

Supplementary information 1

ΔΔG Threshold (kcal/mol)	1.0							2.0						
	Absolute Positives	Absolute Negatives	TPR (%)	FPR (%)	TPR/TPR ratio	TPR 95% confidence interval (%)	FPR 95% confidence interval (%)	Absolute Positives	Absolute Negatives	TPR (%)	FPR (%)	TPR/TPR ratio	TPR 95% confidence interval (%)	FPR 95% confidence interval (%)
Disulphide breakage	2	0	0.46	0.00	N/A	0.63	0.00	2	0	0.91	0.00	N/A	1.26	0.00
Buried Pro introduced	3	1	0.69	0.15	4.49	0.78	0.30	2	2	0.91	0.23	3.97	1.26	0.32
Clash	16	5	3.67	0.77	4.79	1.76	0.67	10	11	4.57	1.27	3.61	2.76	0.74
Buried hydrophilic introduced	10	1	2.29	0.15	14.95	1.41	0.30	6	5	2.74	0.58	4.76	2.16	0.50
Buried charge introduced	11	3	2.52	0.46	5.48	1.47	0.52	7	7	3.20	0.81	3.97	2.33	0.59
Secondary structure altered	0	2	0.00	0.31	0.00	0.00	0.42	0	2	0.00	0.23	0.00	0.00	0.32
Buried charge switch	0	1	0.00	0.15	0.00	0.00	0.30	0	1	0.00	0.12	0.00	0.00	0.23
Disallowed phi/psi	2	6	0.46	0.92	0.50	0.63	0.73	1	7	0.46	0.81	0.57	0.89	0.59
Buried charge replaced	6	10	1.38	1.53	0.90	1.09	0.94	4	12	1.83	1.38	1.32	1.77	0.78
Buried Gly replaced	5	6	1.15	0.92	1.25	1.00	0.73	4	7	1.83	0.81	2.27	1.77	0.59
Buried H-bond breakage	32	27	7.34	4.14	1.77	2.45	1.53	17	42	7.76	4.83	1.61	3.54	1.43
Buried salt bridge breakage	1	4	0.23	0.61	0.37	0.45	0.60	0	5	0.00	0.58	0.00	0.00	0.50
Cavity altered	17	11	3.90	1.69	2.31	1.82	0.99	11	17	5.02	1.96	2.57	2.89	0.92
Buried / exposed switch	20	9	4.59	1.38	3.32	1.96	0.90	16	13	7.31	1.50	4.88	3.45	0.81
Cis pro replaced	2	1	0.46	0.15	2.99	0.63	0.30	2	1	0.91	0.12	7.94	1.26	0.23
Gly in a bend	3	5	0.69	0.77	0.90	0.78	0.67	2	6	0.91	0.69	1.32	1.26	0.55