

Supporting Information

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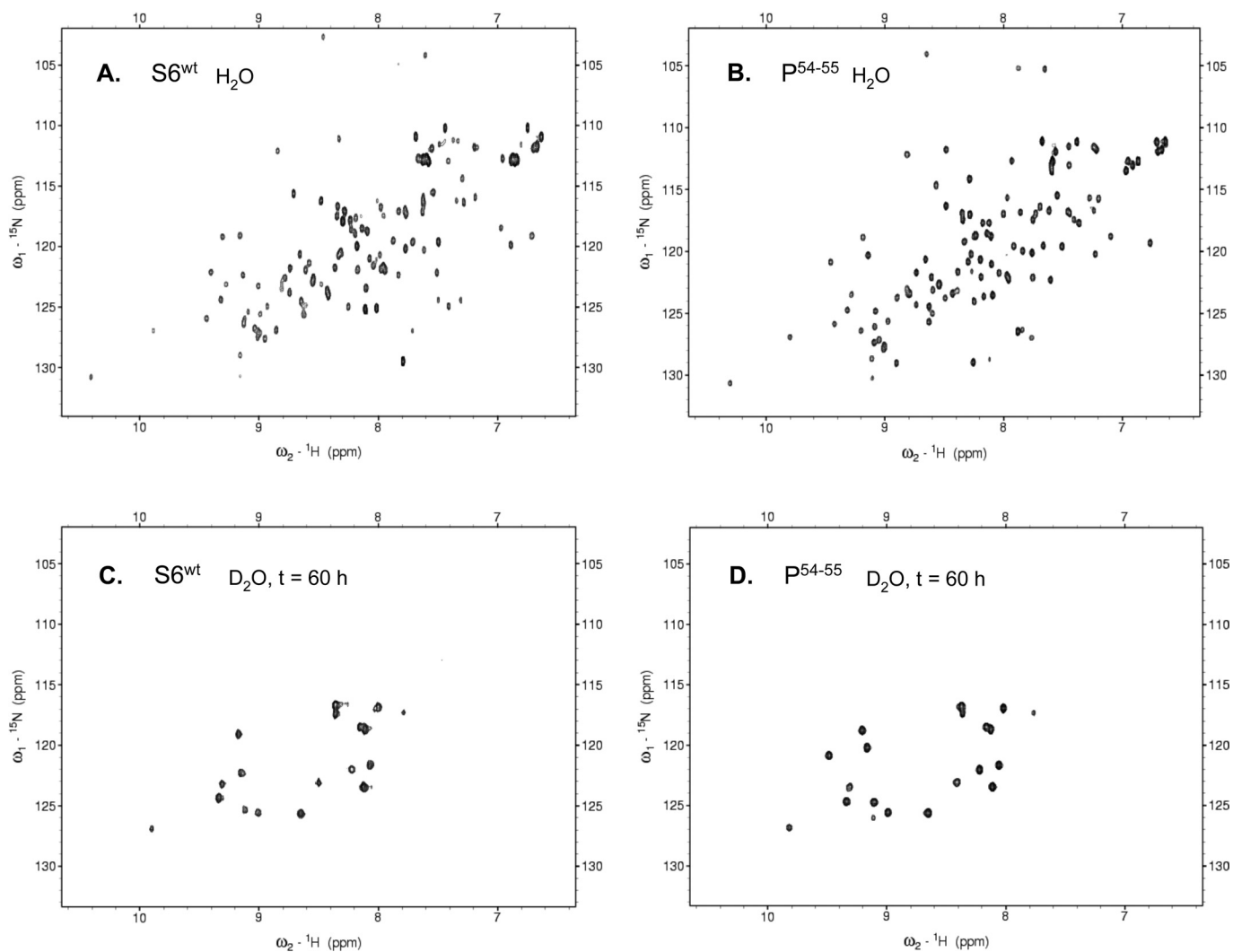


Fig. S1. HSQC spectra of S6^{wt} and P⁵⁴⁻⁵⁵, before and after 60 h of exchange in D₂O. (A) S6^{wt} in H₂O. (B) P⁵⁴⁻⁵⁵ in H₂O. (C) S6^{wt} after 60-h incubation in D₂O. (D) P⁵⁴⁻⁵⁵ after 60-h incubation in D₂O.

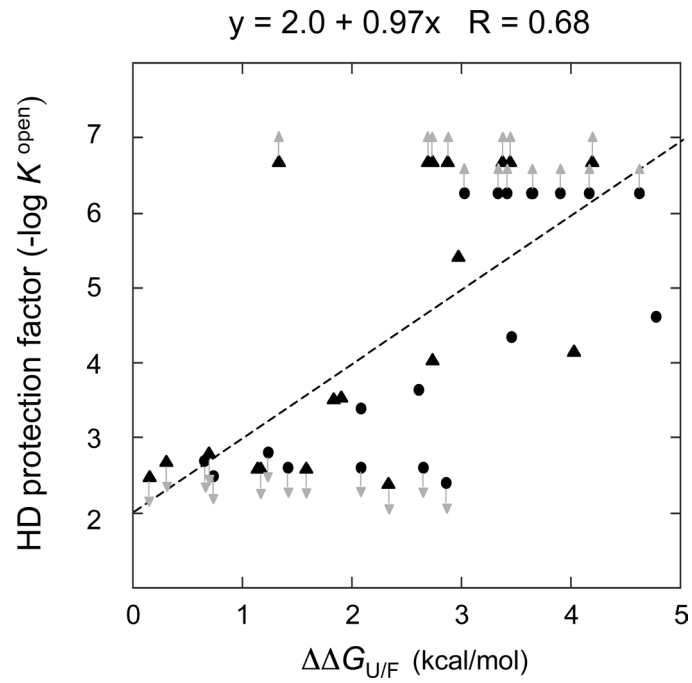
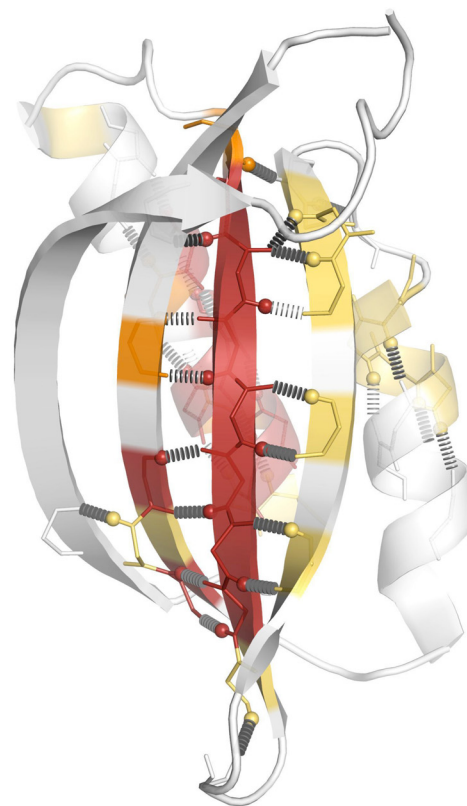


Fig. S3. Plot of HD protection factors (Table 1) vs. local stability ($\Delta\Delta G_{U/F}$, Table S2) as estimated from the stability loss upon point mutation to Ala. The correlation $R = 0.68$ is obtained by fitting to the entire dataset, including the points at the thresholds for global (arrow up) and dead-time exchange (arrow down).

**S6^{wt}****P⁵⁴⁻⁵⁵**

Movie S1. Video showing the HD-exchange patterns of S6^{wt} and P⁵⁴⁻⁵⁵ (Fig. 4 in main text). The protection factors of S6^{wt} and P⁵⁴⁻⁵⁵ are overall very similar and do not respond to the changes in folding pathway induced by circular permutation. The backbone positions are color-coded according to the protection factors (PF) in Fig. S3.

[Movie S1 \(AVI\)](#)

Table S1. NOE factors for S6^{wt} and the permutant P54-55

S6 ^{wt}			P54-55		
Amino acid	NOE	Error	Amino acid	NOE	Error
M1			M1 ₁		
R2	0.59	0.04	R2 ₄₄		
R3	0.53	0.02	R3 ₄₅	0.73	0.01
Y4	0.83	0.03	Y4 ₄₆	0.80	0.02
Q5	0.77	0.02	Q5 ₄₇	0.80	0.02
V6	0.67	0.03	V6 ₄₈	0.76	0.02
N7	0.77	0.02	N7 ₄₉	0.82	0.02
I8	0.94	0.02	I8 ₅₀	0.78	0.02
V9	0.85	0.03	V9 ₅₁	0.79	0.02
L10	0.77	0.03	L10 ₅₂	0.81	0.02
N11			N11 ₅₃		
P12			P12 ₅₄		
N13			N13 ₅₅		
L14	0.66	0.02	L14 ₅₆	0.68	0.01
D15	0.73	0.02	D15 ₅₇	0.75	0.01
Q16	0.76	0.02	Q16 ₅₈	0.76	0.01
S17	0.78	0.01	S17 ₅₉	0.78	0.01
Q18	0.65	0.02	Q18 ₆₀	0.80	0.01
L19	0.81	0.02	L19 ₆₁	0.79	0.01
A20	0.83	0.02	A20 ₆₂	0.80	0.01
L21	0.83	0.01	L21 ₆₃	0.83	0.01
E22	0.71	0.02	E22 ₆₄	0.79	0.01
K23	0.95	0.02	K23 ₆₅	0.82	0.01
E24			E24 ₆₆	0.25	0.01
I25	0.87	0.02	I25 ₆₇	0.84	0.01
I26	0.73	0.02	I26 ₆₈	0.82	0.02
Q27			Q27 ₆₉	0.84	0.01
R28			R28 ₇₀	0.82	0.01
A29	0.74	0.01	A29 ₇₁	0.81	0.01
L30	0.86	0.02	L30 ₇₂	0.80	0.02
Q31	0.77	0.02	Q31 ₇₃	0.82	0.01
N32	0.59	0.01	N32 ₇₄	0.76	0.01
Y33	0.77	0.02	Y33 ₇₅	0.78	0.02
G34	0.76	0.02	G34 ₇₆	0.79	0.02
A35	0.76	0.01	A35 ₇₇	0.74	0.01
R36	0.73	0.02	R36 ₇₈	0.71	0.02
V37	0.79	0.02	V37 ₇₉		
E38	0.78	0.03	E38 ₈₀	0.79	0.02
K39	0.76	0.02	K39 ₈₁	0.74	0.02
V40	0.52	0.02	V40 ₈₂	0.55	0.02
E41	0.84	0.03	E41 ₈₃	0.80	0.02
E42	0.71	0.02	E42 ₈₄		
L43	0.63	0.03	L43 ₈₅	0.77	0.03
G44	0.64	0.03	G44 ₈₆	0.71	0.02
L45			L45 ₈₇		
R46	0.74	0.03	R46 ₈₈	0.78	0.03
R47	0.69	0.02	R47 ₈₉	0.72	0.02
L48	0.57	0.03	L48 ₉₀	0.57	0.02
A49	0.04	0.02	A49 ₉₁	0.16	0.01
Y50			Y50 ₉₂		
P51			P51 ₉₃		
I52			I52 ₉₄		
A53	-0.50	0.04	A53 ₉₅	-6.47	0.08
L54	-0.40	0.04	L54 ₉₆	-2.22	0.02
D55			D55 ₂	-0.27	0.00
P56			P56 ₃		
Q57	0.35	0.02	Q57 ₄	0.62	0.03
G58	0.77	0.03	G58 ₅	0.72	0.03
Y59	0.78	0.03	Y59 ₆	0.82	0.03
F60	0.85	0.03	F60 ₇	0.79	0.03
L61	0.72	0.03	L61 ₈	0.79	0.03
W62	0.72	0.02	W62 ₉	0.75	0.02

S6^{wt}

p54-55

Amino acid	NOE	Error	Amino acid	NOE	Error
Y63			Y63 ₁₀	0.79	0.02
Q64			Q64 ₁₁		
V65	0.84	0.02	V65 ₁₂	0.79	0.02
E66	0.76	0.02	E66 ₁₃	0.85	0.02
M67	0.78	0.02	M67 ₁₄	0.81	0.02
P68			P68 ₁₅		
E69	0.75	0.03	E69 ₁₆	0.73	0.02
D70	0.83	0.01	D70 ₁₇	0.75	0.01
R71	0.70	0.02	R71 ₁₈	0.71	0.02
V72	0.74	0.02	V72 ₁₉	0.82	0.01
N73	0.81	0.02	N73 ₂₀	0.81	0.02
D74			D74 ₂₁	0.15	0.00
L75	0.76	0.02	L75 ₂₂	0.84	0.01
A76	0.95	0.02	A76 ₂₃	0.76	0.01
R77	0.77	0.01	R77 ₂₄	0.81	0.01
E78	0.86	0.02	E78 ₂₅	0.80	0.02
L79	0.81	0.02	L79 ₂₆	0.77	0.02
R80	0.77	0.02	R80 ₂₇	0.78	0.01
I81			I81 ₂₈	0.78	0.02
R82	0.73	0.02	R82 ₂₉	0.76	0.02
D83	0.75	0.02	D83 ₃₀	0.83	0.01
N84	0.77	0.02	N84 ₃₁	0.82	0.02
V85	0.79	0.02	V85 ₃₂	0.79	0.02
R86	0.78	0.03	R86 ₃₃	0.82	0.03
R87	0.70	0.02	R87 ₃₄	0.81	0.02
V88	0.84	0.02	V88 ₃₅	0.80	0.02
M89	0.76	0.02	M89 ₃₆		
V90	0.79	0.02	V90 ₃₇		
V91	0.75	0.03	V91 ₃₈	0.73	0.03
K92	0.76	0.02	K92 _{A39}	0.73	0.02
S93	0.80	0.02	S93 ₄₀	0.71	0.02
Q94	0.56	0.02	Q94 _{T41}	0.66	0.01
E95	0.19	0.02	E95 _{T42}	0.71	0.01
P96			P96 ₄₃		
F97	-0.06	0.02	F97	0.72	0.01
L98	-0.66	0.01	L98		
A99			A99		
N100			N100		
A101			A101		

The residues are labeled according to the S6^{wt} sequence and subscripts refer to P⁵⁴⁻⁵⁵ numbering.

Table S2. ϕ values and free-energy changes upon point mutation ($\Delta \Delta G_{U/F}$) for S6^{wt} and P⁵⁴⁻⁵⁵

Mutation	S6 ^{wt} ϕ	S6 ^{wt} $\Delta \Delta G_{U/F}$	P ⁵⁴⁻⁵⁵ ϕ	P ⁵⁴⁻⁵⁵ $\Delta \Delta G_{U/F}$
V6A ₄₈	0.51 ^{1*}	3.64	0.57*	3.38
I8A ₅₀	0.45*	4.17	0.40*	3.44
L10A ₅₂	0.32	4.62	0.18	4.20
L19A ₆₁	0.25	2.61	0.05	1.90
I26A ₆₈	0.40*	3.03	0.23	1.33
L30A ₇₂	0.34	3.66	0.14	2.87
V37A ₇₉	0.27	2.66	0.07	1.17
V40A ₈₂	—	0.74	—	0.16
L48A ₉₀	—	0.65	—	0.30
F60A ₇	—	1.23	—	0.69
L61A ₈	0.25	3.42	0.08	2.97
Y63A ₁₀	0.21	3.91	0.10	2.69
V65A ₁₂	0.38	3.33	0.17	2.74
V72A ₁₉	0.17	1.42	0.00	1.14
L75A ₂₂	0.41*	2.08	0.51*	1.83
L79A ₂₆	0.17	4.78	0.23	4.03
V85A ₃₂	0.08	3.46	0.15	2.74
V88A ₃₅	0.15	2.09	0.61*	1.59
V90A ₃₇	0.16	2.86	0.56*	2.33

Adapted from data in ref. 1. Subscripts refer to P⁵⁴⁻⁵⁵ numbering.

*The positions with $f > 0.4$ are shown in Fig. 1.

1. Haglund E, Lindberg MO, Oliveberg M (2008) Changes of protein folding pathways by circular permutation. Overlapping nuclei promote global cooperativity *J Biol Chem* 283:27904–27915.

