002	5.9 ± 0.9
$\beta 3$	I341A	25 ± 2	0.57 ± 0.04	29 ± 4
$\alpha 1$	P346G	22 ± 1	0.34 ± 0.02	32 ± 5
$\alpha 1$	A347G	22 ± 1	0.33 ± 0.02	37 ± 5
Loop	L353A	11 ± 1	0.80 ± 0.05	41 ± 6
$\beta 4$	I359V	11 ± 0.5	0.088 ± 0.006	12 ± 2
$\beta 4$	V362A	3.6 ± 0.2	0.098 ± 0.006	9.0 ± 1.3
$\alpha 2$	H372A	140 ± 7.0	0.024 ± 0.002	3.7 ± 0.7
$\alpha 2$	E373A	18 ± 0.9	0.031 ± 0.002	5.8 ± 0.9
$\alpha 2$	E373G	12 ± 0.6	0.056 ± 0.004	9.4 ± 1.4
$\alpha 2$	A375G	5.4 ± 0.3	0.045 ± 0.003	5.8 ± 0.8
$\alpha 2$	A376G	5.7 ± 0.4	0.088 ± 0.006	8.9 ± 1.3
$\alpha 2$	I377A	23 ± 1	0.037 ± 0.003	6.6 ± 1.0
$\alpha 2$	I377G	6.0 ± 0.3	0.074 ± 0.005	10 ± 2
$\alpha 2$	A378G	5.0 ± 0.5	0.47 ± 0.03	32 ± 4
$\alpha 2$	L379A	4.3 ± 0.2	0.090 ± 0.006	9.9 ± 1.4
$\alpha 2$	K380A	42 ± 2	0.025 ± 0.002	4.6 ± 0.7
$\alpha 2$	K380G	17 ± 0.8	0.066 ± 0.005	7.8 ± 1.2
Turn	A382G	9.3 ± 0.6	0.11 ± 0.008	14 ± 2
$\beta 6$	V386A	12 ± 0.6	0.55 ± 0.03	28 ± 4
$\beta 6$	I388V	8.5 ± 0.4	0.16 ± 0.01	18 ± 3
$\beta 6$	Y392A	13 ± 0.9	0.27 ± 0.02	6.9 ± 1.1

The fitted *m* values are as follows: $m_{D\rightarrow 1} = 0.84 \pm 0.01$, $m_{N\rightarrow 1} = 0.66 \pm 0.01$, and $m_p = 0.50 \pm 0.01 \text{ kcal}\cdot\text{mol}^{-1}\cdot\text{M}^{-1}$. Errors are from the global fitting to the sum of Eqs. 1 and 3.

* $k_{u2} = k_u/K_p$.