Supplementary Table 1. T_m value correlations at pH 7.0

Parameter	95% confidence interval	P value	P value summary	R
Abundance	-0.5542 to 0.6420	0.8415	ns	0.0685
Number Amino Acids	-0.5780 to 0.3388	0.5466	ns	0.1522
Instability Index	-0.5879 to 0.3254	0.5081	ns	0.1669
Contact Order	-0.8636 to 0.2848	0.2042	ns	0.4678
Hydropathicity	-0.5812 to 0.3344	0.534	ns	0.1569
pI	-0.2150 to 0.6605	0.2605	ns	0.2800
% amino acids positively charged	-0.5794 to 0.3369	0.5411	ns	0.1543
% amino acids negatively charged	-0.2305 to 0.6512	0.2882	ns	0.2648
% amino acids charged	-0.3891 to 0.5381	0.7074	ns	0.0951
% aromatic amino acids	-0.4202 to 0.5111	0.8191	ns	0.0580
% amino acids hydrophobic	-0.4424 to 0.4906	0.9034	ns	0.0308
Molecular weight	-0.5698 to 0.3495	0.5788	ns	0.1402
Aliphatic Index	-0.4298 to 0.5023	0.8551	ns	0.0463
A	-0.6210 to 0.2779	0.3869	ns	0.2171
C	-0.8908 to -0.3914	0.0007	***	0.7257
D	-0.6978 to 0.1481	0.1642	ns	0.3425
E	-0.3105 to 0.5987	0.4676	ns	0.1829
F	-0.4258 to 0.5061	0.8397	ns	0.0513
G	-0.1223 to 0.7110	0.1358	ns	0.3655
H	-0.6873 to 0.1678	0.1889	ns	0.3245
I	-0.3074 to 0.6008	0.4595	ns	0.1862
K	-0.2258 to 0.6541	0.2795	ns	0.2695
L	-0.2443 to 0.6427	0.3147	ns	0.2512
M	0.2039 to 0.8393	0.0069	*	0.6125
N	-0.1668 to 0.6878	0.1877	ns	0.3254
P	-0.7753 to -0.02136	0.0421	ns	0.4834
Q	-0.4494 to 0.4840	0.9306	ns	0.0221
R	-0.5105 to 0.4209	0.8215	ns	0.0572
S	-0.3516 to 0.5682	0.5854	ns	0.1379
T	-0.5547 to 0.3687	0.6394	ns	0.1185
V	-0.7558 to 0.02572	0.0632	ns	0.4465
W	0.03831 to 0.7820	0.0362	ns	0.4963
Y	-0.7473 to 0.04529	0.0744	ns	0.4307

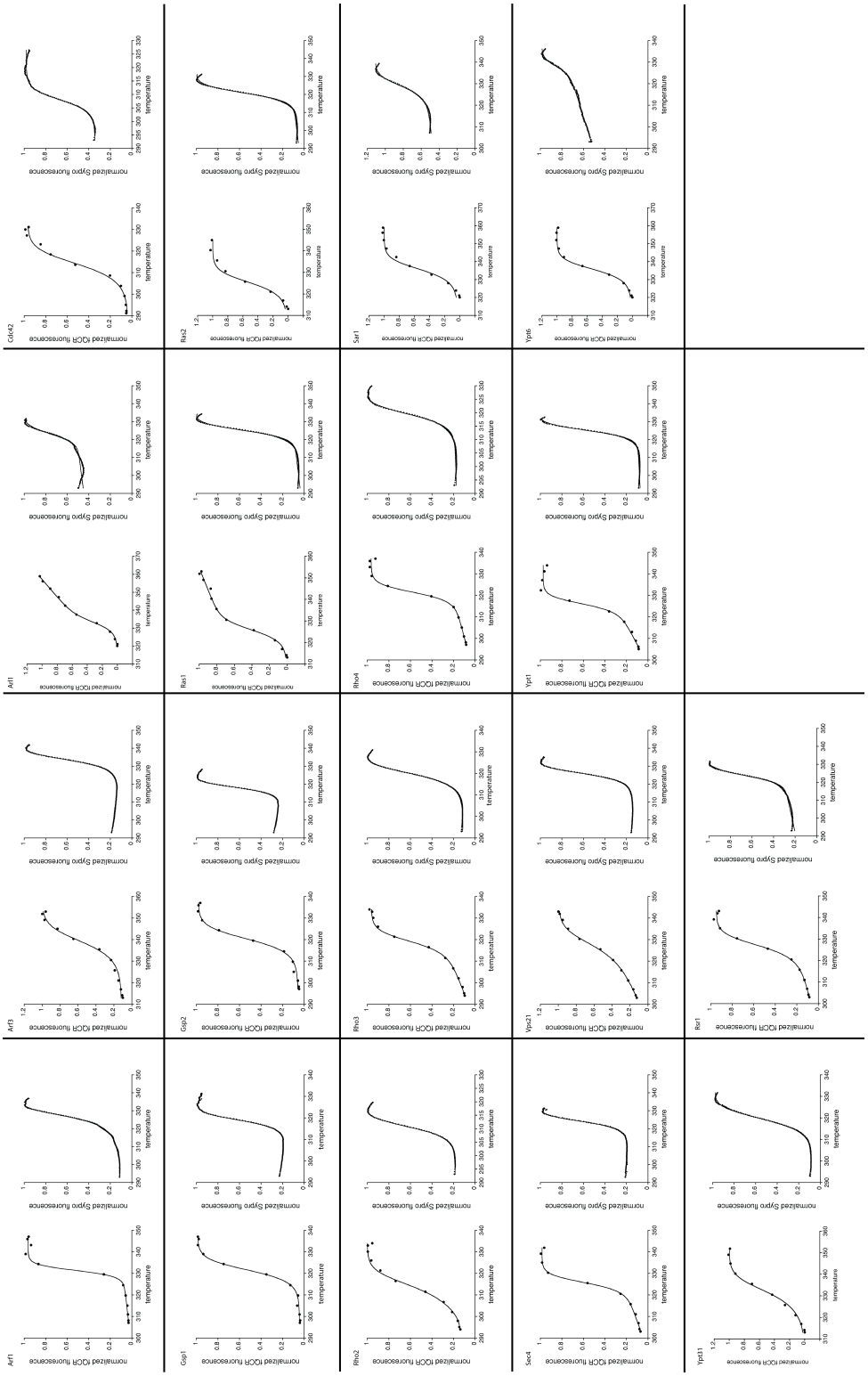
ns = the correlation is not statistically significant

Supplementary Table 2. Primers sequences used in the LIC cloning procedure.

GTPase	Direction	LIC cloning primer sequence
Gsp1	Forward	5' TACTTCCAATCCAATGCG ATGTCTGCCCCAGCTGCTAACG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TTATAAATCAGCATCATCTTCATC 3'
Gsp2	Forward	5' TACTTCCAATCCAATGCG ATGTCAGCACCTGCTCAAAAC 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TTATAAATCAGCATCGTCTTC 3'
Rho2	Forward	5' TACTTCCAATCCAATGCG ATGTCTGAAAAGGCCGTTAGAAG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TTATAAAATTATGCAACAGTTAG 3'
Rho3	Forward	5' TACTTCCAATCCAATGCG ATGTCATTTCTATGTGGGTCAGC 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TTACATAATGGTACAGCTGGATC 3'
Rho4	Forward	5' TACTTCCAATCCAATGCG ATGAATACACTATTATTTAAGCG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TTACATTATAATACACTTGTT 3'
Cdc42	Forward	5' TACTTCCAATCCAATGCG ATGCAAACGCTAAAGTGTGTTG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA CTACAAAATTGCACATTTTTTAC 3'
Ras1	Forward	5' TACTTCCAATCCAATGCG ATGCAGGGAAATAAATCAACTATAAG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TCAACAAATTATACAACAACC 3'
Rho1	Forward	5' TACTTCCAATCCAATGCG ATGTCACAACAAGTTGGTAACAG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA CTATAACAAGACACACTTCTTC 3'
Ras2	Forward	5' TACTTCCAATCCAATGCG ATGCCTTTGAACAAGTCGAACATAAG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TTAACTTATAATACAACAGCCACC 3'
Sar1*	Forward	5' TACTTCCAATCCAATGCG ATGGCTGGTTGGGATATTTTTGGTTGG 3'
	Forward	5' TACTTCCAATCCAATGCG ATGGCTGGTTGGGATATTTTTGGTTGG TCAGAGATGTGTTGGCTTCCC 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TTAAATATATTGAGATAACCATTGG 3'
Rsr1	Forward	5' TACTTCCAATCCAATGCG ATGAGAGACTATAAATTAGTAG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA CTATAGAATAGTGCAAGTGG 3'
Vps21	Forward	5' TACTTCCAATCCAATGCG ATGAACACATCAGTCACTTCC 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA CTAACAACTGCAAGCACTGTTTGC 3'
Arl1	Forward	5' TACTTCCAATCCAATGCG ATGGGTAACATTTTTAGTTCAATG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA CTATAACTGTTCCTCTTTTATAAC 3'
Arf1	Forward	5' TACTTCCAATCCAATGCG ATGGGTTTGTTTGCCTCTAAG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TTAAGTTGAGTTTTTCAAACTG 3'
Arf3	Forward	5' TACTTCCAATCCAATGCG ATGGGCAATTCAATTTCGAAGG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TTATTTCTTTGGAACGTTTGTG 3'
Sec4	Forward	5' TACTTCCAATCCAATGCG ATGTCAGGCTTGAGAACTGTTTC 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TCAACAGCAATTTGATTTAGAAC 3'
Ypt1	Forward	5' TACTTCCAATCCAATGCG ATGAATAGCGAGTACGATTACC 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA TCAACAGCAGCCCCCACCGGTG 3'
Ypt6	Forward	5' TACTTCCAATCCAATGCG ATGAGCAGATCCGGGAAATCATTG 3'
	Reverse	5' TTATCCACTTCCAATGCGCTA CTAACACTGACAAGCGCTTTG 3'

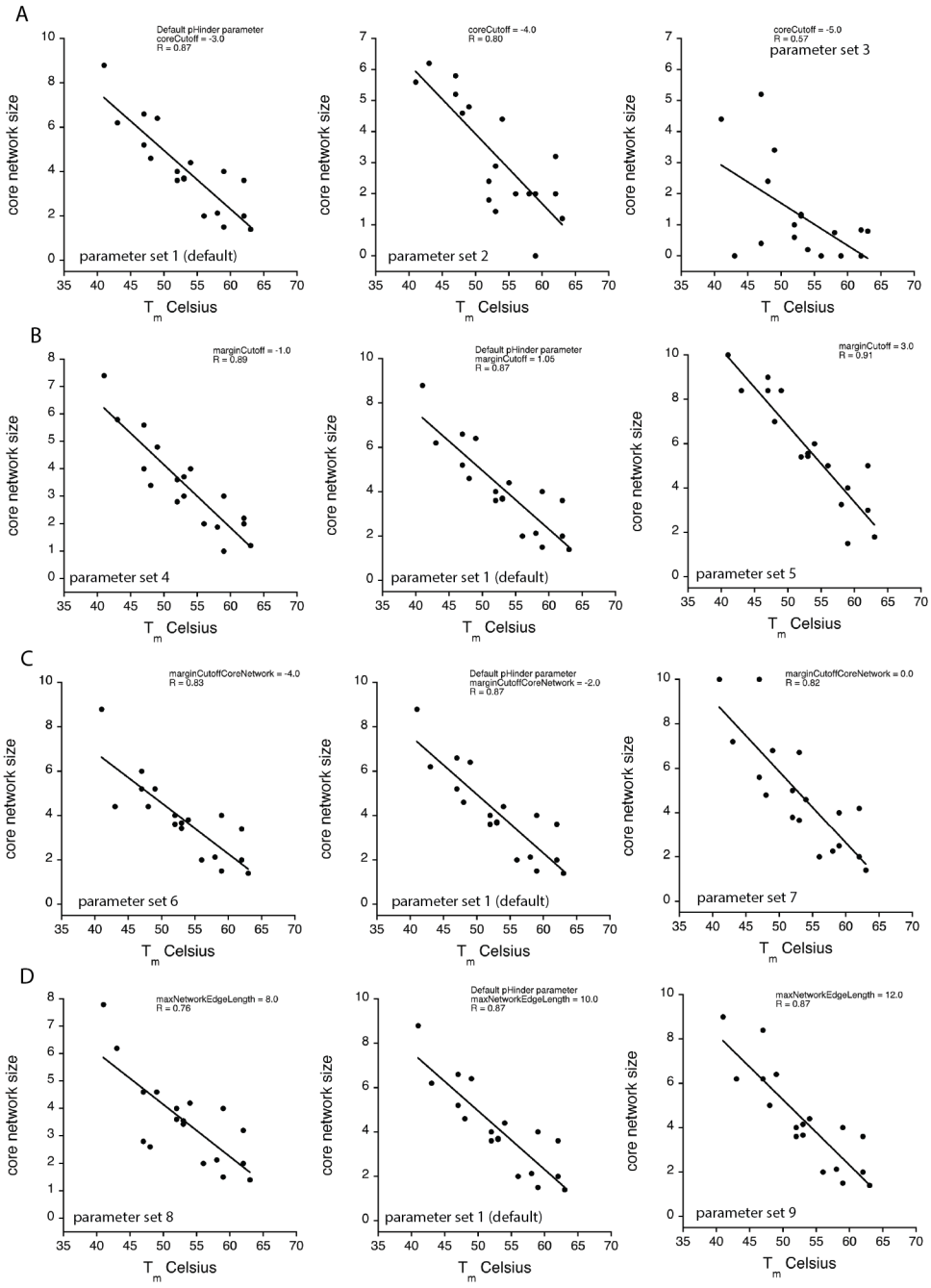
*Cloning required two steps to remove an intron.

Supplementary Figure 1.



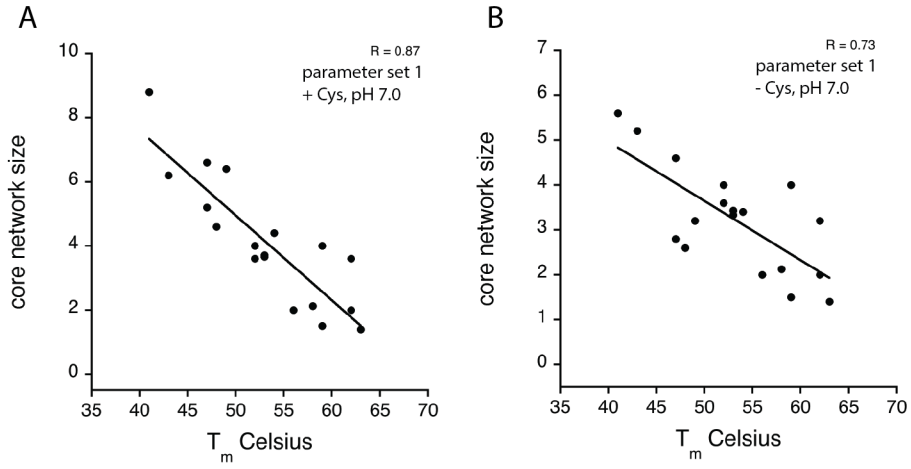
Supplementary Figure Legend 1. Thermal unfolding curves for the set of 18 yeast GTPases at pH 7.0. The black line in each plot indicates a non-linear least squares fit of the Gibbs-Helmholtz equation (Eqs. 1 & 2 in the main text). Temperature is displayed in units of Kelvin (273 + T_m value in degrees Celsius) to accommodate the fitting procedure. Unfolding curves monitored by Sypro fluorescence correspond to the ThermoFluor method.

Supplementary Figure 2.



Supplementary Figure Legend 2. Sensitivity of the correlation between core network size and Ras paralog T_m values to the parameters of the pHinder algorithm. (**A**) The distance constraint for classifying core side chains (*coreCutoff*) is varied ±1.0 Å from a default value of 3.0 Å. (**B-D**) The distance constraints for classifying margin side chains (*marginCutoff*), classifying deep margin side chains (*marginCutoffCoreNetwork*), and setting the maximum network edge length (*maxNetworkEdgeLength*) are varied ±2.0 Å from default values of -1.05 Å, -2.0 Å, and 10.0 Å respectively.

Supplementary Figure 3.



Supplementary Figure Legend 3. Sensitivity of the correlation between core network size and Ras paralog thermostability to the inclusion of Cys residues in the pHinder algorithm.