Supplementary Material for the paper:

Stress induces remodelling of yeast interaction and co-expression networks

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Supplementary Methods

Co-expression network generation

To generate co-expression networks, we first calculated Spearman correlations in gene expression across different genetic variants (that is, knock-out mutants for the microarray data and genetic segregants for the RNAseq data) for all gene pairs, to generate a correlation matrix C:

$C(i,j) = corr(S_i,S_j)$,

where S_i is a vector containing the expression of gene i in each genetic variant. C can be considered as the adjacency matrix of a network. We then eliminated self-loops (C(i,i) = 0) and thresholded C so that it contained either a specific number of edges or only edges above a specific (significant, $p<0.05$) correlation.

Supplementary Results and Discussion

Co-expression network robustness

Because the co-expression networks built from the microarray data set involved only seven mutants, robustness of the correlation coefficients was verified by sequentially eliminating each mutant from the calculation. For significant correlations above 0.9 this resulted in an average change of 0.02 in magnitude of the correlation coefficients. For significant correlations above 0.7, the change was 0.05. Generating networks from the recalculated correlations resulted in a 0.3% edge gain and 6.75% edge loss when thresholding at 0.9 (gain of 0.3% and loss of 2% when thresholding at 0.7). As a further control,we calculated co-expression using a wider pool of mutants including 24 additional mutants (which could not be used for network construction, because they lacked expression data post exposure to stress). The co-expression, as calculated from the 7 mutants correlated (0.6826 Spearman correlation coefficient) with the co-expression as calculated from the larger set of mutants. These results indicate that the correlation calculation is robust despite the relatively small number of mutants.

Generation of control networks

The variance of the average shortest path lengths (i.e. “expected path lengths”) of the 20 control networks was low (standard deviations of the average shortest path length ranged from 0.001 to 0.004 in the 4 sets of 20 control networks). Given this low variability and the computational expense of generating these control networks, we deemed 20 networks to be sufficient to establish the expected path length.

Effect of hierarchical clustering cut-off on Link Communities (LC) overlap

Hierarchical clustering in this paper was performed using a distance cut-off of 0.4. For the co-expression networks, the stress-induced decrease in modular overlap was conserved at other cut-off thresholds (0.3-0.5). For the PPI networks, hierarchical clustering with a threshold of 0.4 assigns the vast majority of nodes to a single module. At lower cut-off values, all edges were assigned into their own module, essentially meaning that the number of modules a node was assigned to was determined by its degree. We were unable to determine a cut-off value for which the clustering did not fall into one of these extremes. It should be noted that full exploration of cut-off values was prohibited by high computational cost.

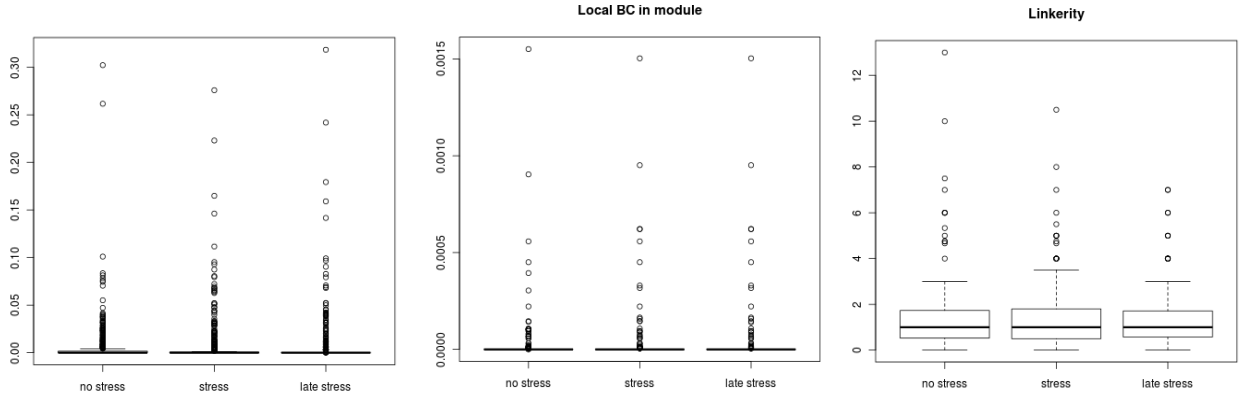
Betweenness centrality analysis

The betweenness centrality (BC) of a node is defined as the proportion of shortest paths in the network which are found to pass through the node:
$BC(v) = \sum_i \sum_j (g\_ivj / g\_ij,\ i \neq j, i \neq v, j \neq v)$,
where g_ij is the number of shortest paths between nodes i and j, and g_ivj is the number of shortest paths passing through node v. In a weighted network, such as our PPI networks, the shortest path calculation assigns the weight as the cost of travelling each edge. As, in our network, weights represent ease, not cost, of travel, we used 1/weight in determining the shortest paths.
We do not see a significant general change between the values of BC, BCsub or linkerity (as defined in (Vaggi et al., 2012)) for stressed and non-stressed networks (Figure S1).

Vaggi, F., Dodgson, J., Bajpai, A., Chessel, A., Jordán, F., Sato, M., Carazo-Salas, R. E., et al. (2012). Linkers of cell polarity and cell cycle regulation in the fission yeast protein interaction network. *PLoS computational biology*, *8*(10), e1002732. doi:10.1371/journal.pcbi.1002732

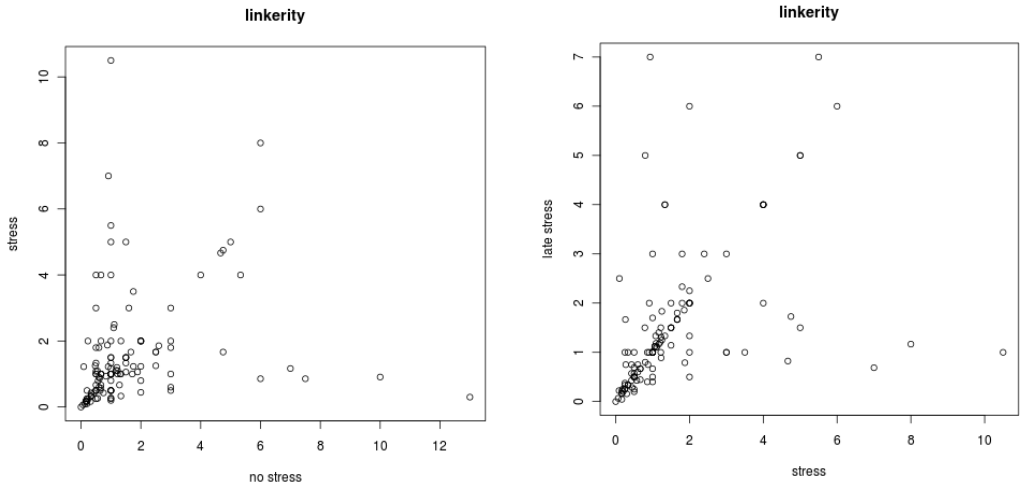
Supplementary Figures:

Supp. Figure S1: Boxplots showing the distributions of BC values in the three conditions (no stress, stress (60 minutes) and late stress (240 minutes) for abundance weighted PPIs (a), corresponding distributions for local BC measured relative to a single sub-network (b) and distribution of the linkerity values (ratio of local to central BC).



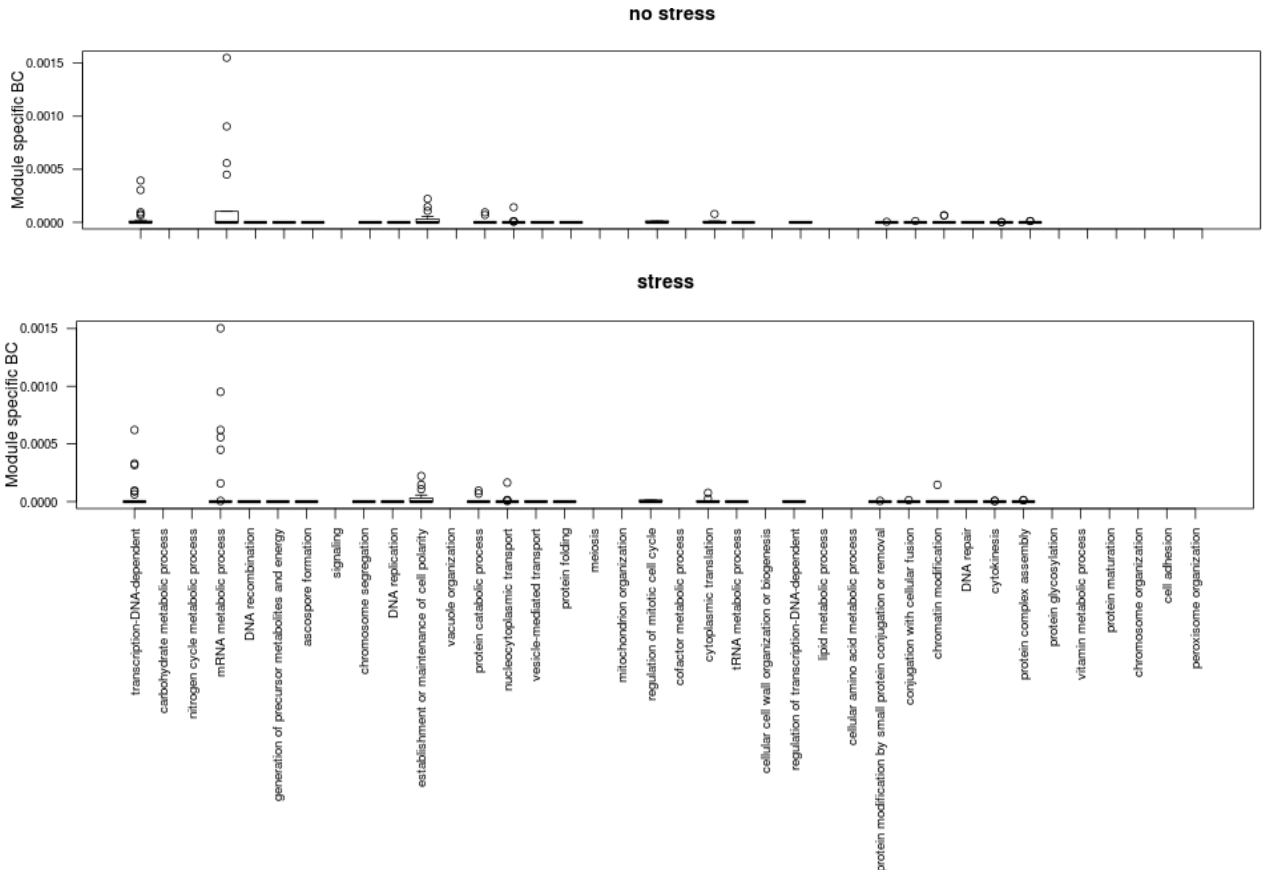
However, we can identify some genes that have higher centrality in the stressed conditions and others that lose centrality with the treatment, especially when considering linkerity (Figure S2).

Supp. Figure S2: Linkerity values for the three difference conditions. Most genes don't change linkerity significantly but there are a few displaying a clear change, meaning that they play a role as a linker between functional modules only in specific conditions.



Some GO category subnetworks show changes in local BC as shown in Figure S3, most changes are driven by single oulying data points. More specific results are shown Table S3 (general statistics), S4 (Top 20 genes that increase BC during stress) and S5 (top genes that increase BC at late stress). Figures S4 and S5 show predicted interactions for these genes. A more thorough analysis of the genes is beyond the scope of this work and will be considered in a future publication.

Supp. Figure S3: Distributions of sub-network specific local BC for the different GO categories for non-stressed and stressed conditions. Very few differences can be seen, mostly due to outliers in the distributions, leading to no general trend.



Supplementary Tables

Supp Table S1: Properties of co-expression networks at various time points in a peroxide stress (0.5mM) time course. Correlations in gene expression were calculated from expression data collected at specific points during the time course in different genetic variants. Networks were generated from the correlation data using two methods: either by drawing connections between a specific number of gene-pairs with the highest correlations, or by considering gene-pairs with a correlation above a specific threshold to be connected. As shown in the table, stress increases network density, shortest average path length and transitivity.

Network	Time point (min)	Threshold	Nodes	Edges	Density	Average Shortest Path Length	Actual/Expected	Size of largest Component	Transitivity
RNAseq	0	Top 40000	2836	40000	0.005	4.85	1.87	2582	0.52397749
RNAseq	60	Top 40000	1980	40000	0.010	6.33	2.71	1768	0.60193717
Microarray	0	Top 60000	4240	60000	0.003	4.58	1.62	4240	0.37599285
Microarray	60	Top 60000	4268	60000	0.003	6.10	2.15	4213	0.41561613
Microarray	0	0.9	4241	81946	0.0091	4.43	1.68034698	4241	0.43247021
Microarray	15	0.9	4359	91406	0.0096	4.45	1.70826335	4359	0.49322151
Microarray	60	0.9	4351	186982	0.0198	4.58	1.94748246	4351	0.56839195
Microarray	0	0.7	4242	309284	0.0344	3.20	1.55585666	4242	0.49175417
Microarray	15	0.7	4395	345603	0.0358	3.19	1.55714104	4395	0.52946568
Microarray	60	0.7	4356	619219	0.0653	3.25	1.62504025	4356	0.60423823
RNAseq	0	0.8	832	4304	0.0125	2.49	1.11982083	259	0.54
RNAseq	60	0.8	2273	54240	0.0210	8.66	1.84501845	2075	0.6

Supp Table S2: Modular properties of co-expression networks, at various points in a peroxide (0.5mM) stress time course, using two different methods of module detection: Moduland (ML) and Link Communities (LC). Using both algorithms, modular overlap (as measured by ModuLand overlap, see Methods, or the average number of Link Communities modules per node) is decreased in response to stress.

Dataset	**Time Point (minutes)**	**Threshold**	**ML Modules**	**Links between modules (ML)**	**Module Density (ML)**	**Average node-wise overlap (ML)**	**Average modules per node (link communities – S = 0.4)**
Microarray	0	0.9	636	200981	*1.00*	94.78	7.60
Microarray	15	0.9	641	202952	*0.99*	92.36	7.70
Microarray	60	0.9	439	93144	*0.97*	42.81	5.74
Microarray	0	Top 60000	458	102313	*0.98*	*7.15*	8.88
Microarray	15	Top 60000	551	143856	*0.95*	7.06	6.50
Microarray	60	Top 60000	339	27816	*0.49*	3.63	3.44
RNAseq	0	Top 10000	131	39	*0.00*	1.10	3.67
RNAseq	60	Top 10000	113	13	*0.00*	1.03	3.34
RNAseq	0	Top 20000	152	228	*0.02*	1.47	4.63
RNAseq	60	Top 20000	104	26	*0.00*	1.06	4.55
RNAseq	0	Top 40000	131	252	*0.03*	1.58	9.98
RNAseq	60	Top 40000	110	35	*0.01*	1.18	6.04

Supp Table S3: Hubs in the netwok which decrease co-expression with their neighbours upon stress treatment.

'SPBP8B7.28c':
SPBP8B7.28c-1 - Meiotic chromosome segregation protein P8B7.28c; Required for meiotic chromosome segregation
'SPAC29A4.08c':
cwf8 - Cell cycle control protein cwf8; Involved in mRNA splicing where it associates with cdc5 and the other cwf proteins as part of the spliceosome
'SPBC6B1.10':
prp17 - Pre-mRNA-processing factor 17; Functions in the second step of pre-mRNA splicing. Involved in splicing intron which are longer than 200 nucleotides
'SPAC644.12':
cdc5 - Pre-mRNA-splicing factor cef1; Involved in mRNA splicing and cell cycle control
'SPBC15D4.03':
slm9 - Histone transcription regulator slm9; Probably required for replication-independent chromatin assembly (By similarity). Required for transcriptional silencing in the outer repeat (otr) centromeric repeats and the Tf2 long terminal repeat retrotransposons. May play an indirect role in the regulation of cdc2 and/or wee1 at the G2/M stage of mitosis
'SPAC1782.03':
SPAC1782.03-1 - Uncharacterized protein C1782.03
'SPBC646.13':
sds23 - Protein sds23/moc1; Required for normal DNA replication and for proper mitosis. Induces sexual development and ascus formation
'SPAC13C5.02':
dre4 - DNA replication protein 4
'SPAC821.07c':
moc3 - Transcriptional regulatory protein moc3; Induces sexual development and ascus formation. Also involved in calcium homeostasis
'SPAC2F3.14c':
SPAC2F3.14c-1 - WW domain-containing protein C2F3.14c
'SPBC6B1.07':
prp1 - Pre-mRNA-splicing factor prp1; Involved in pre-mRNA splicing. Interacts with prp6 and prp13. May also be involved in the regulation of the G0-G1/G2 transition. Required for pre-spliceosome formation, which is the first step of pre-mRNA splicing. This protein is associated with snRNP U5. Has a role in branch site-3' splice site selection. Associates with the branch site-3' splice 3'-exon region
'SPBC11B10.09':
cdc2 - Cell division control protein 2; Plays a key role in the control of the eukaryotic cell cycle. It is required for entry into S-phase and mitosis. When complexed with cig2, plays a role in G1-S phase transition. When activated and complexed with the cyclin cdc13, it leads to the onset of mitosis. p34 is a component of the kinase complex that phosphorylates the repetitive C-terminus of RNA polymerase II. Involved in cell cycle arrest induced by defective RNA splicing. Required for phosphorylation of dis1 to ensure accurate chromosome segregation and for the DNA damage checkpoint
'SPBC947.10':
SPBC947.10 - Uncharacterized RING finger protein C947.10
'SPCC364.02c':
bis1 - Stress response protein bis1; Has a role in maintaining cell viability during stationary phase induced by stress response
'SPAC9G1.06c':
cyk3 - Uncharacterized protein C9G1.06c
'SPBC14F5.08':
med7 - Mediator of RNA polymerase II transcription subunit 7; Component of the Mediator complex, a coactivator involved in the regulated transcription of nearly all RNA polymerase II-dependent genes. Mediator functions as a bridge to convey information from gene-specific regulatory proteins to the basal RNA polymerase II transcription machinery. Mediator is recruited to promoters by direct interactions with regulatory proteins and serves as a scaffold for the assembly of a functional preinitiation complex with RNA polymerase II and the general transcription factors (By similarity)
'SPBC106.04':
ada1 - AMP deaminase; AMP deaminase plays a critical role in energy metabolism
'SPBC83.18c':
SPBC83.18c - C2 domain-containing protein C83.18c

Supp Table S4: Hubs in the netwok which increase co-expression with their neighbours upon stress treatment.

'SPAC12G12.13c':

cid14 - Poly(A) RNA polymerase cid14; Required for 3' polyadenylation of the 5.8S and 25S rRNAs as a prelude ot their degradation in the exosome. Involved in the nucleolar organization to ensure faithful chromosome segregation during mitosis

'SPAC3A12.11c':

cwf2 - Pre-mRNA-splicing factor cwc2; Involved in pre-mRNA splicing

'SPBP35G2.08c':

air1 - Protein air1; Component of the TRAMP (TRF4) and TRAMP5 complexes which have a poly(A) RNA polymerase activity and are involved in a post- transcriptional quality control mechanism limiting inappropriate expression of genetic information. Polyadenylation is required for the degradative activity of the exosome on several of its nuclear RNA substrates like cryptic transcripts generated by RNA polymerase II and III, or hypomethylated pre-tRNAi-Met. Both complexes polyadenylate RNA processing and degradation intermediates of snRNAs, snoRNAs and mRNAs that accumulate in strains lacking a fun [...]

'SPBC1D7.04':

mlo3 - mRNA export protein mlo3; Has a role in the mRNA export process. Interferes with mitotic chromosome segregation when overexpressed

'SPBC409.05':

skp1 - Suppressor of kinetochore protein 1; Required for cig2 degradation in the G2 and M phases of the cell cycle. Together with pof6, essential for septum processing and cell separation. Involved in mitotic progression, essential for the execution of anaphase B; required for coordinated structural alterations of mitotic spindles and segregation of nuclear membrane structures at anaphase. Involved in the DNA damage checkpoint pathway and maintenance of genome integrity

'SPAC31G5.13':

rpn11 - 26S proteasome regulatory subunit rpn11; Acts as a regulatory subunit of the 26 proteasome which is involved in the ATP-dependent degradation of ubiquitinated proteins

'SPBC409.06':

uch2 - Ubiquitin carboxyl-terminal hydrolase 2; Ubiquitin-protein hydrolase is involved both in the processing of ubiquitin precursors and of ubiquinated proteins. This enzyme is a thiol protease that recognizes and hydrolyzes a peptide bond at the C-terminal glycine of ubiquitin

'SPBC12D12.01':

sad1 - Spindle pole body-associated protein sad1; Associates with the spindle pole body and maintains a functional interface between the nuclear membrane and the microtubule motor proteins. Involved in chromosome segregation during meiosis where it associates with the telomeres

'SPAC8E11.02c':

rad24 - DNA damage checkpoint protein rad24; Required for the DNA damage checkpoint that ensures that DNA damage is repaired before mitosis is attempted. Acts as a negative regulator of meiosis by antagonizing the function of mei2. It inhibits the association of meiRNA (a non-coding RNA molecule required for the nuclear mei2 dot formation) to the phosphorylated but not to the unphosphorylated form of mei2 in vitro

'SPAC4F8.13c':

rng2 - Ras GTPase-activating-like protein rng2; Required for cytokinesis. Component of the contractile F-actin ring; required for its construction following assembly of F-actin at the division site

'SPAC664.01c':

swi6 - Chromatin-associated protein swi6; Recognizes and binds histone H3 tails methylated at 'Lys-9', leading to epigenetic repression. Involved in the repression of the silent mating-type loci MAT2 and MAT3. May compact MAT2/3 into a heterochromatin-like conformation which represses the transcription of these silent cassettes

'SPBP16F5.03c':

tra1 - Transcription-associated protein 1; Essential component of histone acetyltransferase (HAT) complexes, which serves as a target for activators during recruitment of HAT complexes. Essential for vegetative growth. Functions as a component of the transcription regulatory histone acetylation (HAT) complexes SAGA, SALSA and SLIK. At the promoters, SAGA is required for recruitment of the basal transcription machinery. It influences RNA polymerase II transcriptional activity through different activities such as TBP interaction and promoter selectivity, interaction with transcription activator [...]

'SPBC28F2.12':

rpb1 - DNA-directed RNA polymerase II subunit rpb1; DNA-dependent RNA polymerase catalyzes the transcription of DNA into RNA using the four ribonucleoside triphosphates as substrates. Largest and catalytic component of RNA polymerase II which synthesizes mRNA precursors and many functional non-coding RNAs. Forms the polymerase active center together with the second largest subunit. Pol II is the central component of the basal RNA polymerase II transcription machinery. It is composed of mobile elements that move relative to each other. RPB1 is part of the core element with the central large cl [...]

'SPAC1687.20c':

mis6 - Inner centromere protein mis6; Has a role in the maintenance of core chromatin structure and kinetochore function...

Supp Table S5: Changes in Betweenness Centrality (BC) and subnetwork specific BC (BCsub) statistics in abundance weighted PPIs at the three time points considered. Only GO sub-networks where significant changes were found are shown.

Statistic	No stress (t=0)	Stress (60')	Late Stress(240')
Maximum BC value	0.30	0.27	0.31
BC standard deviation	0.02	0.02	0.02
Mean BCsub transcription DNA dep.	3.6e-05	5.6e-05	5.6e-05
Mean BCsub cytokinesis	4.5e-07	9.0e-07	9.0e-07
Mean BCsub Nucleocyt. transport	8.5e-06	9.8e-06	9.5e-06
Mean BCsub Chrom. Modification	1.2e-05	1.3e-05	1.4e-05

Supplementary table S6: Genes that have much higher BC after stress (Top 20 genes ranked by fold change)

'SPCC16C4.18c':

taf6 - Transcription initiation factor TFIID subunit 6; TAFs are components of the transcription factor IID (TFIID) complex that are essential for mediating regulation of RNA polymerase transcription (By similarity)

'SPBC4B4.03':

rsc1 - Chromatin structure-remodeling complex subunit rsc1; Component of the chromatin structure remodeling complex (RSC), which is involved in transcription regulation and nucleosome positioning. Controls particularly membrane and organelle development genes

'SPBC3E7.14':

smf1 - Probable small nuclear ribonucleoprotein F; Probable common Sm protein, is found in U1 and U2 snRNPs (By similarity)

'SPBC16C6.07c':

rpt1 - 26S protease regulatory subunit 7 homolog; The 26S protease is involved in the ATP-dependent degradation of ubiquitinated proteins. The regulatory (or ATPase) complex confers ATP dependency and substrate specificity to the 26S complex (By similarity)

'SPBC4.07c':

mts2 - 26S protease regulatory subunit 4 homolog; The 26S protease is involved in the ATP-dependent degradation of ubiquitinated proteins. The regulatory (or ATPase) complex confers ATP dependency and substrate specificity to the 26S complex

'SPBC15D4.14':

taf73 - Transcription initiation factor TFIID subunit taf73; TAFs are components of the transcription factor IID (TFIID) complex that are essential for mediating regulation of RNA polymerase transcription. Regulates the genes involved in ubiquitin-dependent proteolysis during the progression of M-phase of mitosis

'SPBC839.10':

SPBC839.10 - Uncharacterized RNA-binding protein C839.10

'SPBC32F12.11':

SPBC32F12.11-1 - Glyceraldehyde-3-phosphate dehydrogenase 1

SPBC354.12-1 - Glyceraldehyde-3-phosphate dehydrogenase 2

'SPBC16A3.15c':

nda2 - Tubulin alpha-1 chain; Tubulin is the major constituent of microtubules. It binds two moles of GTP, one at an exchangeable site on the beta chain and one at a non-exchangeable site on the alpha-chain

'SPBC409.07c':

wis1 - Protein kinase wis1; Dosage-dependent regulator of mitosis with serine/ threonine protein kinase activity. May play a role in the integration of nutritional sensing with the control over entry into mitosis. It may interact with cdc25, wee1 and win1. May activate sty1

'SPAC19A8.13':

usp101 - U1 small nuclear ribonucleoprotein 70 kDa homolog; Involved in nuclear mRNA splicing (By similarity). Essential for growth

'SPBC16E9.12c':

pab2 - Polyadenylate-binding protein 2

'SPAC22H12.04c':

SPAC13G6.02c-1 - 40S ribosomal protein S3aE-A

SPAC22H12.04c-1 - 40S ribosomal protein S3aE-B

'SPAC23C4.15':

rpb5 - DNA-directed RNA polymerases I, II, and III subunit RPABC1; DNA-dependent RNA polymerase catalyzes the transcription of DNA into RNA using the four ribonucleoside triphosphates as substrates. Common component of RNA polymerases I, II and III which synthesize ribosomal RNA precursors, mRNA precursors and many functional non-coding RNAs, and small RNAs, such as 5S rRNA and tRNAs, respectively. Pol II is the central component of the basal RNA polymerase II transcription machinery. Pols are composed

of mobile elements that move relative to each other. In Pol II, RPB5 is part of the lower j [...]

'SPACUNK4.06c':

rpb7 - DNA-directed RNA polymerase II subunit rpb7; DNA-dependent RNA polymerase catalyzes the transcription of DNA into RNA using the four ribonucleoside triphosphates as substrates. Component of RNA polymerase II which synthesizes mRNA precursors and many functional non-coding RNAs. Pol II is the central component of the basal RNA polymerase II transcription machinery. It is composed of mobile elements that move relative to each other. RPB7 is part of a subcomplex with RPB4 that binds to a pocket formed by RPB1, RPB2 and RPB6 at the base of the clamp element. The RBP4-RPB7 subcomplex seems [...]

'SPAC6F12.15c':

cut9 - Anaphase-promoting complex subunit cut9; Component of the anaphase-promoting complex/cyclosome (APC/C), a cell cycle-regulated E3 ubiquitin-protein ligase complex that controls progression through mitosis and the G1 phase of the cell cycle. The APC/C is thought to confer substrate specificity and, in the presence of ubiquitin-conjugating E2 enzymes, it catalyzes the formation of protein-ubiquitin conjugates that are subsequently degraded by the 26S proteasome. May play a pivotal role in the control of anaphase

'SPAC2C4.03c':

smd2 - Probable small nuclear ribonucleoprotein Sm D2; Required for pre-mRNA splicing. Required for snRNP biogenesis (By similarity)

'SPBC19G7.05c':

bgs1 - 1,3-beta-glucan synthase component bgs1; Required for the assembly of the division setum and maintenance of cell polarity

'SPAC9G1.02':

wis4 - MAP kinase kinase kinase wis4; Involved in a signal transduction pathway that is activated in under conditions of heat shock, oxidative stress or limited nutrition. Unlike win1, it is not activated by changes in the osmolarity of the extracellular environment. Activates the wis1 MAP kinase kinase by phosphorylation

'SPAC18B11.10':

tup11 - Transcriptional repressor tup11; Transcriptional repressor

Corresponding BC values:

	BC	BC stress (60)	BC stress (240)	BC stress 60/BC
SPCC16C4.18c	0.00	0.02	0.00	904.00
SPBC4B4.03	5.9e-05	0.01	0.00	100.64
SPBC3E7.14	0.00	0.04	0.01	26.98
SPBC16C6.07c	5.4e-06	0.00	0.00	22.32
SPBC4.07c	0.01	0.08	0.05	16.03
SPBC15D4.14	0.00	0.03	0.00	13.35
SPBC839.10	0.01	0.08	0.01	8.29
SPBC32F12.11	0.02	0.15	0.16	6.45
SPBC16A3.15c	0.00	0.01	0.00	5.81
SPBC409.07c	0.00	0.01	0.02	5.52
SPAC19A8.13	0.02	0.09	0.03	5.02
SPBC16E9.12c	6.3e-06	3.1e-05	0.00	4.92
SPAC22H12.04c	0.01	0.06	0.00	4.83
SPAC23C4.15	0.00	0.00	0.00	4.72
SPACUNK4.06c	0.04	0.16	0.18	4.37
SPAC6F12.15c	0.00	0.01	0.00	4.08
SPAC2C4.03c	0.01	0.05	0.07	4.01
SPBC19G7.05c	0.00	0.02	0.02	3.89
SPAC9G1.02	0.00	0.01	0.02	3.80
SPAC18B11.10	0.01	0.02	0.02	3.69

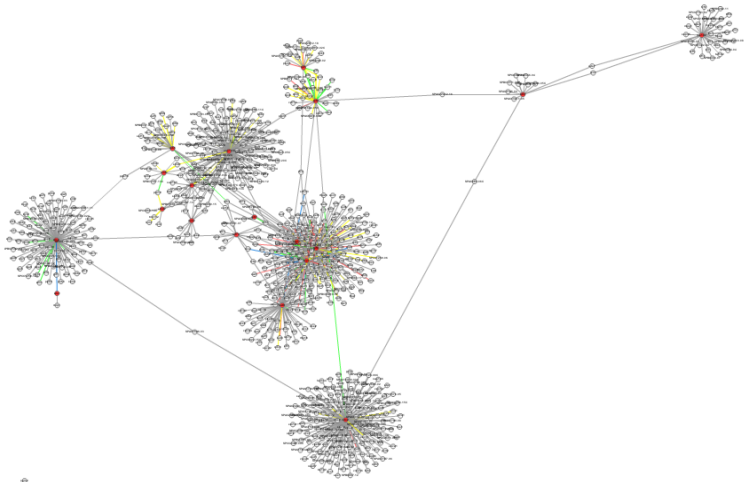


Figure S4: Network of predicted and known (coloured) interactions for the top 20 genes increasing BC upon stress-treatment. Note the connections between the different proteins in the set (red). From www.bahlerlab.info/PInt, see website for more details.

Supplementary table S7: Genes that have higher BC at the late time-point(240') compared to 60' (Top 20 genes ranked by fold change)

'SPBC16A3.05c':	
	rae1 - Poly(A)+ RNA export protein; Required for mitotic cell growth as well as for spore germination. Functions in cell cycle progression through trafficking of proteins required for mitosis. Has a role in the mRNA export process
'SPBC646.09c':	
	int6 - Eukaryotic translation initiation factor 3 subunit E; Component of the eIF-3 complex, which binds to the 40S ribosome and promotes the binding of methionyl-tRNAi and mRNA. Required for maintaining the basal level of atf1 and for transcriptional activation of core environmental stress response genes (CESR genes) in response to histidine starvation. May positively regulate proteasome activity. Required for nuclear localization of the proteasome subunit rpn501/rpn502
'SPBC17D11.05':	
	tif32 - Eukaryotic translation initiation factor 3 subunit A; Component of the eukaryotic translation initiation factor 3 (eIF-3) complex, which is involved in protein synthesis and, together with other initiation factors, stimulates binding of mRNA and methionyl-tRNAi to the 40S ribosome
'SPAC23E2.01':	
	fep1 - Iron-sensing transcription factor 1; Represses the expression of the iron transporter fio1 in response to high iron concentrations. Binds to the consensus sequence 5'-[AT]GATAA-3'. Also represses the expression of str1, str2 and str3
'SPBC14F5.04c':	
	pgk1 - Phosphoglycerate kinase
'SPCC1795.11':	
	ded1 - ATP-dependent RNA helicase ded1; ATP-binding RNA helicase involved in translation initiation. Remodels RNA in response to ADP and ATP concentrations by facilitating disruption, but also formation of RNA duplexes (By similarity). Inactivation of ded1 blocks mitotic cell cycle progression at G1 and G2/M. Induces sexual development and ascus formation
'SPAC4F10.11':	
	spn1 - Septin homolog spn1; Plays a role in the cell cycle. Involved in a late stage of septum formation leading to the separation of the daughter cells
'SPBC409.07c':	
	wis1 - Protein kinase wis1; Dosage-dependent regulator of mitosis with serine/ threonine protein kinase activity. May play a role in the integration of nutritional sensing with the control over entry into mitosis. It may interact with cdc25, wee1 and win1. May activate sty1
'SPAC29A4.08c':	
	cwf8 - Cell cycle control protein cwf8; Involved in mRNA splicing where it associates with cdc5 and the other cwf proteins as part of the spliceosome
'SPAC9G1.02':	
	wis4 - MAP kinase kinase kinase wis4; Involved in a signal transduction pathway that is activated in under conditions of heat shock, oxidative stress or limited nutrition. Unlike win1, it is not activated by changes in the osmolarity of the extracellular environment. Activates the wis1 MAP kinase kinase by phosphorylation
'SPCC18B5.11c':	
	Cds1 - Serine/threonine-protein kinase cds1; Has a role in the DNA replication-monitoring S/G2 checkpoint system. It is responsible for blocking mitosis in the S phase. It monitors DNA synthesis by interacting with DNA polymerase alpha and sends a signal to block the onset of mitosis while DNA synthesis is in progress. Phosphorylates rad60
'SPAC22E12.07':	
	rna1 - Ran GTPase-activating protein 1; GTPase activator for the nuclear Ras-related regulatory protein spi1 (Ran), converting it to the putatively inactive GDP- bound state
'SPCC576.03c':	
	tpx1 - Peroxiredoxin tpx1; Physiologically important antioxidant which constitutes an enzymatic defense against sulfur-containing radicals. Can provide protection against a thiol-containing oxidation system but not against an oxidation system without thiol. Required for the peroxide-induced activation of pap1 via its oxidation and for the nuclear accumulation of pap1. Required also for activation of sty1. Reduced by srx1 and this regulation acts as a molecular switch controlling the transcriptional response to hydrogen peroxide
'SPCC622.09':	
	htb1 - Histone H2B-alpha; Core component of nucleosome. Nucleosomes wrap and compact DNA into chromatin, limiting DNA accessibility to the cellular machineries which require DNA as a template. Histones thereby play a central role in transcription regulation, DNA repair, DNA replication and chromosomal stability. DNA accessibility is regulated via a complex set of post-translational modifications of histones, also called histone code, and nucleosome remodeling
'SPAC13G7.08c':	
	crb3 - Pre-rRNA-processing protein crb3/ipi3; Involved in the processing of ITS2 sequences from 35S pre-rRNA (By similarity)
'SPAC20G8.05c':	
	cdc15 - Cell division control protein 15; After the onset of mitosis, forms a ring-like structure which colocalizes with the medial actin ring. Appears to mediate cytoskeletal rearrangements required for cytokinesis. Essential for viability

'SPAC11H11.06':

arp2 - Actin-related protein 2; Functions as ATP-binding component of the Arp2/3 complex which is involved in regulation of actin polymerization and together with an activating nucleation-promoting factor (NPF) mediates the formation of branched actin networks. Seems to contact the pointed end of the daughter actin filament (By similarity). During cytokinesis it colocalizes to the cortical actin patches until spetation is complete. Has a role in the mobility of these patches. Essential for viability

'SPAC3C7.14c':

obr1 - P25 protein; Unknown. Target of pap1 transcription factor. Confers brefeldin A resistance in S.pombe

'SPBC800.05c':

tub1 - Tubulin alpha-2 chain; Tubulin is the major constituent of microtubules. It binds two moles of GTP, one at an exchangeable site on the beta chain and one at a non-exchangeable site on the alpha-chain

'SPAC2C4.03c':

smd2 - Probable small nuclear ribonucleoprotein Sm D2; Required for pre-mRNA splicing. Required for snRNP biogenesis (By similarity)

Corresponding BC values:

	BC	BC stress (60)	BC stress (240)	BC stress (60) / BC	BC stress (240) / BC stress (60)
SPBC16A3.05c	0.00	0.00	0.01	0.33	14.24
SPBC646.09c	0.01	0.01	0.02	0.41	4.95
SPBC17D11.05	0.01	0.01	0.04	1.34	4.58
SPAC23E2.01	0.00	0.00	0.00	0.52	3.80
SPBC14F5.04c	0.01	0.00	0.01	0.27	2.41
SPCC1795.11	0.08	0.07	0.14	0.79	2.15
SPAC4F10.11	2.5e-06	6.3e-06	1.2e-05	2.52	1.90
SPBC409.07c	0.00	0.01	0.02	5.52	1.92
SPAC29A4.08c	0.08	0.05	0.10	0.62	1.91
SPAC9G1.02	0.00	0.01	0.02	3.80	1.84
SPCC18B5.11c	0.01	0.01	0.02	0.66	1.80
SPAC22E12.07	0.00	0.00	0.01	1.28	1.53
SPCC576.03c	0.02	0.00	0.00	0.14	1.51
SPCC622.09	0.00	0.01	0.01	1.58	1.48
SPAC13G7.08c	0.02	0.02	0.02	0.77	1.47
SPAC20G8.05c	0.03	0.02	0.03	0.84	1.47
SPAC11H11.06	0.00	0.00	0.00	0.86	1.38
SPAC3C7.14c	0.01	0.01	0.01	1.35	1.34
SPBC800.05c	0.01	0.01	0.01	0.65	1.34
SPAC2C4.03c	0.01	0.05	0.07	4.01	1.31

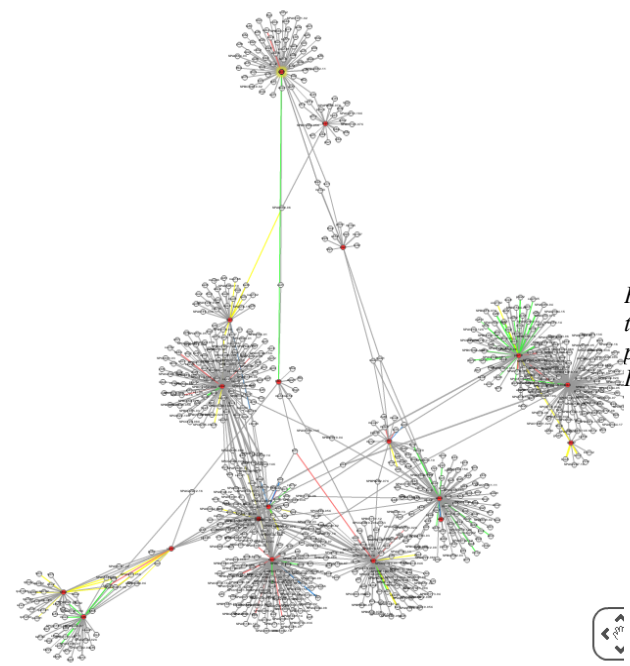


Figure S5:Network of predicted and known (coloured) interactions for the top 20 genes increasing BC in late stress compared to stress. Note the presence of many interactions interconnecting the proteins in the set (red). From www.bahlerlab.info/PInt, see website for more details.