Supplementary Material

Table S1. Energy difference between wild-type and alanine mutants for all energy contributions regarded in the alanine-scanning calculation ($\Delta\Delta = \Delta_{wild\text{-}type} - \Delta_{mutant}$)

energy contribution	Tyr295Ala		Asp296Ala		Val300Ala		Arg303Ala	
	mean	**std**	**mean**	**std**	**mean**	**std**	**mean**	**std**
$\Delta\Delta E_{electrostatic}$	-6.82	2.2	95.2	0.05	-0.07	0.02	-257.69	0.94
$\Delta\Delta E_{vdW}$	-5.88	0.16	-1.45	0.26	-2.38	0.05	-0.60	0.07
$\Delta\Delta E_{gas}$	-12.71	2.19	93.73	0.01	-2.46	0.11	-258.29	0.83
$\Delta\Delta G_{nonpolar}$	-0.59	-	-0.10	-	-0.12	0.05	-0.37	0.01
$\Delta\Delta G_{PB}$	10.99	1.63	-94.76	0.77	-0.18	0.18	256.01	1.43
$\Delta\Delta G_{binding}$	**-2.31**	**0.38**	**-1.13**	**0.22**	**-2.76**	**0.05**	**-2.65**	**0.17**
energy contribution	**Leu304Ala**		**Lys307Ala**		**Val314Ala**		**Val319Ala**	
	mean	**std**	**mean**	**std**	**mean**	**std**	**mean**	**std**
$\Delta\Delta E_{electrostatic}$	0.50	0.02	-270.72	0.35	-0.18	0.01	-0.17	0.00
$\Delta\Delta E_{vdW}$	-0.61	-	-0.48	0.35	-0.20	-	-0.39	0.04
$\Delta\Delta E_{gas}$	0.12	0.01	-271.21	0.68	0.39	0.10	-0.57	0.06
$\Delta\Delta G_{nonpolar}$	-0.08	-	-0.19	-	0.00	0.01	-0.05	0.01
$\Delta\Delta G_{PB}$	-0.30	0.05	268.61	1.28	0.25	0.08	0.32	0.02
$\Delta\Delta G_{binding}$	**-0.50**	**0.01**	**-2.79**	**0.23**	**-0.13**	**0.05**	**-0.29**	**0.03**
energy contribution	**Ser316Ala**		**Gln320Ala**		**Leu321Ala**		**Arg324Ala**	
	mean	**std**	**mean**	**std**	**mean**	**std**	**mean**	**Std**
$\Delta\Delta E_{electrostatic}$	-0.87	0.01	-0.23	0.09	-0.31	0.02	-145.41	2.66
$\Delta\Delta E_{vdW}$	-0.03	0.01	-0.07	-	-2.57	0.03	-4.92	0.11
$\Delta\Delta E_{gas}$	-0.91	0.02	-0.30	0.08	-2.89	0.11	-150.33	2.68
$\Delta\Delta G_{nonpolar}$	0.00	-	0.01	-	-0.16	0.01	-0.45	-
$\Delta\Delta G_{PB}$	0.89	0.04	0.26	0.08	-2.64	0.17	154.81	1.45
$\Delta\Delta G_{binding}$	**-0.02**	**0.01**	**-0.04**	**0.01**	**-0.41**	**0.15**	**4.02**	**0.37**

Dashes indicate that the standard deviation was smaller than 0.01 kcal mol^{-1}.