

1 chaperoned by Hsp90 change as a result of this altered affinity for one of the client
2 proteins. Solid and dotted red, blue and black lines correspond to those in (A).

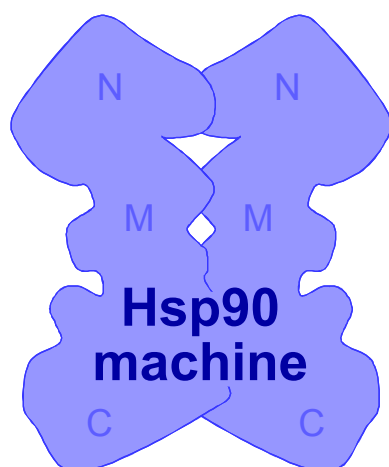
3
4 **Figure 5. Hypothesis: the Hsp90 transistor tunes multiple cellular outputs in**
5 **response to thermal input.** Thermal fluctuations influence Hsp90 availability and
6 probably the affinity of the Hsp90 chaperone machine for certain client proteins (see
7 text). Hsp90 modulates the activity of many client proteins, which include regulators
8 in key signalling pathways. Hence the Hsp90 chaperone machine is proposed to act
9 like a transistor that modulates the activity of these signalling pathways in response
10 to thermal (and other proteotoxic) inputs. As a result, temperature modulates cell
11 division, adaptation, growth and morphogenesis through the Hsp90 transistor.

12
13 **Supplementary Figure. The fungal Hsp90 chaperone machine and its client**
14 **proteins.** Once again, the shape of the Hsp90 machine is adapted from Pearl *et al.*
15 (2008)²⁶, illustrating the amino- (N), middle (M) and carboxy-terminal (C) domains.
16 The specificity of an Hsp90 complex depends on which co-chaperone it binds. This
17 figure combines lists of Hsp90 client proteins identified in *S. cerevisiae* and
18 *C. albicans* by Zhao *et al.* (2005)⁷⁸, McClellan *et al.* (2007)⁹² and Diezmann *et al.*
19 (2012)⁶⁷. The Hsp90 client proteins from Zhao *et al.* (2005)⁷⁸ include those listed in
20 their table listing proteins in specific complexes and processes that are affected by
21 Hsp90. The Hsp90 client proteins from McClellan *et al.* (2007)⁹² are from their 30°C
22 and 37°C datasets and include those proteins that are included in their ranked lists
23 with average Ratio values (Rv) of <0.5 and those proteins in their lists of top 5%
24 proteins with significantly enriched PFAM designations. Dubious ORFs are not
25 included. Hsp90 client proteins from Diezmann *et al.* (2012)⁶⁷ are those included in
26 the global *C. albicans* Hsp90 genetic interaction network. *S. cerevisiae* Hsp90 client
27 proteins are in black, *C. albicans* Hsp90 client proteins are in blue, and those
28 identified in both yeasts are in bold.

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31 **Other display items:**

32
33 **Text Box 1. Modelling the structure and dynamics of regulatory networks.**
34 Systems biologists use different modelling approaches, depending on the specific

Supplementary Figure: Leach *et al.*



Hsp90 co-chaperone machinery

Aha1 Cdc37 Cns1
Cpr6 Cpr7 Pih1 Sba1
Sgt1 Sti1 Tah1

Cell growth and division

Bem2, Bem3, **Bmh1**, Bub1, Clb2, Cdc10, Cdc26, **Cdc28**, Cna1, Cyk3, Ecm17, Glc8, Hof1, Gin1, Jnm1, Lrg1, Pde2, Pin4, Ras2, Sla2, Slm1, Swm1, Whi3, [1x orf19]

Chromatin remodelling

Ada2, Eaf3, Gcn5, Hos2, Ngg1, **Spt3**, Spt4, Spt7, Spt15, Swi1, Snf2, Snf11, **Srb8**, [2x orf19s],

Other chaperones and co-chaperones

Caj1, Hlj1, Jem1, Scj1

Hsp90 client proteins

Transcription factors

Ada2, **Adr1**, Aft2, **Ahr1**, Arg81, Aro80, Asg1, Bas1, Bcr1, Cdr1, Cha4, Cap1, Cap4, Cph1, Cst6, Cta4, Cta7, Czf1, Dal81, Fcr3, Gat1, Gis2, Gln3, Gzf3, Hal9, Hap5, Hap43, Hmc1, Imp2, Lys143, Mcm1, Met32, Mdm34, Mig1, Mig2, Mot3, Msn4, Nut1, Pdr1, Pho4, Pkc1, Ppr1, Rad18, Rgt1, Rim101, Rrn10, **Rtg3**, Sef1, Sip5, Spt8, Spt15, Spt20, Ssn2, Stb5, Swi1, Tac1, Taf11, Taf14, Tec1, Thi20, Tup1, Ume7, Upc2, Yap3, Yer028c, Zcf2, Zcf6, Zcf13, Zcf14, Zcf16, Zcf18, Zcf19, Zcf25, Zcf34, [11x orf19s]

Protein kinases

Cbk1, Cbk2, Cdc15, **Cek2**, **Cka1**, Cka2, **Ckb1**, Cla4, Cmk1, Ctk1, Ctk2, Dbf2, Elm1, Fab1, Fun31, Hal4, **Hog1**, Hsl1, Hst7, **Ire1**, Kcc4, Kcs1, Kns1, Mck1, **Mkc1/Slt2**, Mkk2, Nbn1, Pbs2, Pkh1, Pro1, Prr1, Prr2, Prs3, Prs5, Ptp1, Rim11, Rim15, Sip3, Smk1, Ssk2, Snf1, **Ssn3**, **Ssn8**, Tom1, Tpk3, Yak1, Yck2, Ypk1, [4x orf19s]

Metabolism

Aat2, Adr1, Avt6, Bas1, Cha4, Dal7, Erg2, Erg5, Erg6, Erg28, Flc2, Gap1, Gat1, Git1, Gln3, Gtr1, Gua1, Hxk2, Hxt4, Hxt12, Leu3, Lip6, Lpg20, Mal11, Mot3, Opi3, Osh1, Osh3, Pgc1, Pho4, Pho84, Pho86, Pho88, Ptr2, Sam1, Scs2, Sno1, Sur1, Sur2, Sur4, Tdh1, Tps1,

Intracellular trafficking

Age2, Apl1, Apl2, **Apl5**, Apl6, Apm1, Apm3, Aps3, Arl1, Arl3, Bre5, Bro1, Bst1, Cog5, Cog6, Cog7, Cog8, Did4, Die2, Fti1, Gvp36, Msn5, Pep8, Ppa1, Prm9, Rav1, Rav2, Rtg1, Sac1, Sec34, Sec72, Sgt2, Snc2, **Snf7**, Snf8, Srn2, Stp22, Swh1, Sys1, Vam6, Vam7, Vma9, Vma10, Vma13, Vph1, Vps5, Vps8, Vps9, **Vps15**, **Vps16**, Vps17, Vps21, Vps24, Vps25, Vps27, **Vps28**, Vps29, **Vps34**, Vps35, Vps36, Vps60, Vps61, Vtc1, Vti1, Yel048c, Yjr088c, Ypr091c Ypt6, Ypt7, [1x orf19]

Ubiquitination, pH adaptation, cell wall and other functions

Aim26, Als7, Arr3, Bmt5, Chs5, Csf1, Cue1, Ccw12, Ccw14, Doa4, Eap1, Ecm9, Ecm14, Ecm25, Ecm32, Fig4, Frq1, Gcd14, Hit1, Hoc1, Hsm3, Hwp2, Hyr1, Ifk2, Ime4, Irs34 Kin2, Kin3, Kis1, Kre1, Lpf1, Mft1, Mnn9, Nuo84, Oca1, Pan3, Pib1, Phr3, Pho23, Pmp3, Pna1, Puf3, Qdr2, Rei1, Rgs2, Rhr2, Ric1, Rim8, Rim20, Rim21, Rim13, Rlm9, Rph2, Rod1, Slk19, Snt2, Spr1, Stn1, Sun41, Syg1, Tao3, Thp2, Trm7, Ubc15, Ubp3, Ubp14, Wsc1, Yil029c, Ypl225w, Yrl407w, Zcf29, [37x orf19s]