



Supporting Online Material for

Rewiring of Genetic Networks in Response to DNA Damage

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Published 3 December 2010, *Science* **330**, 1385 (2010)
DOI: 10.1126/science.1195618

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Other Supporting Online Material for this manuscript includes the following: (available at www.sciencemag.org/cgi/content/full/330/6009/1385/DC1)

Table S2 as a zipped archive: [1195618 table s2.zip](#)

MATERIALS AND METHODS

E-MAP experiments. Strain construction, plating of mutants, mutant selection, and scoring of genetic interactions in each condition were performed using a previously defined protocol (S_1 , S_2). Using a replica pinning robot (Singer Instruments; UK), haploid double mutants were simultaneously grown at 30 degrees C on agar plates which were either untreated or contained MMS. For the MMS map, double mutants were grown under the prescribed selective media with the addition of 0.02% MMS for 72 hours. Plates were photographed and analyzed quantitatively to measure colony size. In either untreated or MMS-treated conditions, colony sizes were based on 12 replicate measurements: 3 independent cultures \times 2 colony replicas per plate \times 2 marker orientations (*geneA* Δ ::Kan *geneB* Δ ::Nat vs. *geneB* Δ ::Kan *geneA* Δ ::Nat). For a given double mutant combination, the resulting experimental data were used to assign a quantitative S -score based on a modified T-test that compares the observed double mutant growth rate to that expected assuming no interaction exists. As in previous work, $S \leq -2.5$ was considered a significant negative interaction indicating synthetic sickness or lethality, and $S \geq 2.0$ was considered a significant positive interaction indicating an alleviating or epistatic genetic interaction (S_1).

Differential interaction scoring system. Differential interactions were evaluated by first computing the difference in S -score ($S_1 - S_2$) of a double gene deletion strain grown in two conditions 1 and 2. To estimate the null distribution of this difference, replicate S -scores were obtained from a set of 8,018 double deletions assayed in untreated conditions in both of two previously published E-MAPs (**fig. S3**) (S_3, S_4). We found that this null distribution had a standard deviation that increased non-linearly with the magnitude of S -score (**fig. S3**). This deviation was estimated as a non-parametric function $\sigma(S_1 + S_2)$ of the sum of S -scores using a sliding window. The differential interaction p -value was then computed:

$$p = 1 - \Phi \left| \frac{S_1 - S_2}{\sigma} \right|$$

where Φ is the cumulative distribution function of the standard normal distribution. To categorize this p -value, the direction of change in S -score of condition 1 relative to condition 2 was used. In our study, condition 1 was set to MMS-treated media and condition 2 was set to

untreated media. Thus, an interaction in which the S-score in condition 1 is higher than that of condition 2 is considered “positive differential”, and an interaction in which condition 1 is less than that of condition 2 is considered “negative differential” (**table S2**). This procedure was largely insensitive to whether the null model was generated based on comparison of untreated or MMS-treated E-MAP scores.

In static maps, the S-score of a double mutant is proportional to the ratio of its observed-to-expected growth rates. For example, a negative genetic interaction implies that the observed double mutant growth rate is less than its expected growth rate (SI). Thus, a change from a positive interaction in untreated (UT) conditions to a negative interaction in MMS (a negative differential interaction) indicates that:

$$\left(\frac{O_{UT}}{E_{UT}}\right) > 1 > \left(\frac{O_{MMS}}{E_{MMS}}\right) \text{ or, equivalently: } \left(\frac{O_{MMS}}{O_{UT}}\right) < \left(\frac{E_{MMS}}{E_{UT}}\right)$$

Where O_x and E_x represent the observed and expected double mutant growth rates with respect to condition x . Thus, the observed double-mutant fitness in MMS with respect to UT is less than expected, resulting in differential sickness or lethality. Positive differential interactions are computed similarly, with the inequalities reversed.

Network enrichment. The untreated, MMS-treated, and differential genetic networks were each evaluated for their enrichment for genes involved in DNA damage response (**Fig. 1E**) as well as other functional categories (**Fig. 1F**). Network enrichment is based on a hypergeometric test that determines if the rate of interaction is statistically higher for genes in a functional category than for all 418 genes included in the E-MAP:

$$p = \sum_{i=x}^n \frac{\binom{M}{i} \binom{N-M}{n-i}}{\binom{N}{n}}$$

i : Number of interactions observed that involve genes in category

n : Number of interactions possible that involve genes in category

M : Total number of interactions observed over all genes

N : Total number of interactions possible over all genes

Identification and comparison of modules by hierarchical clustering. Separately, each of the MMS and untreated maps were subjected to consensus hierarchical clustering (S5). For each condition, the top of the hierarchy defines one module encompassing all 418 genes in the map, and the bottom of the hierarchy defines 418 modules with each module containing exactly one gene. A specified number of modules is defined by extracting clusters at the appropriate level of the hierarchy. The set of modules is decomposed into a network containing all possible within-module gene pairs. The overlap of these networks across conditions or with protein-protein interaction networks is then determined. The expected overlap is computed by randomly shuffling the assignment of genes to modules in the untreated map.

Assembly of the module map. The module map (Fig. 4B) was generated as previously described (S6) with the following modifications. A physical protein-protein interaction network was downloaded from the BioGRID database excluding interactions annotated as “genetic” and limited to interactions supported by two or more publications (table S4). These data were combined with interactions based on tandem affinity purification followed by mass spectrometry having PE-score ≥ 2 (S7). Members of a module were required to form a connected component within this physical network. Modules were initially identified using the maximum absolute value of the *S*-score in either condition using a cluster reward of 5. Within-module scores were calculated using both the genetic interaction strength as well as correlation of genetic interaction profiles. Links between modules were determined based on the hypergeometric enrichment for either positive or negative differential interactions among all possible pairs of members between modules. Modules links with enrichment *p*-value ≤ 0.01 are shown (table S6).

Real-time PCR. Cultures of cells were grown in triplicate to an OD600 of 0.8 and either treated with 0.03% MMS for 1 hour or left untreated. RNA was extracted using Trizol reagent (Invitrogen: CA, USA) and contaminating genomic DNA was removed using DNaseI (Ambion: TX, USA). RNA was reversed transcribed using Superscript III (Invitrogen) and amplified using an iCycler (BioRad; CA, USA). The resulting mRNA expression levels were tested against ACT1 mRNA levels as control. Resulting data was analyzed using the $\Delta\Delta C_t$ method, error bars indicate standard deviation.

Western blotting and FACS. To probe for activity of γ H2AX, cells were grown to an OD600 of 0.8 in media containing 2% glucose and shifted to media containing 2% galactose for 3 hours to

induce expression of P_{gal1} -*CBF1*, then further treated with 0.03% MMS for 1 hour. Total protein was extracted using YEX lysis (S8) and probed with anti- γ H2AX (Activemotif; NY, USA) and anti-PGK1 (Invitrogen) antibodies. For all FACS experiments involving overexpression of *CBF1*, samples were shifted to galactose media for three hours prior to MMS treatment to induce expression of P_{gal1} -*CBF1*. FACS is performed as described (S9). Htz1 acetylation analysis was performed as described (S10). Anti-Rpn8 is a gift from Dan Finley (Harvard Medical School; MA, USA). Anti-acetyl K8, K10 and K14 antibodies are from Millipore (CA, USA). All *mec1* Δ strains are in the *sml1* Δ background (S11, S12).

Phospho-proteomics analysis. Whole cell lysate from yeast wild-type and *pph3* Δ strains were analyzed and quantified using a label free phospho-proteomic method as described in detail in (S13).

SUPPLEMENTAL FIGURES

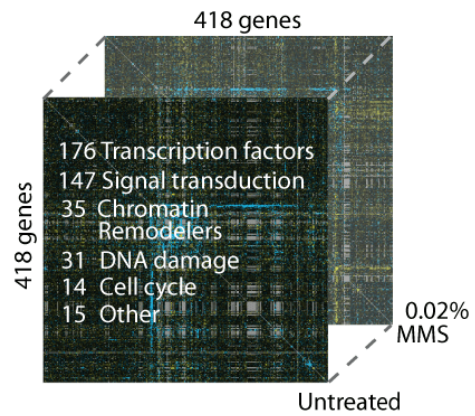


Fig. S1: Composition of the 418 genes in this study. Double mutants were measured in both untreated and 0.02% MMS.

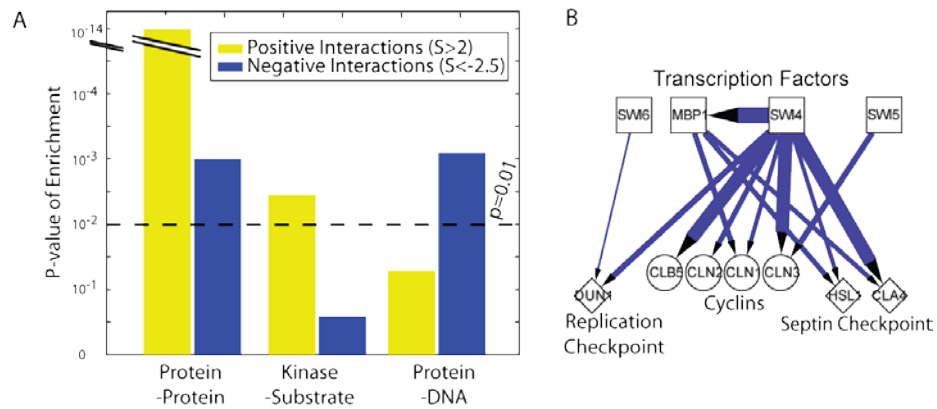


Fig. S2: Analysis of physical interactions overlapping with the untreated E-MAP. **(A)** Enrichment of positive and negative genetic interactions for various physical interaction datasets. Sources: Protein-protein ($S7$); Kinase-substrate ($S4$); Protein-DNA ($S14$). Enrichment was calculated based on a hypergeometric overlap of two interaction datasets as in ref. ($S6$). **(B)** Subnetwork highlighting negative genetic interactions among cell-cycle transcription factors (top layer) and their downstream target genes as measured previously by physical protein-DNA interactions (bottom layer). Thickness of edge corresponds to strength of negative interactions.

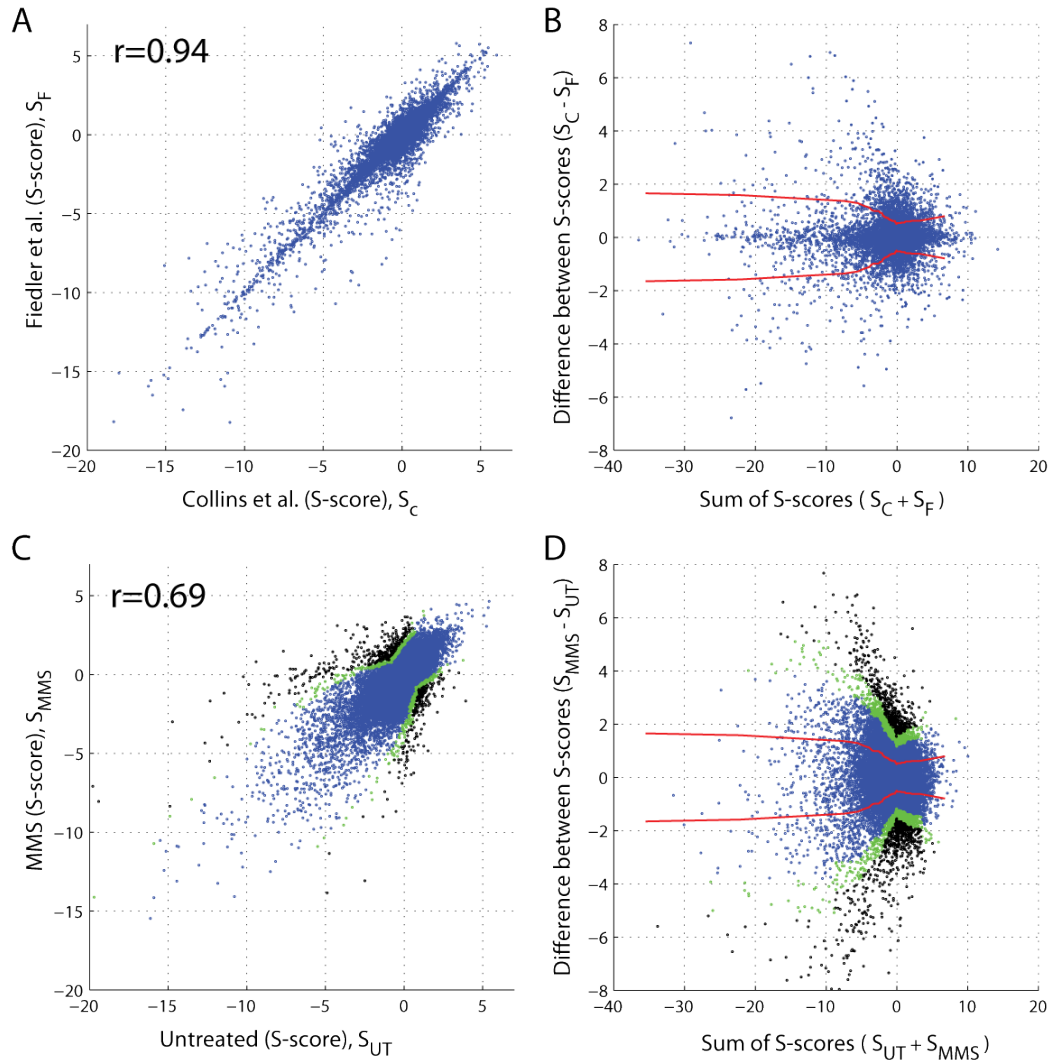


Fig. S3: Determination of differential genetic interactions. When comparing two untreated E-MAPs, we found that the difference in S-score over the same gene pair was linked with the magnitude of S. **(A)** Background model comparing S-scores for 8,018 double mutants measured independently in two different E-MAPs (S_3 , S_4). Pearson correlation (r) of scores is shown. **(B)** Same data plotted as the sum of S-scores on the x-axis and the difference between S-scores on the y-axis. Along a sliding window, the observed mean difference is near zero but the variance (red line) increases with stronger negative S-scores or positive S-scores. **(C)** Scatterplot of untreated versus MMS-treated S-scores from the growth data generated in this study. **(D)** Same data plotted as in (B). Double deletions whose difference in S-score between conditions is significantly greater than expected are indicated (green, $p \leq 0.01$; black, $p \leq 0.001$).

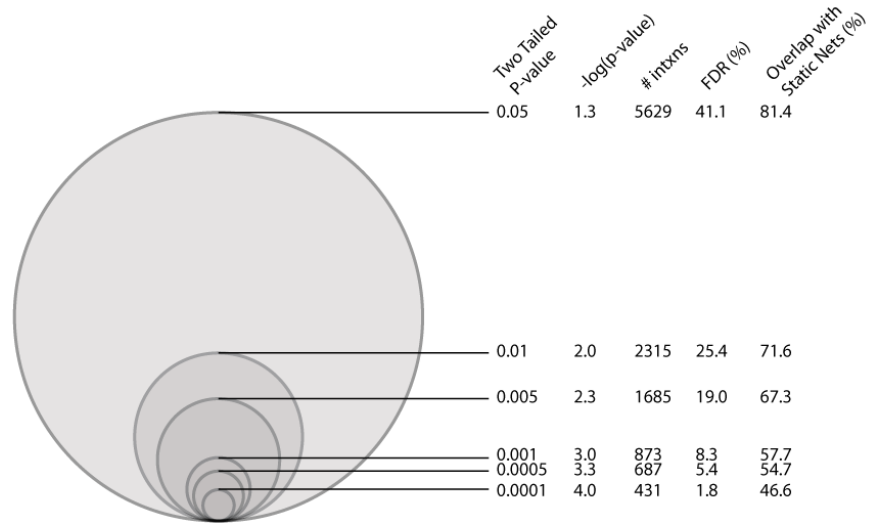


Fig S4: Characterization of differential genetic interactions assigned at increasing levels of significance. The False Discovery Rate (FDR) is based on the number of interactions expected at random after thresholding at the p-values listed. For each differential network size, the percentage overlap with genetic interactions identified in either static network (untreated or MMS-treated) is shown.

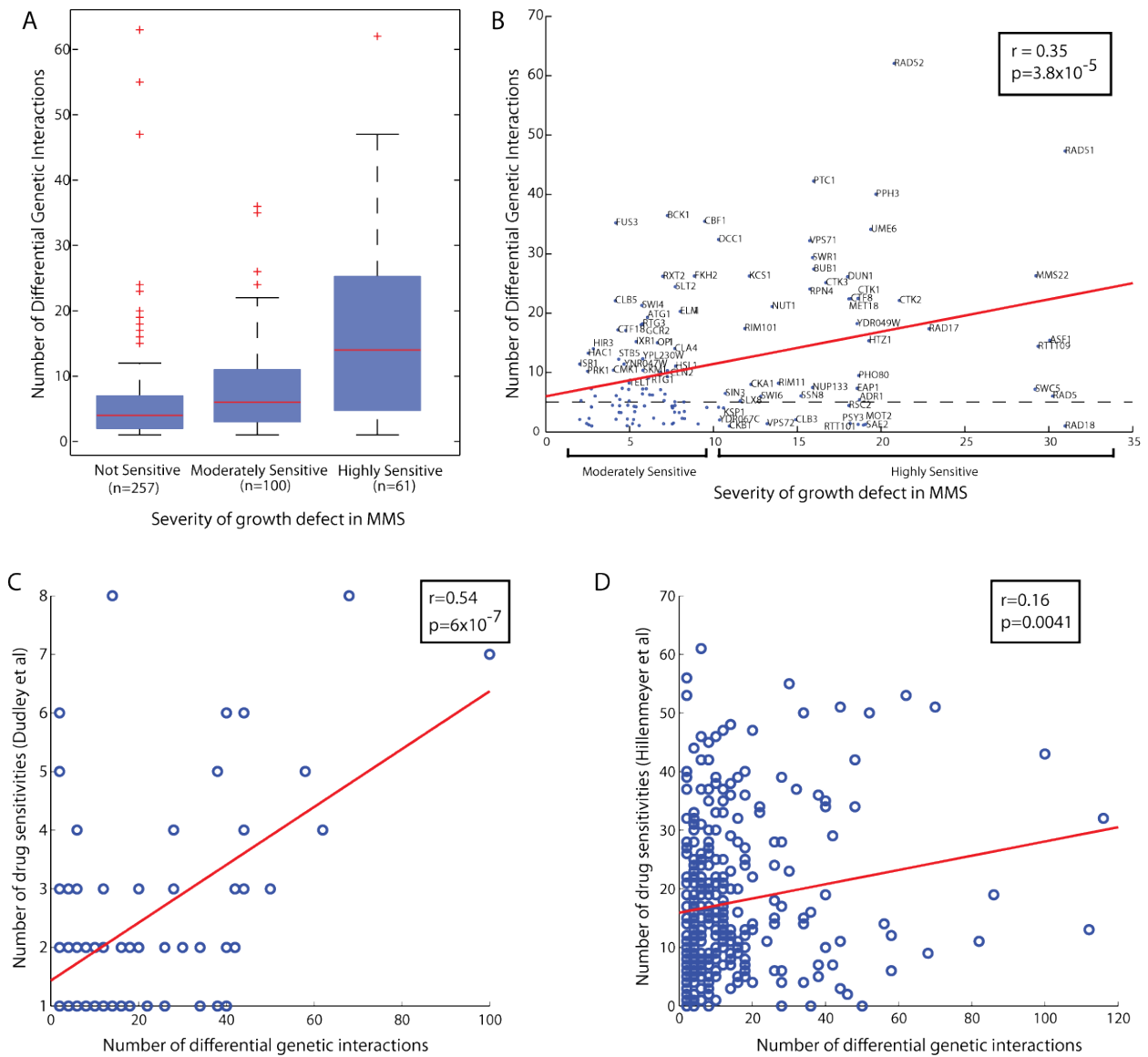


Fig. S5: The number of differential genetic interactions predicts sensitivity to MMS and to multiple drugs. **(A)** All 418 genes in the E-MAP are binned based on the MMS growth defect of the corresponding gene knockout strain (*S15*). The distribution of interactions in each bin is summarized with a standard box plot. **(B)** For genes identified as MMS sensitive, quantitative estimates of that sensitivity are significantly correlated with the number of differential genetic interactions for each gene (red regression line). The average number of differential genetic interactions over all genes is shown (dotted line). **(C, D)** Previous studies have measured single-gene knockout sensitivities against a broad panel of drugs and conditions. The number of differential genetic interactions for a gene is plotted against the number of drugs for which the gene knockout is sensitive in (C) Dudley *et al.* (*S16*) or (D) Hillenmeyer *et al.* (*S17*).

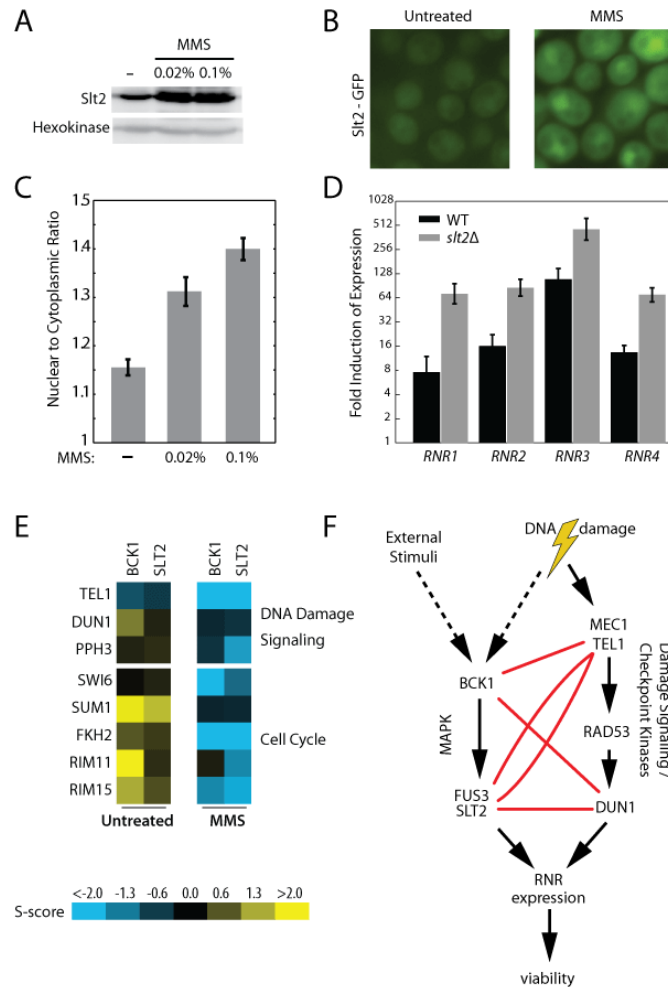


Fig. S6: MAPK pathways in the DNA damage response. **(A)** Immunoblot of GFP-tagged Slt2 indicates an increase in abundance in response to MMS treatment for 1 hour. Hexokinase is used as a loading control. **(B)** Fluorescence microscopy of Slt2-GFP cells before and after exposure to 0.1% MMS for 1 hour. Exposure time is the same for both panels. **(C)** Nuclear accumulation of Slt2 in response to MMS. Mean cytoplasmic versus nuclear fluorescent intensity was quantified for 20 random cells in each condition. Error bars are s.e.m. **(D)** Increase in expression of RNR subunits in response to 0.03% MMS for 1 hour using real-time PCR in wild-type cells and an *slt2Δ* mutant. **(E)** MAPK pathway members *BCK1* and *SLT2* show negative differential interactions with DNA damage signaling pathway members and with cell cycle regulators. **(F)** Potential role of MAPK pathways in the response to DNA damage based on negative differential interactions (red). This role is consistent with a previous report in which human p38/MAPK pathways have been suggested to regulate the cell cycle in a parallel pathway to *CHK1/CHK2* after UV-induced DNA damage (*S18*). It is possible that the Slt2 MAPK pathway operates in an independent but redundant fashion with the *MEC1/TEL1* checkpoint kinase pathway.

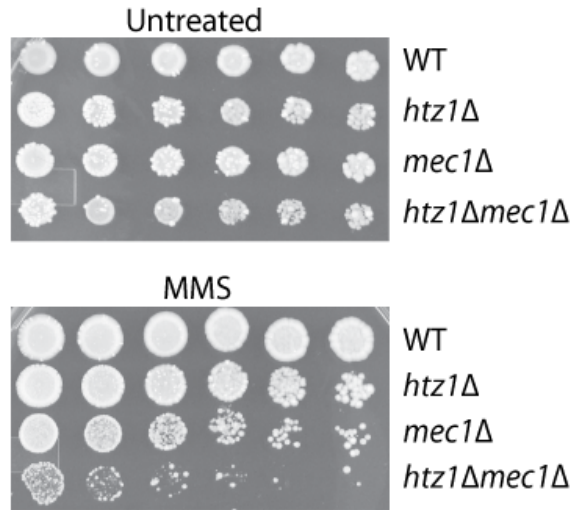


Fig. S7: Synthetic sickness of *htz1Δ* with *mec1Δ* in MMS. Plates were grown for 3 days at 30 degrees with 0.02% MMS. All *mec1Δ* strains were generated in an *sml1Δ* background (*S11*, *S12*).

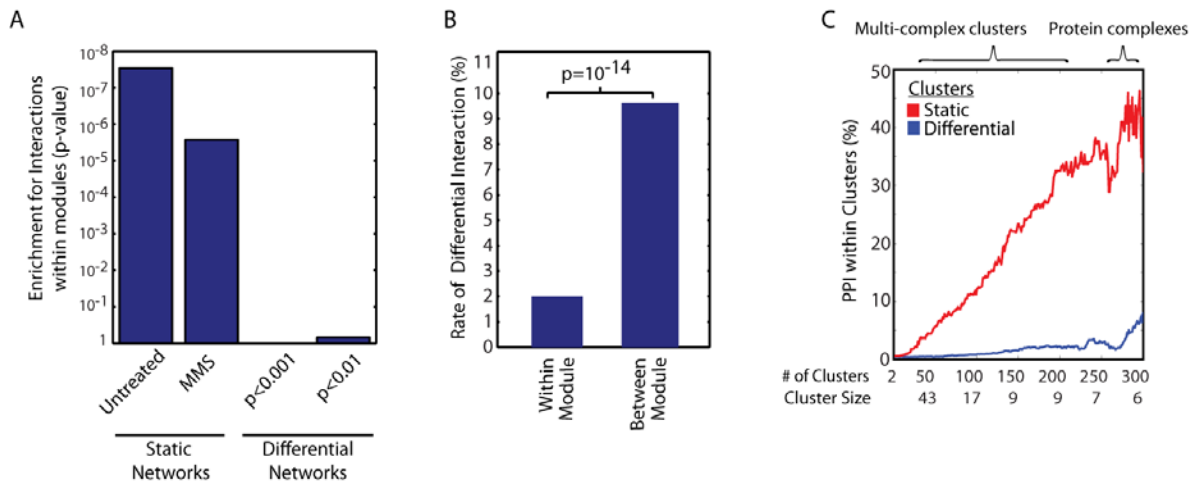


Fig. S8: Differential interactions reflect biological modularity **(A)** Enrichment of various static and differential networks for known protein complexes and pathways (modules, **table S1**). Static networks were defined based on S -score ($S \geq +2$ or $S \leq -2.5$) in each condition, differential networks were based on both positive and negative differential interactions identified at a p -value threshold. Enrichment is calculated based on the hypergeometric test as in (S6). **(B)** Percentage of gene pairs within and between modules that have differential interactions. **(C)** Alternative view in which modules are defined by hierarchical clustering of genetic interaction profiles independently in each condition, with the total number of clusters running from 2 to 300 over a series of clustering runs. Cluster Size refers to the maximum number of genes assigned to any cluster. Y-axis shows the percentage of physical interactions among gene pairs that cluster together in both conditions (static, red) versus those that cluster together in one condition only (differential, blue).

SUPPLEMENTAL REFERENCES

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SUPPLEMENTARY TABLES

Supplementary Table S1: List of genes in the E-MAP and their annotations. Functional annotations of function and module membership were curated manually. MMS sensitivity is from Begley et al. (S15).

Supplementary Table S2: List of S-scores and differential p-values determined in this study. For each gene pair the Untreated S-Score, the MMS S-score, and the conditional p-value are listed. For the differential p-value, positive values indicate positive differential interactions and negative values indicate negative differential interactions. This table is included separately as a compressed Excel spreadsheet.

Supplementary Table S3: Phosphopeptides up and down regulated upon deletion of *PPH3* based on phospho-proteomic screening. Peptide target indicated the phosphorylated residues, Fold-change and p-value indicate relative abundance compared to wild-type and are calculated as in Huber et al. (S13).

Supplementary Table S4: List of Protein Interactions used for module finding. PE scores were taken from (S7). Other interactions were downloaded from the BioGrid database excluding interactions which were of the genetic variety, and had more than two literature citations.

Supplementary Table S5: Multi-gene modules identified in this study

Supplementary Table S6: Module-Module interactions identified in this study

Supplementary Table S1
List of genes in the E-MAP and their annotations

GENE	ORF	Annotation	FUNCTION	ANNOTATED MODULE	MMS SENSITIVITY	Num Intxns Untreated ($S > 2, S < -2.5$)	Num Intxns MMS ($S > 2, S < -2.5$)	# Differential Interactions (differential p-value < 0.01)
ACA1	YER045C	Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, may regulate transcription of genes involved in utilization of non-optimal carbon sources	TF	-	0	2	4	0
ACE2	YLR131C	Transcription factor that activates expression of early G1-specific genes, localizes to daughter cell nuclei after cytokinesis and delays G1 progression in daughters, localization is regulated by phosphorylation; potential Cdc28p substrate	TF	-	0	7	14	4
ADA2	YDR448W	Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes	Chromatin	-	4	25	5	4
ADR1	YDR216W	Carbon source-responsive zinc-finger transcription factor, required for transcription of the glucose-repressed gene ADH2, of peroxisomal protein genes, and of genes required for ethanol, glycerol, and fatty acid utilization	TF	-	18	7	10	3
AFT2	YPL202C	Iron-regulated transcriptional activator; activates genes involved in intracellular iron use and required for iron homeostasis and resistance to oxidative stress; similar to Aft1p	TF	-	0	2	2	0
AHC1	YOR023C	Subunit of the Ada histone acetyltransferase complex, required for structural integrity of the complex	Chromatin	-	0	9	6	0
AKL1	YBR059C	Ser-Thr protein kinase, member (with Ark1p and Prk1p) of the Ark kinase family; involved in endocytosis and actin cytoskeleton organization	Signaling	-	6	7	9	6
ARG80	YMR042W	Transcription factor involved in regulation of arginine-responsive genes; acts with Arg81p and Arg82p	TF	-	0	0	0	0

ARG81	YML099C	Zinc-finger transcription factor of the Zn(2)-Cys(6) binuclear cluster domain type, involved in the regulation of arginine-responsive genes; acts with Arg80p and Arg82p	TF	-	0	5	11	5
ARG82	YDR173C	Inositol polyphosphate multikinase (IPMK), sequentially phosphorylates Ins(1,4,5)P3 to form Ins(1,3,4,5,6)P5; putative nuclear lipid inositol PI3-kinase; regulates arginine-, phosphate-, and nitrogen-responsive genes	Signaling	-	4	8	15	0
ARK1	YNL020C	Serine/threonine protein kinase involved in regulation of the cortical actin cytoskeleton; involved in control of endocytosis	Signaling	-	0	4	4	0
ARO80	YDR421W	Zinc finger transcriptional activator of the Zn2Cys6 family; activates transcription of aromatic amino acid catabolic genes in the presence of aromatic amino acids	TF	-	4	1	1	0
ARP8	YOR141C	Nuclear actin-related protein involved in chromatin remodeling, component of chromatin-remodeling enzyme complexes	Chromatin	INO80	5	28	43	0
ARR1	YPR199C	Transcriptional activator of the bZIP family, required for transcription of genes involved in resistance to arsenic compounds	TF	-	0	1	1	0
ASF1	YJL115W	Nucleosome assembly factor, involved in chromatin assembly and disassembly, anti-silencing protein that causes derepression of silent loci when overexpressed	Chromatin	-	30	11	2	14
ASH1	YKL185W	Zinc-finger inhibitor of HO transcription; mRNA is localized and translated in the distal tip of anaphase cells, resulting in accumulation of Ash1p in daughter cell nuclei and inhibition of HO expression; potential Cdc28p substrate	TF	-	4	6	7	4
ASK10	YGR097W	Component of the RNA polymerase II holoenzyme, phosphorylated in response to oxidative stress; has a role in destruction of Ssn8p, which relieves repression of stress-response genes	TF	-	0	5	4	0
ATG1	YGL180W	Protein serine/threonine kinase, required for autophagy and for the cytoplasm-to-vacuole targeting (Cvt) pathway	Signaling	-	6	7	20	6
AZF1	YOR113W	Zinc-finger transcription factor, involved in induction of CLN3 transcription in response to glucose; genetic and physical interactions indicate a possible role in mitochondrial transcription or genome maintenance	TF	-	0	8	5	0
BAS1	YKR099W	Myb-related transcription factor involved in regulating basal and induced expression of genes of the purine and histidine biosynthesis pathways; also involved in regulation of meiotic recombination at specific genes	TF	-	0	19	22	3
BCK1	YJL095W	Mitogen-activated protein (MAP) kinase kinase kinase acting in the protein kinase C signaling pathway, which controls cell integrity; upon activation by Pkc1p phosphorylates downstream kinases Mkk1p and Mkk2p	Signaling	MAPK	7	23	48	13
BDF1	YLR399C	Protein involved in transcription initiation at TATA-containing promoters; associates with the basal transcription factor TFIID; contains two bromodomains; corresponds to the C-terminal region of mammalian TAF1; redundant with Bdf2p	TF	-	19	2	1	0

BUB1	YGR188C	Protein kinase that forms a complex with Mad1p and Bub3p that is crucial in the checkpoint mechanism required to prevent cell cycle progression into anaphase in the presence of spindle damage, associates with centromere DNA via Skp1p	Signaling	-	15	77	51	21
BYE1	YKL005C	Negative regulator of transcription elongation, contains a TFIIIS-like domain and a PHD finger, multicopy suppressor of temperature-sensitive <i>ess1</i> mutations, probably binds RNA polymerase II large subunit	TF	-	0	2	1	1
CAD1	YDR423C	AP-1-like bZIP transcriptional activator involved in multiple stress responses, iron metabolism, and pleiotropic drug resistance; controls a set of genes involved in stabilizing proteins, binds consensus sequence TTACTAA; 5' UTR contains uORFs	TF	-	0	2	3	0
CAT8	YMR280C	Zinc cluster transcriptional activator necessary for derepression of a variety of genes under non-fermentative growth conditions, active after diauxic shift, binds carbon source responsive elements	TF	-	0	1	2	0
CBF1	YJR060W	Helix-loop-helix protein that binds the motif CACRTG, which is present at several sites including MET gene promoters and centromere DNA element I (CDEI); required for nucleosome positioning at this motif; targets <i>Isw1p</i> to DNA	TF	-	9	53	64	19
CDC28	YBR160W	Catalytic subunit of the main cell cycle cyclin-dependent kinase (CDK); alternately associates with G1 cyclins (CLNs) and G2/M cyclins (CLBs) which direct the CDK to specific substrates	Cell Cycle	-	0	2	2	0
CHA4	YLR098C	DNA binding transcriptional activator, mediates serine/threonine activation of the catabolic L-serine (L-threonine) deaminase (CHA1); Zinc-finger protein with Zn[2]-Cys[6] fungal-type binuclear cluster domain	TF	-	0	19	28	5
CHK1	YBR274W	DNA damage checkpoint effector kinase, mediates mitotic cell cycle arrest via phosphorylation of <i>Pds1p</i> ; phosphorylated by checkpoint signal transducer kinase <i>Mec1p</i> ; homolog of <i>S. pombe</i> and mammalian Chk1 checkpoint kinase	DNA Repair	CHKPT	0	2	8	2
CIN5	YOR028C	Basic leucine zipper transcriptional factor of the γ AP-1 family that mediates pleiotropic drug resistance and salt tolerance; localizes constitutively to the nucleus	TF	-	4	9	14	1
CKA1	YIL035C	Alpha catalytic subunit of casein kinase 2, a Ser/Thr protein kinase with roles in cell growth and proliferation; the holoenzyme also contains CKA2, CKB1 and CKB2, the many substrates include transcription factors and all RNA polymerases	Signaling	-	12	10	18	7
CKA2	YOR061W	Alpha' catalytic subunit of casein kinase 2, a Ser/Thr protein kinase with roles in cell growth and proliferation; the holoenzyme also contains CKA1, CKB1 and CKB2, the many substrates include transcription factors and all RNA polymerases	Signaling	-	0	12	13	6
CKB1	YGL019W	Beta regulatory subunit of casein kinase 2, a Ser/Thr protein kinase with roles in cell growth and proliferation; the holoenzyme also contains CKA1, CKA2 and CKB2, the many substrates include transcription factors and all RNA polymerases	Signaling	-	10	10	6	0

CKB2	YOR039W	Beta' regulatory subunit of casein kinase 2, a Ser/Thr protein kinase with roles in cell growth and proliferation; the holoenzyme also contains CKA1, CKA2 and CKB1, the many substrates include transcription factors and all RNA polymerases	Signaling	-	15	7	3	0
CK1	YLR133W	Choline kinase, catalyzes the first step in the CDP-choline pathway phosphatidylcholine synthesis (Kennedy pathway); mRNA expression is regulated by inositol and choline, enzyme activity is stimulated by phosphorylation by protein kinase	Signaling	-	0	5	12	6
CLA4	YNL298W	Cdc42p activated signal transducing kinase of the PAK (p21-activated kinase) family, involved in septin ring assembly and cytokinesis; directly phosphorylates septins Cdc3p and Cdc10p; other yeast PAK family members are Ste20p and Skm1p	Signaling	-	7	48	42	0
CLB1	YGR108W	B-type cyclin involved in cell cycle progression; activates Cdc28p to promote the transition from G2 to M phase; accumulates during G2 and M, then targeted via a destruction box motif for ubiquitin-mediated degradation by the proteasome	Cell Cycle	-	0	2	6	0
CLB2	YPR119W	B-type cyclin involved in cell cycle progression; activates Cdc28p to promote the transition from G2 to M phase; accumulates during G2 and M, then targeted via a destruction box motif for ubiquitin-mediated degradation by the proteasome	Cell Cycle	-	13	6	6	0
CLB3	YDL155W	B-type cyclin involved in cell cycle progression; activates Cdc28p to promote the G2/M transition; may be involved in DNA replication and spindle assembly; accumulates during S phase and G2, then targeted for ubiquitin-mediated degradation	Cell Cycle	-	14	12	4	0
CLB4	YLR210W	B-type cyclin involved in cell cycle progression; activates Cdc28p to promote the G2/M transition; may be involved in DNA replication and spindle assembly; accumulates during S phase and G2, then targeted for ubiquitin-mediated degradation	Cell Cycle	-	0	3	2	3
CLB5	YPR120C	B-type cyclin involved in DNA replication during S phase; activates Cdc28p to promote initiation of DNA synthesis; functions in formation of mitotic spindles along with Clb3p and Clb4p; most abundant during late G1 phase	Cell Cycle	-	4	15	27	14
CLB6	YGR109C	B-type cyclin involved in DNA replication during S phase; activates Cdc28p to promote initiation of DNA synthesis; functions in formation of mitotic spindles along with Clb3p and Clb4p; most abundant during late G1	Cell Cycle	-	0	2	4	1
CLN1	YMR199W	G1 cyclin involved in regulation of the cell cycle; activates Cdc28p kinase to promote the G1 to S phase transition; late G1 specific expression depends on transcription factor complexes, MBF (Swi6p-Mbp1p) and SBF (Swi6p-Swi4p)	Cell Cycle	-	0	43	56	42
CLN2	YPL256C	G1 cyclin involved in regulation of the cell cycle; activates Cdc28p kinase to promote the G1 to S phase transition; late G1 specific expression depends on transcription factor complexes, MBF (Swi6p-Mbp1p) and SBF (Swi6p-Swi4p)	Cell Cycle	-	7	10	9	9

CLN3	YAL040C	G1 cyclin involved in cell cycle progression; activates Cdc28p kinase to promote the G1 to S phase transition; plays a role in regulating transcription of the other G1 cyclins, CLN1 and CLN2; regulated by phosphorylation and proteolysis	Cell Cycle	-	0	11	12	1
CMK1	YFR014C	Calmodulin-dependent protein kinase; may play a role in stress response, many CA ⁺⁺ /calmodulin dependent phosphorylation substrates demonstrated in vitro, amino acid sequence similar to Cmk2p and mammalian Cam Kinase II	Signaling	-	4	3	4	5
CMK2	YOL016C	Calmodulin-dependent protein kinase; may play a role in stress response, many CA ⁺⁺ /calmodulin dependent phosphorylation substrates demonstrated in vitro, amino acid sequence similar to Cmk1p and mammalian Cam Kinase II	Signaling	-	0	7	7	0
CMP2	YML057W	Calcineurin A; one isoform (the other is CNA1) of the catalytic subunit of calcineurin, a Ca ⁺⁺ /calmodulin-regulated protein phosphatase which regulates Crz1p (a stress-response transcription factor), the other calcineurin subunit is CNB1	Signaling	-	0	4	2	2
CNA1	YLR433C	Calcineurin A; one isoform (the other is CMP2) of the catalytic subunit of calcineurin, a Ca ⁺⁺ /calmodulin-regulated protein phosphatase which regulates Crz1p (a stress-response transcription factor), the other calcineurin subunit is CNB1	Signaling	-	0	4	3	7
CRZ1	YNL027W	Transcription factor that activates transcription of genes involved in stress response; nuclear localization is positively regulated by calcineurin-mediated dephosphorylation	TF	-	0	4	1	1
CTF18	YMR078C	Subunit of a complex with Ctf8p that shares some subunits with Replication Factor C and is required for sister chromatid cohesion; may have overlapping functions with Rad24p in the DNA damage replication checkpoint	DNA Repair	RFC	4	9	3	10
CTF8	YHR191C	Subunit of a complex with Ctf18p that shares some subunits with Replication Factor C and is required for sister chromatid cohesion	DNA Repair	RFC	18	24	29	16
CTI6	YPL181W	Protein that relieves transcriptional repression by binding to the Cyc8p-Tup1p corepressor and recruiting the SAGA complex to the repressed promoter; contains a PHD finger domain	Chromatin	RPD3L	9	15	19	0
CTK1	YKL139W	Catalytic (alpha) subunit of C-terminal domain kinase I (CTDK-I), which phosphorylates the C-terminal repeated domain of the RNA polymerase II large subunit (Rpo21p) to affect both transcription and pre-mRNA 3' end processing	Signaling	CTK-C	18	55	46	15
CTK2	YJL006C	Beta subunit of C-terminal domain kinase I (CTDK-I), which phosphorylates the C-terminal repeated domain of the RNA polymerase II large subunit (Rpo21p) to affect both transcription and pre-mRNA 3' end processing; has similarity to cyclins	Signaling	CTK-C	21	34	30	13
CTK3	YML112W	Gamma subunit of C-terminal domain kinase I (CTDK-I), which phosphorylates the C-terminal repeated domain of the RNA polymerase II large subunit (Rpo21p) to affect both transcription and pre-mRNA 3' end processing	Signaling	CTK-C	16	66	55	21

CUP2	YGL166W	Copper-binding transcription factor; activates transcription of the metallothionein genes CUP1-1 and CUP1-2 in response to elevated copper concentrations	TF	-	0	1	2	0
CUP9	YPL177C	Homeodomain-containing transcriptional repressor of PTR2, which encodes a major peptide transporter; imported peptides activate ubiquitin-dependent proteolysis, resulting in degradation of Cup9p and de-repression of PTR2 transcription	TF	-	0	8	9	5
CYC8	YBR112C	General transcriptional co-repressor, acts together with Tup1p; also acts as part of a transcriptional co-activator complex that recruits the SWI/SNF and SAGA complexes to promoters	TF	-	0	5	3	0
DAL80	YKR034W	Negative regulator of genes in multiple nitrogen degradation pathways; expression is regulated by nitrogen levels and by Gln3p; member of the GATA-binding family, forms homodimers and heterodimers with Deh1p	TF	-	0	5	5	1
DAL81	YIR023W	Positive regulator of genes in multiple nitrogen degradation pathways; contains DNA binding domain but does not appear to bind the dodecanucleotide sequence present in the promoter region of many genes involved in allantoin catabolism	TF	-	9	5	3	3
DAL82	YNL314W	Positive regulator of allophanate inducible genes; binds a dodecanucleotide sequence upstream of all genes that are induced by allophanate; contains an UISALL DNA-binding, a transcriptional activation, and a coiled-coil domain	TF	-	0	11	15	4
DAT1	YML113W	DNA binding protein that recognizes oligo(dA).oligo(dT) tracts; Arg side chain in its N-terminal pentad Gly-Arg-Lys-Pro-Gly repeat is required for DNA-binding; not essential for viability	TF	-	0	2	3	1
DBF20	YPR111W	Ser/Thr kinase involved in late nuclear division, one of the mitotic exit network (MEN) proteins; necessary for the execution of cytokinesis	Signaling	-	0	4	4	0
DCC1	YCL016C	Subunit of a complex with Ctf8p and Ctf18p that shares some components with Replication Factor C, required for sister chromatid cohesion and telomere length maintenance	DNA Repair	RFC	10	24	43	19
DCN1	YLR128W	Putative Nedd8 ligase; binds Nedd8; involved in cullin neddylation; not essential; similar to C.elegans DCN-1; contains UBA-like ubiquitin-binding domain and a DUF298 domain	Other	-	0	3	2	0
DIA3	YDL024C	Protein of unknown function, involved in invasive and pseudohyphal growth	Signaling	-	0	3	5	0
DIG1	YPL049C	Regulatory protein of unknown function, constitutively-expressed, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription	TF	FUS/DIG	0	5	8	0
DMA1	YHR115C	Protein involved in regulating spindle position and orientation, functionally redundant with Dma2p; homolog of S. pombe Dma1 and H. sapiens Chfr	Other	-	0	5	6	1
DMA2	YNL116W	Protein involved in regulating spindle position and orientation, functionally redundant with Dma1p; homolog of S. pombe Dma1 and H. sapiens Chfr	Other	-	0	15	16	2

DOT6	YER088C	Protein of unknown function, involved in telomeric gene silencing and filamentation	TF	-	7	DOT6	6	2
DUN1	YDL101C	Cell-cycle checkpoint serine-threonine kinase required for DNA damage-induced transcription of certain target genes, phosphorylation of Rad55p and Sml1p, and transient G2/M arrest after DNA damage; also regulates postreplicative DNA repair	DNA Repair	CHKPT	18	14	31	6
EA3	YPR023C	Esa1p-associated factor, nonessential component of the NuA4 acetyltransferase complex, homologous to Drosophila dosage compensation protein MSL3	Chromatin	NUA4	7	3	5	0
EA5	YEL018W	Esa1p-associated factor, subunit of the NuA4 acetyltransferase complex	Chromatin	-	0	13	6	0
EA7	YNL136W	Subunit of the NuA4 histone acetyltransferase complex, which acetylates the N-terminal tails of histones H4 and H2A	Chromatin	-	5	11	11	0
EAP1	YKL204W	eIF4E-associated protein, binds eIF4E and inhibits cap-dependent translation, also functions independently of eIF4E to maintain genetic stability; plays a role in cell growth, implicated in the TOR signaling cascade	Other	-	18	4	3	5
ECM22	YLR228C	Sterol regulatory element binding protein, regulates transcription of the sterol biosynthetic genes ERG2 and ERG3; member of the fungus-specific Zn[2]-Cys[6] binuclear cluster family of transcription factors; homologous to Upc2p	TF	-	0	4	8	3
EDS1	YBR033W	Putative zinc cluster protein; YBR033W is not an essential gene	TF	-	3	5	6	1
ELM1	YKL048C	Serine/threonine protein kinase that regulates cellular morphogenesis, septin behavior, and cytokinesis; required for the regulation of other kinases; forms part of the bud neck ring	Signaling	SEPTIN	8	29	45	7
ELP3	YPL086C	Subunit of Elongator complex, which is required for modification of wobble nucleosides in tRNA; exhibits histone acetyltransferase activity that is directed to histones H3 and H4; disruption confers resistance to K. lactis zymotoxin	Chromatin	-	0	17	6	0
FAB1	YFR019W	1-phosphatidylinositol-3-phosphate 5-kinase; vacuolar membrane kinase that generates phosphatidylinositol (3,5)P2, which is involved in vacuolar sorting and homeostasis	Signaling	-	15	2	3	0
FAR10	YLR238W	Protein involved in G1 cell cycle arrest in response to pheromone, in a pathway different from the Far1p-dependent pathway; interacts with Far3p, Far7p, Far8p, Far9p, and Far11p; potential Cdc28p substrate	Signaling	-	0	2	2	2
FIG4	YNL325C	Protein that forms a complex with Vac14p and is involved in turnover of PI3,5P2 (phosphatidylinositol 3,5-bisphosphate) after hyperosmotic shock; required for efficient mating; member of a protein family with a domain homologous to Sac1p	Signaling	-	7	2	2	0
FKH1	YIL131C	Forkhead family transcription factor with a minor role in the expression of G2/M phase genes; negatively regulates transcriptional elongation; positive role in chromatin silencing at HML and HMR; regulates donor preference during switching	TF	-	0	6	8	3

FKH2	YNL068C	Forkhead family transcription factor with a major role in the expression of G2/M phase genes; positively regulates transcriptional elongation; negative role in chromatin silencing at HML and HMR; substrate of the Cdc28p/Clb5p kinase	TF	-	8	25	54	6
FMP48	YGR052W	Putative protein of unknown function; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies	TF	-	0	6	6	0
FUS3	YBL016W	Mitogen-activated protein kinase involved in mating pheromone response; activated by phosphorylation by Ste7p; provides specificity during the mating vs. filamentous growth response by phosphorylating transcriptional and cytoplasmic targets	Signaling	FUS/DIG	4	39	58	8
FZF1	YGL254W	Transcription factor involved in sulfite metabolism, sole identified regulatory target is SSU1, overexpression suppresses sulfite-sensitivity of many unrelated mutants due to hyperactivation of SSU1, contains five zinc fingers	TF	-	2	0	1	1
GAL3	YDR009W	Transcriptional regulator involved in activation of the GAL genes in response to galactose; forms a complex with Gal80p to relieve Gal80p inhibition of Gal4p; binds galactose and ATP but does not have galactokinase activity	TF	-	0	0	1	0
GAL4	YPL248C	DNA-binding transcription factor required for the activation of the GAL genes in response to galactose; repressed by Gal80p and activated by Gal3p	TF	-	0	1	2	0
GAL80	YML051W	Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding	TF	-	0	1	3	6
GAT1	YFL021W	Transcriptional activator of genes involved in nitrogen catabolite repression, member of the GATA family of DNA binding proteins; activity and localization regulated by nitrogen limitation and Ure2p	TF	-	5	1	2	0
GAT2	YMR136W	Protein containing GATA family zinc finger motifs; similar to Gln3p and Dal80p; expression repressed by leucine	TF	-	0	2	5	0
GAT3	YLR013W	Protein containing GATA family zinc finger motifs	TF	-	0	2	3	0
GAT4	YIR013C	Protein containing GATA family zinc finger motifs	TF	-	0	0	3	1
GCN2	YDR283C	Protein kinase, phosphorylates the alpha-subunit of translation initiation factor eIF2 (Sui2p) in response to starvation; activated by uncharged tRNAs and the Gcn1p-Gcn20p complex	Signaling	-	0	7	8	3
GCR2	YNL199C	Transcriptional activator of genes involved in glycolysis; interacts and functions with the DNA-binding protein Gcr1p	TF	-	5	17	36	14
GIS1	YDR096W	JmjC domain-containing histone demethylase; transcription factor involved in the expression of genes during nutrient limitation; also involved in the negative regulation of DPP1 and PHR1	TF	-	0	10	13	2
GLN3	YER040W	Transcriptional activator of genes regulated by nitrogen catabolite repression (NCR), localization and activity regulated by quality of nitrogen source	TF	-	0	17	13	0

GLO3	YER122C	ADP-ribosylation factor GTPase activating protein (ARF GAP), involved in ER-Golgi transport; shares functional similarity with Gcs1p	Signaling	-	0	15	6	0
GPT2	YKR067W	Glycerol-3-phosphate acyltransferase located in both lipid particles and the ER; involved in the stepwise acylation of glycerol-3-phosphate and dihydroxyacetone, which are intermediate steps in lipid biosynthesis	Signaling	-	7	2	2	2
GTS1	YGL181W	Protein containing a zinc-finger in the N-terminus and a long Gln-rich region in the C-terminus; regulates ultradian rhythm, cell size, cell cycle, lifespan, sporulation, heat tolerance, and multidrug transport	TF	-	0	1	0	0
GZF3	YJL110C	GATA zinc finger protein and Dal80p homolog that negatively regulates nitrogen catabolic gene expression by competing with Gat1p for GATA site binding; function requires a repressive carbon source; dimerizes with Dal80p and binds to Tor1p	TF	-	2	5	13	0
HAA1	YPR008W	Transcriptional activator involved in the transcription of TPO2, HSP30 and other genes encoding membrane stress proteins; despite sequence similarity with the transcription factor Ace1p, it is not subject to metalloregulation	TF	-	0	3	7	1
HAC1	YFL031W	bZIP transcription factor (ATF/CREB1 homolog) that regulates the unfolded protein response, via UPR binding, and membrane biogenesis; ER stress-induced splicing pathway utilizing Ire1p, Trl1p and Ada5p facilitates efficient Hac1p synthesis	TF	UPR	2	7	10	2
HAL5	YJL165C	Putative protein kinase; overexpression increases sodium and lithium tolerance, whereas gene disruption increases cation and low pH sensitivity and impairs potassium uptake, suggesting a role in regulation of Trk1p and/or Trk2p transporters	Signaling	-	0	7	10	4
HAL9	YOL089C	Putative transcription factor containing a zinc finger; overexpression increases salt tolerance through increased expression of the ENA1 (Na ⁺ /Li ⁺ extrusion pump) gene while gene disruption decreases both salt tolerance and ENA1 expression	TF	-	0	7	8	4
HAP2	YGL237C	Subunit of the heme-activated, glucose-repressed Hap2p/3p/4p/5p CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; contains sequences sufficient for both complex assembly and DNA binding	TF	HAP	0	3	9	3
HAP3	YBL021C	Subunit of the heme-activated, glucose-repressed Hap2p/3p/4p/5p CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; contains sequences contributing to both complex assembly and DNA binding	TF	HAP	0	13	12	1
HAP5	YOR358W	Subunit of the heme-activated, glucose-repressed Hap2/3/4/5 CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; required for assembly and DNA binding activity of the complex	TF	HAP	0	11	5	1
HAT1	YPL001W	Catalytic subunit of the Hat1p-Hat2p histone acetyltransferase complex that uses the cofactor acetyl coenzyme A, to acetylate free nuclear and cytoplasmic histone H4; involved in telomeric silencing and DNA double-strand break repair	Chromatin	-	0	3	4	0

HCM1	YCR065W	Forkhead transcription factor that drives S-phase specific expression of genes involved in chromosome segregation, spindle dynamics, and budding; suppressor of calmodulin mutants with specific SPB assembly defects; telomere maintenance role	TF	-	0	15	16	4
HDA1	YNL021W	Putative catalytic subunit of a class II histone deacetylase complex that also contains Hda2p and Hda3p; Hda1p interacts with the Hda2p-Hda3p subcomplex to form an active tetramer; deletion increases histone H2B, H3 and H4 acetylation	Chromatin	-	5	22	16	0
HEX3	YDL013W	Protein containing a RING finger domain that interacts with Slx8p; mutant phenotypes and genetic interactions suggest a role in sumoylation and in genome stability	DNA Repair	RING/SUMO	8	17	11	0
HIR1	YBL008W	Non-essential transcriptional corepressor involved in the cell cycle-regulated transcription of histone H2A, H2B, H3 and H4 genes; contributes to nucleosome formation, heterochromatic gene silencing, and formation of functional kinetochores	TF	HIR	0	9	14	6
HIR2	YOR038C	Non-essential transcriptional corepressor involved in the cell cycle-regulated transcription of histone H2A, H2B, H3, and H4 genes; recruits Swi-Snf complexes to histone gene promoters; promotes heterochromatic gene silencing with Asf1p	TF	HIR	0	13	14	3
HIR3	YJR140C	Transcriptional corepressor involved in the cell cycle-regulated transcription of histone genes HTA1, HTB1, HHT1, and HHT2; involved in position-dependent gene silencing and nucleosome reassembly	TF	HIR	2	9	12	9
HMS1	YOR032C	Basic helix-loop-helix (bHLH) protein with similarity to myc-family transcription factors; overexpression confers hyperfilamentous growth and suppresses the pseudohyphal filamentation defect of a diploid mep1 mep2 homozygous null mutant	TF	HMS	0	10	10	7
HMS2	YJR147W	Protein with similarity to heat shock transcription factors; overexpression suppresses the pseudohyphal filamentation defect of a diploid mep1 mep2 homozygous null mutant	TF	HMS	0	2	2	0
HOG1	YLR113W	Mitogen-activated protein kinase involved in osmoregulation via three independent osmosensors; mediates the recruitment and activation of RNA Pol II at Hot1p-dependent promoters; localization regulated by Ptp2p and Ptp3p	Signaling	-	7	1	1	0
HOT1	YMR172W	Transcription factor required for the transient induction of glycerol biosynthetic genes GPD1 and GPP2 in response to high osmolarity; targets Hog1p to osmostress responsive promoters; has similarity to Msn1p and Gcr1p	TF	-	0	3	5	1
HRK1	YOR267C	Protein kinase implicated in activation of the plasma membrane H(+)-ATPase Pma1p in response to glucose metabolism; plays a role in ion homeostasis	Signaling	-	0	5	19	5
HSL1	YKL101W	Nim1p-related protein kinase that regulates the morphogenesis and septin checkpoints; associates with the assembled septin filament; required along with Hsl7p for bud neck recruitment, phosphorylation, and degradation of Swe1p	Signaling	SEPTIN	7	23	34	6

HST3	YOR025W	Member of the Sir2 family of NAD(+)-dependent protein deacetylases; involved along with Hst4p in telomeric silencing, cell cycle progression, radiation resistance, genomic stability and short-chain fatty acid metabolism	Chromatin	-	0	6	6	0
HTZ1	YOL012C	Histone variant H2AZ, exchanged for histone H2A in nucleosomes by the SWR1 complex; involved in transcriptional regulation through prevention of the spread of silent heterochromatin	Chromatin	SWR1C	19	9	0	13
IES3	YLR052W	Subunit of the INO80 chromatin remodeling complex	Chromatin	INO80	0	16	17	0
IME1	YJR094C	Master regulator of meiosis that is active only during meiotic events, activates transcription of early meiotic genes through interaction with Ume6p, degraded by the 26S proteasome following phosphorylation by Ime2p	TF	-	0	6	10	2
IME2	YJL106W	Serine/threonine protein kinase involved in activation of meiosis, associates with Ime1p and mediates its stability, activates Ndt80p; IME2 expression is positively regulated by Ime1p	Signaling	-	7	4	8	2
INO2	YDR123C	Component of the heteromeric Ino2p/Ino4p basic helix-loop-helix transcription activator that binds inositol/choline-responsive elements (ICREs), required for derepression of phospholipid biosynthetic genes in response to inositol depletion	TF	INO	0	19	18	2
INO4	YOL108C	Transcription factor required for derepression of inositol-choline-regulated genes involved in phospholipid synthesis; forms a complex, with Ino2p, that binds the inositol-choline-responsive element through a basic helix-loop-helix domain	TF	INO	0	6	3	0
IRE1	YHR079C	Serine-threonine kinase and endoribonuclease; transmembrane protein that initiates the unfolded protein response signal by regulating synthesis of Hac1p through HAC1 mRNA splicing	Signaling	UPR	0	15	13	4
ISR1	YPR106W	Predicted protein kinase, overexpression causes sensitivity to staurosporine, which is a potent inhibitor of protein kinase C	Signaling	-	2	2	10	3
ISW1	YBR245C	Member of the imitation-switch (ISWI) class of ATP-dependent chromatin remodeling complexes; ATPase that forms a complex with Ioc2p and Ioc4p to regulate transcription elongation, and a complex with Ioc3p to repress transcription initiation	Chromatin	-	12	2	3	0
IXR1	YKL032C	Protein that binds DNA containing intrastrand cross-links formed by cisplatin, contains two HMG (high mobility group box) domains, which confer the ability to bend cisplatin-modified DNA; mediates aerobic transcriptional repression of COX5b	TF	-	5	44	55	4
JHD1	YER051W	JmjC domain family histone demethylase specific for H3-K36, similar to proteins found in human, mouse, drosophila, X. laevis, C. elegans, and S. pombe	Chromatin	-	0	0	1	0
KAR4	YCL055W	Transcription factor required for gene regulation in response to pheromones; also required during meiosis; exists in two forms, a slower-migrating form more abundant during vegetative growth and a faster-migrating form induced by pheromone	TF	-	0	3	5	2

KCC4	YCL024W	Protein kinase of the bud neck involved in the septin checkpoint, associates with septin proteins, negatively regulates Swe1p by phosphorylation, shows structural homology to bud neck kinases Gin4p and Hsl1p	Signaling	-	0	4	12	2
KCS1	YDR017C	Inositol hexakisphosphate (IP6) kinase, also has inositol heptakisphosphate (IP7) kinase activity, required for proper vacuole morphology and involved in salt stress response; contains two leucine heptad repeats	Signaling	-	12	139	146	11
KIN2	YLR096W	Serine/threonine protein kinase involved in regulation of exocytosis; localizes to the cytoplasmic face of the plasma membrane; closely related to Kin1p	Signaling	-	0	3	9	9
KIN3	YAR018C	Nonessential protein kinase with unknown cellular role	Signaling	-	0	10	7	3
KIN4	YOR233W	Kinase that acts by inhibiting the mitotic exit network (MEN) when the spindle position checkpoint is activated; localized asymmetrically to mother cell cortex, spindle pole body and bud neck	Signaling	-	0	4	3	0
KIN82	YCR091W	Putative serine/threonine protein kinase, most similar to cyclic nucleotide-dependent protein kinase subfamily and the protein kinase C subfamily	Signaling	-	0	4	6	1
KKQ8	YKL168C	Putative serine/threonine protein kinase with unknown cellular role	Signaling	-	0	0	3	0
KNS1	YLL019C	Nonessential putative protein kinase of unknown cellular role; member of the LAMMER family of protein kinases, which are serine/threonine kinases also capable of phosphorylating tyrosine residues	Signaling	-	0	4	7	0
KSP1	YHR082C	Nonessential putative serine/threonine protein kinase of unknown cellular role; overproduction causes allele-specific suppression of the prp20-10 mutation	Signaling	-	10	7	7	1
KSS1	YGR040W	Mitogen-activated protein kinase (MAPK) involved in signal transduction pathways that control filamentous growth and pheromone response	Signaling	-	0	4	4	1
LCB4	YOR171C	Sphingoid long-chain base kinase, responsible for synthesis of long-chain base phosphates, which function as signaling molecules, regulates synthesis of ceramide from exogenous long-chain bases, localizes to the Golgi and late endosomes	Signaling	-	0	9	14	2
LCB5	YLR260W	Minor sphingoid long-chain base kinase, paralog of Lcb4p responsible for few percent of the total activity, possibly involved in synthesis of long-chain base phosphates, which function as signaling molecules	Signaling	-	0	9	11	8
LEU3	YLR451W	Zinc-finger transcription factor that regulates genes involved in branched chain amino acid biosynthesis and ammonia assimilation; positively regulated by alpha-isopropylmalate, an intermediate in leucine biosynthesis	TF	-	0	2	4	4
LTP1	YPR073C	Protein phosphotyrosine phosphatase of unknown cellular role; activated by adenine	Signaling	-	0	3	4	0
MAC1	YMR021C	Copper-sensing transcription factor involved in regulation of genes required for high affinity copper transport	TF	-	0	6	5	0

MAL13	YGR288W	MAL-activator protein, part of complex locus MAL1; nonfunctional in genomic reference strain S288C	TF	-	0	5	3	3
MAL33	YBR297W	MAL-activator protein, part of complex locus MAL3; nonfunctional in genomic reference strain S288C	TF	-	0	3	4	3
MBF1	YOR298C-A	Transcriptional coactivator that bridges the DNA-binding region of Gcn4p and TATA-binding protein Spt15p; suppressor of frameshift mutations	TF	-	0	2	5	1
MBP1	YDL056W	Transcription factor involved in regulation of cell cycle progression from G1 to S phase, forms a complex with Swi6p that binds to MluI cell cycle box regulatory element in promoters of DNA synthesis genes	Cell Cycle	-	0	10	10	6
MDS3	YGL197W	Protein with an N-terminal kelch-like domain, putative negative regulator of early meiotic gene expression; required, with Pmd1p, for growth under alkaline conditions	TF	-	0	9	15	0
MEC1	YBR136W	Genome integrity checkpoint protein and PI kinase superfamily member; signal transducer required for cell cycle arrest and transcriptional responses prompted by damaged or unreplicated DNA; monitors and participates in meiotic recombination	DNA Repair	CHKPT	0	0	1	0
MEK1	YOR351C	Meiosis-specific serine/threonine protein kinase, functions in meiotic checkpoint, phosphorylates Red1p, interacts with Hop1p; required for meiotic recombination and normal spore viability	Signaling	-	0	1	2	1
MET18	YIL128W	DNA repair and TFIIH regulator, required for both nucleotide excision repair (NER) and RNA polymerase II (RNAP II) transcription; involved in telomere maintenance	TF	-	18	91	101	9
MET28	YIR017C	Transcriptional activator in the Cbf1p-Met4p-Met28p complex, participates in the regulation of sulfur metabolism	TF	-	0	0	2	1
MET31	YPL038W	Zinc-finger DNA-binding protein, involved in regulating expression of the methionine biosynthetic genes, similar to Met32p	TF	-	0	2	2	0
MET32	YDR253C	Zinc-finger DNA-binding protein, involved in regulating expression of the methionine biosynthetic genes, similar to Met31p	TF	-	2	4	12	2
MGA1	YGR249W	Protein similar to heat shock transcription factor; multicopy suppressor of pseudohyphal growth defects of ammonium permease mutants	TF	-	0	2	2	1
MGA2	YIR033W	ER membrane protein involved in regulation of OLE1 transcription, acts with homolog Spt23p; inactive ER form dimerizes and one subunit is then activated by ubiquitin/proteasome-dependent processing followed by nuclear targeting	TF	-	0	11	6	5
MIG1	YGL035C	Transcription factor involved in glucose repression; sequence specific DNA binding protein containing two Cys2His2 zinc finger motifs; regulated by the SNF1 kinase and the GLC7 phosphatase	TF	-	7	3	10	6
MIG2	YGL209W	Protein containing zinc fingers, involved in repression, along with Mig1p, of SUC2 (invertase) expression by high levels of glucose; binds to Mig1p-binding sites in SUC2 promoter	TF	-	0	2	2	3
MIG3	YER028C	Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes	TF	-	0	0	1	0

MIH1	YMR036C	Protein tyrosine phosphatase involved in cell cycle control; regulates the phosphorylation state of Cdc28p; homolog of <i>S. pombe</i> cdc25	Signaling	-	0	4	3	0
MKK1	YOR231W	Mitogen-activated kinase kinase involved in protein kinase C signaling pathway that controls cell integrity; upon activation by Bck1p phosphorylates downstream target, Slk2p; functionally redundant with Mkk2p	Signaling	-	8	6	9	1
MKK2	YPL140C	Mitogen-activated kinase kinase involved in protein kinase C signaling pathway that controls cell integrity; upon activation by Bck1p phosphorylates downstream target, Slk2p; functionally redundant with Mkk1p	Signaling	-	7	4	9	3
MMS1	YPR164W	Protein likely involved in protection against replication-dependent DNA damage; mutants are sensitive to methyl methanesulfonate (MMS); implicated in regulation of Ty1 transposition	DNA Repair	-	30	4	5	0
MMS22	YLR320W	Protein involved in resistance to ionizing radiation; acts with Mms1p in a repair pathway that may be involved in resolving replication intermediates or preventing the damage caused by blocked replication forks	DNA Repair	-	29	6	31	19
MOT2	YER068W	Component of the CCR4-NOT complex, which has multiple roles in transcription regulation, mRNA degradation, and post-transcriptional modifications; with Ubc4p, ubiquitylates subunits of the nascent polypeptide-associated complex (NAC)	TF	-	19	3	4	0
MOT3	YMR070W	Nuclear transcription factor with two Cys2-His2 zinc fingers; involved in repression of a subset of hypoxic genes by Rox1p, repression of several DAN/TIR genes during aerobic growth, and repression of ergosterol biosynthetic genes	TF	-	0	7	6	0
MRC1	YCL061C	S-phase checkpoint protein found at replication forks, required for DNA replication; also required for Rad53p activation during DNA replication stress, where it forms a replication-pausing complex with Tof1p and is phosphorylated by Mec1p; protein involved in replication checkpoint	DNA Repair	9-1-1	8	5	11	0
MRE11	YMR224C	Subunit of a complex with Rad50p and Xrs2p (RMX complex) that functions in repair of DNA double-strand breaks and in telomere stability, exhibits nuclease activity that appears to be required for RMX function; widely conserved	DNA Repair	-	0	11	2	6
MRK1	YDL079C	Glycogen synthase kinase 3 (GSK-3) homolog; one of four GSK-3 homologs in <i>S. cerevisiae</i> that function to activate Msn2p-dependent transcription of stress responsive genes and that function in protein degradation	Signaling	-	0	5	6	0
MSG5	YNL053W	Dual-specificity protein phosphatase required for maintenance of a low level of signaling through the cell integrity pathway; regulates and is regulated by Slk2p; also required for adaptive response to pheromone	Signaling	-	0	5	6	6
MSN1	YOL116W	Transcriptional activator involved in regulation of invertase and glucoamylase expression, invasive growth and pseudohyphal differentiation, iron uptake, chromium accumulation, and response to osmotic stress; localizes to the nucleus	TF	-	0	3	4	0

MSN2	YMR037C	Transcriptional activator related to Msn4p; activated in stress conditions, which results in translocation from the cytoplasm to the nucleus; binds DNA at stress response elements of responsive genes, inducing gene expression	TF	MSN	0	8	17	4
MSN4	YKL062W	Transcriptional activator related to Msn2p; activated in stress conditions, which results in translocation from the cytoplasm to the nucleus; binds DNA at stress response elements of responsive genes, inducing gene expression	TF	MSN	0	10	18	2
MSS11	YMR164C	Transcription factor involved in regulation of invasive growth and starch degradation; controls the activation of MUC1 and STA2 in response to nutritional signals	TF	-	0	3	2	0
MTH1	YDR277C	Negative regulator of the glucose-sensing signal transduction pathway, required for repression of transcription by Rgt1p; interacts with Rgt1p and the Snf3p and Rgt2p glucose sensors; phosphorylated by Yck1p, triggering Mth1p degradation	Signaling	-	2	2	2	0
NDT80	YHR124W	Meiosis-specific transcription factor required for exit from pachytene and for full meiotic recombination; activates middle sporulation genes; competes with Sum1p for binding to promoters containing middle sporulation elements (MSE)	TF	-	0	4	6	3
NHP10	YDL002C	Protein related to mammalian high mobility group proteins; likely component of the INO80 complex, which is an ATP-dependent chromatin-remodeling complex	Chromatin	INO80	0	5	10	0
NNF2	YGR089W	Protein that exhibits physical and genetic interactions with Rpb8p, which is a subunit of RNA polymerases I, II, and III; computational analysis of large-scale protein-protein interaction data suggests a role in chromosome segregation	Chromatin	-	4	6	10	2
NPR1	YNL183C	Protein kinase that stabilizes several plasma membrane amino acid transporters by antagonizing their ubiquitin-mediated degradation	Signaling	-	0	10	20	2
NRG1	YDR043C	Transcriptional repressor that recruits the Cyc8p-Tup1p complex to promoters; mediates glucose repression and negatively regulates a variety of processes including filamentous growth and alkaline pH response	TF	-	0	10	15	7
NRG2	YBR066C	Transcriptional repressor that mediates glucose repression and negatively regulates filamentous growth; has similarity to Nrg1p	TF	-	0	5	4	0
NUP133	YKR082W	Subunit of the Nup84p subcomplex of the nuclear pore complex (NPC), localizes to both sides of the NPC, required to establish a normal nucleocytoplasmic concentration gradient of the GTPase Gsp1p	Other	-	15	22	29	4
NUT1	YGL151W	Component of the RNA polymerase II mediator complex, which is required for transcriptional activation and also has a role in basal transcription	Chromatin	MEDIATOR	13	15	14	17
OAF1	YAL051W	Oleate-activated transcription factor, acts alone and as a heterodimer with Pip2p; activates genes involved in beta-oxidation of fatty acids and peroxisome organization and biogenesis	TF	-	0	3	1	0
OCA1	YNL099C	Putative protein tyrosine phosphatase, required for cell cycle arrest in response to oxidative damage of DNA	Signaling	OCA	0	5	4	0

OPI1	YHL020C	Transcriptional regulator of a variety of genes; phosphorylation by protein kinase A stimulates Opi1p function in negative regulation of phospholipid biosynthetic genes; involved in telomere maintenance	TF	-	6	13	14	8
OTU1	YFL044C	Deubiquitylation enzyme that binds to the chaperone-ATPase Cdc48p; may contribute to regulation of protein degradation by deubiquitylating substrates that have been ubiquitylated by Ufd2p; member of the Ovarian Tumor (OTU) family	Other	-	0	0	2	3
PBS2	YJL128C	MAP kinase kinase that plays a pivotal role in the osmosensing signal-transduction pathway, activated under severe osmotic stress	Signaling	-	5	13	22	2
PDR1	YGL013C	Zinc cluster protein that is a master regulator involved in recruiting other zinc cluster proteins to pleiotropic drug response elements (PDREs) to fine tune the regulation of multidrug resistance genes	TF	-	0	11	7	0
PDR3	YBL005W	Transcriptional activator of the pleiotropic drug resistance network, regulates expression of ATP-binding cassette (ABC) transporters through binding to cis-acting sites known as PDREs (PDR responsive elements)	TF	-	0	0	0	0
PGD1	YGL025C	Subunit of the Mediator global transcriptional cofactor complex, which is part of the RNA polymerase II holoenzyme and plays an essential role in basal and activated transcription; direct target of the Cyc8p-Tup1p transcriptional corepressor	TF	-	0	1	0	0
PHD1	YKL043W	Transcriptional activator that enhances pseudohyphal growth; regulates expression of FLO11, an adhesin required for pseudohyphal filament formation; similar to StuA, an A. nidulans developmental regulator; potential Cdc28p substrate	TF	-	0	4	7	5
PHO2	YDL106C	Homeobox transcription factor; regulatory targets include genes involved in phosphate metabolism; binds cooperatively with Pho4p to the PHO5 promoter; phosphorylation of Pho2p facilitates interaction with Pho4p	TF	-	0	3	2	0
PHO23	YNL097C	Probable component of the Rpd3 histone deacetylase complex, involved in transcriptional regulation of PHO5; C-terminus has similarity to human candidate tumor suppressor p33(ING1)	Chromatin	RPD3L	4	33	38	4
PHO3	YBR092C	Constitutively expressed acid phosphatase similar to Pho5p; brought to the cell surface by transport vesicles; hydrolyzes thiamin phosphates in the periplasmic space, increasing cellular thiamin uptake; expression is repressed by thiamin	Signaling	-	5	7	5	2
PHO4	YFR034C	Basic helix-loop-helix (bHLH) transcription factor; binds cooperatively with Pho2p to the PHO5 promoter; function is regulated by phosphorylation at multiple sites and by phosphate availability	TF	-	0	6	6	2
PHO5	YBR093C	Repressible acid phosphatase (1 of 3) that also mediates extracellular nucleotide-derived phosphate hydrolysis; secretory pathway derived cell surface glycoprotein; induced by phosphate starvation and coordinately regulated by PHO4 and PHO2	Signaling	-	0	0	2	0
PHO80	YOL001W	Cyclin, negatively regulates phosphate metabolism; Pho80p-Pho85p (cyclin-CDK complex) phosphorylates Pho4p and Swi5p; deletion of PHO80 leads to aminoglycoside supersensitivity; truncated form of PHO80 affects vacuole inheritance	Cell Cycle	-	18	21	22	5

PIP2	YOR363C	Autoregulatory oleate-specific transcriptional activator of peroxisome proliferation, contains Zn(2)-Cys(6) cluster domain, forms heterodimer with Oaf1p, binds oleate response elements (OREs), activates beta-oxidation genes	TF	-	0	2	1	0
PKH1	YDR490C	Serine/threonine protein kinase involved in sphingolipid-mediated signaling pathway that controls endocytosis; activates Ypk1p and Ykr2p, components of signaling cascade required for maintenance of cell wall integrity; redundant with Pkh2p	Signaling	-	0	1	4	0
PKH2	YOL100W	Serine/threonine protein kinase involved in sphingolipid-mediated signaling pathway that controls endocytosis; activates Ypk1p and Ykr2p, components of signaling cascade required for maintenance of cell wall integrity; redundant with Pkh1p	Signaling	-	0	2	4	0
PKH3	YDR466W	Protein kinase with similarity to mammalian phosphoinositide-dependent kinase 1 (PDK1) and yeast Pkh1p and Pkh2p, two redundant upstream activators of Pkc1p; identified as a multicopy suppressor of a pkh1 pkh2 double mutant	Signaling	-	0	4	8	2
PLM2	YDR501W	Protein required for partitioning of the 2-micron plasmid	TF	-	0	12	18	3
PML1	YLR016C	Subunit of the RES complex, which is required for nuclear retention of unspliced pre-mRNAs; acts in the same pathway as Pml39p and Mlp1p	Other	-	0	8	8	0
PPG1	YNR032W	Putative serine/threonine protein phosphatase, required for glycogen accumulation; interacts with Tap42p, which binds to and regulates other protein phosphatases	Signaling	-	0	12	16	2
PPH21	YDL134C	Catalytic subunit of protein phosphatase 2A, functionally redundant with Pph22p; methylated at C terminus; forms alternate complexes with several regulatory subunits; involved in signal transduction and regulation of mitosis	Signaling	PP2A	0	14	13	0
PPH22	YDL188C	Catalytic subunit of protein phosphatase 2A, functionally redundant with Pph21p; methylated at C terminus; forms alternate complexes with several regulatory subunits; involved in signal transduction and regulation of mitosis	Signaling	PP2A	0	7	9	2
PPH3	YDR075W	Catalytic subunit of an evolutionarily conserved protein phosphatase complex containing Psy2p and the regulatory subunit Psy4p; required for cisplatin resistance; involved in activation of Gln3p	DNA Repair	PPH3-C	19	4	26	17
PPQ1	YPL179W	Putative protein serine/threonine phosphatase; null mutation enhances efficiency of translational suppressors	Signaling	-	0	8	5	5
PPR1	YLR014C	Zinc finger transcription factor containing a Zn(2)-Cys(6) binuclear cluster domain, positively regulates transcription of genes involved in uracil biosynthesis; activity may be modulated by interaction with Tup1p	TF	-	4	6	10	0
PPS1	YBR276C	Protein phosphatase with specificity for serine, threonine, and tyrosine residues; has a role in the DNA synthesis phase of the cell cycle	Signaling	-	0	5	3	0
PPT1	YGR123C	Protein serine/threonine phosphatase with similarity to human phosphatase PP5; present in both the nucleus and cytoplasm; expressed during logarithmic growth	Signaling	-	0	2	1	0

PPZ1	YML016C	Serine/threonine protein phosphatase Z, isoform of Ppz2p; involved in regulation of potassium transport, which affects osmotic stability, cell cycle progression, and halotolerance	Signaling	-	6	14	13	2
PPZ2	YDR436W	Serine/threonine protein phosphatase Z, isoform of Ppz1p; involved in regulation of potassium transport, which affects osmotic stability, cell cycle progression, and halotolerance	Signaling	-	0	10	16	7
PRE9	YGR135W	20S proteasome beta-type subunit; the only nonessential 20S subunit	Other	-	0	10	11	0
PRK1	YIL095W	Protein serine/threonine kinase; regulates the organization and function of the actin cytoskeleton through the phosphorylation of the Pan1p-Sla1p-End3p protein complex	Signaling	-	2	6	6	4
PRR1	YKL116C	Protein kinase with a possible role in MAP kinase signaling in the pheromone response pathway	Signaling	-	0	2	7	3
PRR2	YDL214C	Protein kinase with a possible role in MAP kinase signaling in the pheromone response pathway	Signaling	-	0	8	7	3
PSK2	YOL045W	One of two (see also PSK1) PAS domain containing S/T protein kinases; regulates sugar flux and translation in response to an unknown metabolite by phosphorylating Ugp1p and Gsy2p (sugar flux) and Caf20p, Tif11p and Sro9p (translation)	Signaling	-	5	2	2	0
PSY2	YNL201C	Putative subunit of an evolutionarily conserved protein phosphatase complex containing the catalytic subunit Pph3p and the regulatory subunit Psy4p; required for cisplatin and oxaliplatin resistance; localizes to nucleus	DNA Repair	PPH3-C	12	4	3	0
PSY3	YLR376C	Protein of unknown function; deletion results in a mutator phenotype suggesting a role for this protein as a mutational suppressor; deletion increases sensitivity to anticancer drugs oxaliplatin and cisplatin but not mitomycin C	DNA Repair	-	18	2	3	0
PSY4	YBL046W	Putative regulatory subunit of an evolutionarily conserved protein phosphatase complex containing the catalytic subunit Pph3p and a third subunit Psy2p; required for cisplatin resistance; GFP-fusion protein localizes to the nucleus	DNA Repair	PPH3-C	0	3	4	0
PTC1	YDL006W	Type 2C protein phosphatase (PP2C); inactivates the osmosensing MAPK cascade by dephosphorylating Hog1p; mutation delays mitochondrial inheritance; deletion reveals defects in precursor tRNA splicing, sporulation and cell separation	Signaling	-	15	65	41	38
PTC2	YER089C	Type 2C protein phosphatase; dephosphorylates Hog1p to limit maximal osmostress induced kinase activity; dephosphorylates Ire1p to downregulate the unfolded protein response; dephosphorylates Cdc28p; role in DNA checkpoint inactivation	Signaling	-	0	4	14	13
PTC3	YBL056W	Type 2C protein phosphatase; dephosphorylates Hog1p (see also Ptc2p) to limit maximal kinase activity induced by osmotic stress; dephosphorylates T169 phosphorylated Cdc28p (see also Ptc2p); role in DNA checkpoint inactivation	Signaling	-	0	1	1	0

PTC4	YBR125C	Cytoplasmic type 2C protein phosphatase; identified as a high-copy number suppressor of the synthetic lethality of a <i>cnb1 mpk1</i> double deletion; overexpression decreases high-osmolarity induced Hog1p phosphorylation and kinase activity	Signaling	-	0	7	7	0
PTC5	YOR090C	Mitochondrially localized type 2C protein phosphatase involved in regulation of pyruvate dehydrogenase activity; contains Mg ²⁺ /Mn ²⁺ -dependent casein phosphatase activity in vitro	Signaling	-	0	0	1	0
PTK1	YKL198C	Putative serine/threonine protein kinase that regulates spermine uptake; involved in polyamine transport; possible mitochondrial protein	Signaling	-	0	2	1	4
PTK2	YJR059W	Putative serine/threonine protein kinase involved in regulation of ion transport across plasma membrane; enhances spermine uptake	Signaling	-	2	18	16	4
PTP1	YDL230W	Phosphotyrosine-specific protein phosphatase that dephosphorylates a broad range of substrates in vivo, including Fpr3p; localized to the cytoplasm and the mitochondria	Signaling	-	0	3	2	0
PTP2	YOR208W	Phosphotyrosine-specific protein phosphatase involved in the inactivation of mitogen-activated protein kinase (MAPK) during osmolarity sensing; dephosphorylates Hog1p MAPK and regulates its localization; localized to the nucleus	Signaling	-	0	2	4	1
PUT3	YKL015W	Transcriptional activator of proline utilization genes, constitutively binds PUT1 and PUT2 promoter sequences and undergoes a conformational change to form the active state; has a Zn(2)-Cys(6) binuclear cluster domain	TF	-	0	3	5	0
RAD17	YOR368W	Checkpoint protein, involved in the activation of the DNA damage and meiotic pachytene checkpoints; with Mec3p and Ddc1p, forms a clamp that is loaded onto partial duplex DNA; homolog of human and <i>S. pombe</i> Rad1 and <i>U. maydis</i> Rec1 proteins	DNA Repair	-	22	8	29	14
RAD18	YCR066W	Protein involved in postreplication repair; binds single-stranded DNA and has single-stranded DNA dependent ATPase activity; forms heterodimer with Rad6p; contains RING-finger motif	DNA Repair	-	30	3	2	0
RAD5	YLR032W	Single-stranded DNA-dependent ATPase, involved in postreplication repair; contains RING finger domain	DNA Repair	-	30	1	6	5
RAD51	YER095W	Strand exchange protein, forms a helical filament with DNA that searches for homology; involved in the recombinational repair of double-strand breaks in DNA during vegetative growth and meiosis; homolog of Dmc1p and bacterial RecA protein	DNA Repair	RADEG	30	11	32	42
RAD52	YML032C	Protein that stimulates strand exchange by facilitating Rad51p binding to single-stranded DNA; anneals complementary single-stranded DNA; involved in the repair of double-strand breaks in DNA during vegetative growth and meiosis	DNA Repair	RADEG	20	21	23	52
RAD53	YPL153C	Protein kinase, required for cell-cycle arrest in response to DNA damage; activated by trans autophosphorylation when interacting with hyperphosphorylated Rad9p; also interacts with ARS1 and plays a role in initiation of DNA replication	DNA Repair	CHKPT	0	0	1	0

RAD9	YDR217C	DNA damage-dependent checkpoint protein, required for cell-cycle arrest in G1/S, intra-S, and G2/M; transmits checkpoint signal by activating Rad53p and Chk1p; hyperphosphorylated by Mec1p and Tel1p; potential Cdc28p substrate	DNA Repair	-	18	5	3	0
RCK1	YGL158W	Protein kinase involved in the response to oxidative stress; identified as suppressor of <i>S. pombe</i> cell cycle checkpoint mutations	Signaling	-	4	5	4	2
RCK2	YLR248W	Protein kinase involved in the response to oxidative and osmotic stress; identified as suppressor of <i>S. pombe</i> cell cycle checkpoint mutations	Signaling	-	0	3	6	5
RCO1	YMR075W	Essential subunit of the histone deacetylase Rpd3S complex; interacts with Eaf3p	Chromatin	NUA4	7	19	28	2
RCS1	YGL071W	Transcription factor involved in iron utilization and homeostasis; binds the consensus site PyPuCACCCPu and activates the expression of target genes in response to changes in iron availability	TF	-	0	20	27	50
RDR1	YOR380W	Transcriptional repressor involved in the control of multidrug resistance; negatively regulates expression of the PDR5 gene; member of the Gal4p family of zinc cluster proteins	TF	-	0	2	0	5
RDS1	YCR106W	Zinc cluster protein involved in conferring resistance to cycloheximide	TF	-	0	0	2	0
RDS2	YPL133C	Zinc cluster protein involved in conferring resistance to ketoconazole	TF	-	4	0	0	0
REI1	YBR267W	Cytoplasmic pre-60S factor; required for the correct recycling of shuttling factors Alb1, Arx1 and Tif6 at the end of the ribosomal large subunit biogenesis; involved in bud growth in the mitotic signaling network	Other	-	0	64	31	0
RFX1	YLR176C	Protein involved in DNA damage and replication checkpoint pathway; recruits repressors Tup1p and Cyc8p to promoters of DNA damage-inducible genes; similar to a family of mammalian DNA binding RFX1-4 proteins	DNA Repair	-	0	12	9	0
RGM1	YMR182C	Putative transcriptional repressor with proline-rich zinc fingers; overproduction impairs cell growth	TF	-	0	0	3	0
RGT1	YKL038W	Glucose-responsive transcription factor that regulates expression of several glucose transporter (HXT) genes in response to glucose; binds to promoters and acts both as a transcriptional activator and repressor	TF	-	0	0	2	4
RIM101	YHL027W	Transcriptional repressor involved in response to pH and in cell wall construction; required for alkaline pH-stimulated haploid invasive growth and sporulation; activated by proteolytic processing; similar to <i>A. nidulans</i> PacC	TF	-	11	64	66	9
RIM11	YMR139W	Protein kinase required for signal transduction during entry into meiosis; promotes the formation of the Ime1p-Ume6p complex by phosphorylating Ime1p and Ume6p; shares similarity with mammalian glycogen synthase kinase 3-beta	Signaling	-	13	5	6	1
RIM15	YFL033C	Glucose-repressible protein kinase involved in signal transduction during cell proliferation in response to nutrients, specifically the establishment of stationary phase; identified as a regulator of IME2; substrate of Pho80p-Pho85p kinase	Signaling	-	0	7	15	1

RLM1	YPL089C	MADS-box transcription factor, component of the protein kinase C-mediated MAP kinase pathway involved in the maintenance of cell integrity; phosphorylated and activated by the MAP-kinase Sit2p	TF	-	0	5	6	2
RME1	YGR044C	Zinc finger protein involved in control of meiosis; prevents meiosis by repressing IME1 expression and promotes mitosis by activating CLN2 expression; directly repressed by a1-a2 regulator; mediates cell type control of sporulation	TF	-	0	1	0	0
ROX1	YPR065W	Heme-dependent repressor of hypoxic genes; contains an HMG domain that is responsible for DNA bending activity	TF	-	6	9	16	4
RPD3	YNL330C	Histone deacetylase; regulates transcription and silencing	Chromatin	-	0	36	11	12
RPH1	YER169W	JmjC domain-containing histone demethylase which can specifically demethylate H3K36 tri- and dimethyl modification states; transcriptional repressor of PHR1; Rph1p phosphorylation during DNA damage is under control of the MEC1-RAD53 pathway	Chromatin	-	0	3	6	4
RPI1	YIL119C	Putative transcriptional regulator; overexpression suppresses the heat shock sensitivity of wild-type RAS2 overexpression and also suppresses the cell lysis defect of an mpk1 mutation	TF	-	0	2	2	1
RPN4	YDL020C	Transcription factor that stimulates expression of proteasome genes; Rpn4p levels are in turn regulated by the 26S proteasome in a negative feedback control mechanism; RPN4 is transcriptionally regulated by various stress responses	TF	-	15	43	44	13
RRI1	YDL216C	Catalytic subunit of the COP9 signalosome (CSN) complex that acts as an isopeptidase in cleaving the ubiquitin-like protein Nedd8 from SCF ubiquitin ligases; metalloendopeptidase involved in the adaptation to pheromone signaling	Other	-	0	6	6	0
RSC1	YGR056W	Component of the RSC chromatin remodeling complex; required for expression of mid-late sporulation-specific genes; contains two essential bromodomains, a bromo-adjacent homology (BAH) domain, and an AT hook	Chromatin	-	8	23	24	2
RSC2	YLR357W	Component of the RSC chromatin remodeling complex; required for expression of mid-late sporulation-specific genes; involved in telomere maintenance	Chromatin	-	18	25	28	0
RSF2	YJR127C	Zinc-finger protein involved in transcriptional control of both nuclear and mitochondrial genes, many of which specify products required for glycerol-based growth, respiration, and other functions	TF	-	0	5	3	0
RTG1	YOL067C	Transcription factor (bHLH) involved in interorganelle communication between mitochondria, peroxisomes, and nucleus	TF	RTG	6	19	23	2
RTG2	YGL252C	Sensor of mitochondrial dysfunction; regulates the subcellular location of Rtg1p and Rtg3p, transcriptional activators of the retrograde (RTG) and TOR pathways; Rtg2p is inhibited by the phosphorylated form of Mks1p	Other	-	2	4	5	0
RTG3	YBL103C	Basic helix-loop-helix-leucine zipper (bHLH/Zip) transcription factor that forms a complex with another bHLH/Zip protein, Rtg1p, to activate the retrograde (RTG) and TOR pathways	TF	RTG	5	64	93	3

RTT101	YJL047C	Cullin subunit of a Roc1p-dependent E3 ubiquitin ligase complex; deletion phenotype suggests a role in anaphase progression; interacts with Mms22p and implicated in Mms22-dependent DNA repair; modified by the ubiquitin-like protein, Rub1p	DNA Repair	-	18	6	8	0
RTT109	YLL002W	Histone acetyltransferase critical for cell survival in the presence of DNA damage during S phase, acetylates H3-K56; plays a role in regulation of Ty1 transposition	DNA Repair	-	29	4	11	8
RUB1	YDR139C	Ubiquitin-like protein with similarity to mammalian NEDD8; conjugation (neddylation) substrates include the cullins Cdc53p, Rtt101p, and Cul3p; activated by Ula1p and Uba3p (E1 enzyme pair); conjugation mediated by Ubc12p (E2 enzyme)	Other	-	0	3	4	0
RXT2	YBR095C	Subunit of the histone deacetylase Rpd3L complex; possibly involved in cell fusion and invasive growth	Chromatin	RPD3L	6	33	40	12
SAE2	YGL175C	Protein with a role in accurate meiotic and mitotic double-strand break repair; phosphorylated in response to DNA damage and required for normal resistance to DNA-damaging agents	DNA Repair	-	18	4	5	0
SAK1	YER129W	Upstream kinase for the SNF1 complex; partially redundant function with Elm1p and Tos3p; members of this family of kinases have functional orthology with LKB1, a mammalian kinase associated with Peutz-Jeghers cancer-susceptibility syndrome	Signaling	-	0	6	6	0
SAT4	YCR008W	Ser/Thr protein kinase involved in salt tolerance; functions in regulation of Trk1p-Trk2p potassium transporter; partially redundant with Hal5p; has similarity to Npr1p	Signaling	-	0	18	40	6
SCY1	YGL083W	Putative kinase, suppressor of GTPase mutant, similar to bovine rhodopsin kinase	Signaling	-	0	0	0	1
SDP1	YIL113W	Stress-inducible dual-specificity MAP kinase phosphatase, negatively regulates Slt2p MAP kinase by direct dephosphorylation, diffuse localization under normal conditions shifts to punctate localization after heat shock	Signaling	-	0	3	2	0
SEF1	YBL066C	Putative transcription factor, has homolog in <i>Kluyveromyces lactis</i>	TF	-	0	0	0	0
SER2	YGR208W	Phosphoserine phosphatase of the phosphoglycerate pathway, involved in serine and glycine biosynthesis, expression is regulated by the available nitrogen source	Signaling	-	0	4	6	0
SET1	YHR119W	Histone methyltransferase, subunit of the COMPASS (Set1C) complex which methylates histone H3 on lysine 4; required in transcriptional silencing near telomeres and at the silent mating type loci; contains a SET domain	Chromatin	-	0	21	24	0
SET2	YJL168C	Histone methyltransferase with a role in transcriptional elongation, methylates a lysine residue of histone H3; associates with the C-terminal domain of Rpo21p; histone methylation activity is regulated by phosphorylation status of Rpo21p	Chromatin	RPD3S	7	29	32	3
SET3	YKR029C	Defining member of the SET3 histone deacetylase complex which is a meiosis-specific repressor of sporulation genes; necessary for efficient transcription by RNAPII; one of two yeast proteins that contains both SET and PHD domains	Chromatin	-	8	14	13	0

SFL1	YOR140W	Transcription repressor involved in regulation of flocculation-related genes, inhibits transcription by recruiting general corepressor Cyc8p-Tup1p to different promoters; negatively regulated by cAMP-dependent protein kinase A subunit Tpk2p	TF	-	7	3	2	0
Signaling1	YDR122W	Serine/threonine protein kinase involved in regulation of exocytosis; localizes to the cytoplasmic face of the plasma membrane; closely related to Kin2p	Signaling	-	0	3	8	4
SIN3	YOL004W	Component of the Sin3p-Rpd3p histone deacetylase complex, involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis; involved in the maintenance of chromosomal integrity	Chromatin	-	10	23	12	0
SIP3	YNL257C	Protein that activates transcription through interaction with DNA-bound Snf1p, C-terminal region has a putative leucine zipper motif; potential Cdc28p substrate	TF	-	0	8	10	0
SIP4	YJL089W	C6 zinc cluster transcriptional activator that binds to the carbon source-responsive element (CSRE) of gluconeogenic genes; involved in the positive regulation of gluconeogenesis; regulated by Snf1p protein kinase; localized to the nucleus	TF	-	0	4	6	2
SIW14	YNL032W	Tyrosine phosphatase that plays a role in actin filament organization and endocytosis; localized to the cytoplasm	Signaling	-	0	2	5	1
SKM1	YOL113W	Member of the PAK family of serine/threonine protein kinases with similarity to Ste20p and Cla4p; proposed to be a downstream effector of Cdc42p during polarized growth	Signaling	-	5	3	4	6
SKN7	YHR206W	Nuclear response regulator and transcription factor, part of a branched two-component signaling system; required for optimal induction of heat-shock genes in response to oxidative stress; involved in osmoregulation	TF	-	0	21	18	16
SKO1	YNL167C	Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, forms a complex with Tup1p and Ssn6p to both activate and repress transcription; cytosolic and nuclear protein involved in osmotic and oxidative stress responses	TF	-	0	5	6	3
SKS1	YPL026C	Putative serine/threonine protein kinase; involved in the adaptation to low concentrations of glucose independent of the SNF3 regulated pathway	Signaling	-	0	2	3	0
SKY1	YMR216C	SR protein kinase (SRPK) involved in regulating proteins involved in mRNA metabolism and cation homeostasis; similar to human SRPK1	Signaling	-	7	10	8	2
SLT2	YHR030C	Serine/threonine MAP kinase involved in regulating the maintenance of cell wall integrity and progression through the cell cycle; regulated by the PKC1-mediated signaling pathway	Signaling	MAPK	7	32	29	14
SLX8	YER116C	Protein containing a RING finger domain that interacts with Hex3p; mutant phenotypes and genetic interactions suggest a role in sumoylation and in genome stability	DNA Repair	RING/SUMO	11	24	17	3
SMK1	YPR054W	Middle sporulation-specific mitogen-activated protein kinase (MAPK) required for production of the outer spore wall layers; negatively regulates activity of the glucan synthase subunit Gsc2p	Signaling	-	4	0	4	5

SMP1	YBR182C	Putative transcription factor involved in regulating the response to osmotic stress; member of the MADS-box family of transcription factors	TF	-	5	0	0	0
SNF1	YDR477W	AMP-activated serine/threonine protein kinase found in a complex containing Snf4p and members of the Sip1p/Sip2p/Gal83p family; required for transcription of glucose-repressed genes, thermotolerance, sporulation, and peroxisome biogenesis	Signaling	-	0	12	14	3
SNT2	YGL131C	DNA binding protein with similarity to the <i>S. pombe</i> Snt2 protein	TF	-	0	5	8	2
SOK2	YMR016C	Nuclear protein that plays a regulatory role in the cyclic AMP (cAMP)-dependent protein kinase (PKA) signal transduction pathway; negatively regulates pseudohyphal differentiation; homologous to several transcription factors	Signaling	-	0	30	30	2
SPS18	YNL204C	Protein of unknown function, contains a putative zinc-binding domain; expressed during sporulation	TF	-	0	3	3	0
SPT2	YER161C	Protein involved in negative regulation of transcription; required for RNA polyadenylation; exhibits regulated interactions with both histones and SWI-SNF components, has similarity to mammalian HMG1 proteins	TF	-	6	7	12	4
SPT23	YKL020C	ER membrane protein involved in regulation of OLE1 transcription, acts with homolog Mga2p; inactive ER form dimerizes and one subunit is then activated by ubiquitin/proteasome-dependent processing followed by nuclear targeting	TF	-	0	5	10	1
SSK2	YNR031C	MAP kinase kinase kinase of the HOG1 mitogen-activated signaling pathway; interacts with Ssk1p, leading to autophosphorylation and activation of Ssk2p which phosphorylates Pbs2p; also mediates actin cytoskeleton recovery from osmotic stress	Signaling	-	2	10	15	0
SSK22	YCR073C	MAP kinase kinase kinase of the HOG1 mitogen-activated signaling pathway; functionally redundant with, and homologous to, Ssk2p; interacts with and is activated by Ssk1p; phosphorylates Pbs2p	Signaling	-	0	0	3	5
SSN3	YPL042C	Cyclin-dependent protein kinase, component of RNA polymerase II holoenzyme; involved in phosphorylation of the RNA polymerase II C-terminal domain; involved in glucose repression	Signaling	MEDIATOR	0	32	36	9
SSN8	YNL025C	Cyclin-like component of the RNA polymerase II holoenzyme, involved in phosphorylation of the RNA polymerase II C-terminal domain; involved in glucose repression and telomere maintenance	Signaling	MEDIATOR	15	16	25	3
STB1	YNL309W	Protein with a role in regulation of MBF-specific transcription at Start, phosphorylated by Cln-Cdc28p kinases in vitro; unphosphorylated form binds Swi6p and binding is required for Stb1p function; expression is cell-cycle regulated	TF	-	0	3	8	4
STB2	YMR053C	Protein that interacts with Sin3p in a two-hybrid assay and is part of a large protein complex with Sin3p and Stb1p	TF	-	0	3	5	3
STB4	YMR019W	Protein that binds Sin3p in a two-hybrid assay; contains a Zn(II)2Cys6 zinc finger domain characteristic of DNA-binding proteins	TF	-	0	7	5	0

STB5	YHR178W	Activator of multidrug resistance genes, forms a heterodimer with Pdr1p; contains a Zn(II)2Cys6 zinc finger domain that interacts with a PDRE (pleiotropic drug resistance element) in vitro; binds Sin3p in a two-hybrid assay	TF	-	4	16	17	6
STB6	YKL072W	Protein that binds Sin3p in a two-hybrid assay	Other	-	0	3	1	4
STP1	YDR463W	Transcription factor, activated by proteolytic processing in response to signals from the SPS sensor system for external amino acids; activates transcription of amino acid permease genes and may have a role in tRNA processing	TF	-	4	1	2	4
STP2	YHR006W	Transcription factor, activated by proteolytic processing in response to signals from the SPS sensor system for external amino acids; activates transcription of amino acid permease genes	TF	-	0	1	6	5
SUM1	YDR310C	Transcriptional repressor required for mitotic repression of middle sporulation-specific genes; involved in telomere maintenance, regulated by the pachytene checkpoint	TF	-	5	17	21	3
SUT1	YGL162W	Transcription factor of the Zn(II)2Cys6 family involved in sterol uptake; involved in induction of hypoxic gene expression	TF	-	0	2	2	1
SWC5	YBR231C	Protein of unknown function, component of the SWR1 complex, which exchanges histone variant H2AZ (Htz1p) for chromatin-bound histone H2A	Chromatin	SWR1C	29	16	14	6
SWE1	YJL187C	Protein kinase that regulates the G2/M transition by inhibition of Cdc28p kinase activity; localizes to the nucleus and to the daughter side of the mother-bud neck; homolog of <i>S. pombe</i> Wee1p; potential Cdc28p substrate	Signaling	-	0	4	7	1
SWI4	YER111C	DNA binding component of the SBF complex (Swi4p-Swi6p), a transcriptional activator that in concert with MBF (Mbp1-Swi6p) regulates late G1-specific transcription of targets including cyclins and genes required for DNA synthesis and repair	Cell Cycle	SBF	5	42	48	14
SWI5	YDR146C	Transcription factor that activates transcription of genes expressed at the M/G1 phase boundary and in G1 phase; localization to the nucleus occurs during G1 and appears to be regulated by phosphorylation by Cdc28p kinase	TF	-	7	12	10	0
SWI6	YLR182W	Transcription cofactor, forms complexes with DNA-binding proteins Swi4p and Mbp1p to regulate transcription at the G1/S transition; involved in meiotic gene expression; localization regulated by phosphorylation; potential Cdc28p substrate	Cell Cycle	SBF	12	16	19	1
SWR1	YDR334W	Swi2/Snf2-related ATPase that is the structural component of the SWR1 complex, which exchanges histone variant H2AZ (Htz1p) for chromatin-bound histone H2A	Chromatin	SWR1C	15	34	39	12
TBS1	YBR150C	Putative protein of unknown function; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies	TF	-	0	5	5	0
TEA1	YOR337W	Ty1 enhancer activator required for full levels of Ty enhancer-mediated transcription; C6 zinc cluster DNA-binding protein	TF	-	0	4	4	2

TEC1	YBR083W	Transcription factor required for full Ty1 expression, Ty1-mediated gene activation, and haploid invasive and diploid pseudohyphal growth; TEA/ATTS DNA-binding domain family member	TF	-	0	5	8	2
TEL1	YBL088C	Protein kinase primarily involved in telomere length regulation; contributes to cell cycle checkpoint control in response to DNA damage; functionally redundant with Mec1p; homolog of human ataxia telangiectasia (ATM) gene	DNA Repair	CHKPT	4	1	8	4
TEP1	YNL128W	Homolog of human tumor suppressor gene PTEN/MMAC1/TEP1 that has lipid phosphatase activity and is linked to the phosphatidylinositol signaling pathway; plays a role in normal sporulation	Signaling	-	0	0	0	0
THI2	YBR240C	Zinc finger protein of the Zn(II)2Cys6 type, probable transcriptional activator of thiamine biosynthetic genes	TF	-	5	2	1	0
TOF1	YNL273W	Subunit of a replication-pausing checkpoint complex (Tof1p-Mrc1p-Csm3p) that acts at the stalled replication fork to promote sister chromatid cohesion after DNA damage, facilitating gap repair of damaged DNA; interacts with the MCM helicase	DNA Repair	9-1-1	12	5	7	0
TOR1	YJR066W	PIK-related protein kinase and rapamycin target; subunit of TORC1, a complex that controls growth in response to nutrients by regulating translation, transcription, ribosome biogenesis, nutrient transport and autophagy; involved in meiosis	Signaling	-	0	4	3	0
TOS3	YGL179C	Protein kinase, related to and functionally redundant with Elm1p and Sak1p for the phosphorylation and activation of Snf1p; functionally orthologous to LKB1, a mammalian kinase associated with Peutz-Jeghers cancer-susceptibility syndrome	Signaling	-	0	10	7	3
TOS4	YLR183C	Transcription factor that binds to a number of promoter regions, particularly promoters of some genes involved in pheromone response and cell cycle; potential Cdc28p substrate; expression is induced in G1 by bound SBF	TF	-	0	3	4	6
TOS8	YGL096W	Homeodomain-containing transcription factor; SBF regulated target gene that in turn regulates expression of genes involved in G1/S phase events such as bud site selection, bud emergence and cell cycle progression; similarity to Cup9p	TF	-	0	1	2	0
TPK1	YJL164C	Subunit of cytoplasmic cAMP-dependent protein kinase, which contains redundant catalytic subunits Tpk1p, Tpk2p, and Tpk3p and regulatory subunit Bcy1p; promotes vegetative growth in response to nutrients; inhibits filamentous growth	Signaling	TPK	0	6	18	3
TPK2	YPL203W	Subunit of cytoplasmic cAMP-dependent protein kinase, which contains redundant catalytic subunits Tpk1p, Tpk2p, and Tpk3p and regulatory subunit Bcy1p; promotes vegetative growth in response to nutrients; activates filamentous growth	Signaling	TPK	4	2	3	0
TPK3	YKL166C	Subunit of cAMP-dependent protein kinase, which contains Tpk1p, Tpk2p, Tpk3p, and regulatory subunit Bcy1p; promotes growth in response to nutrients; mediates induction of apoptosis due to actin-mediated hyperactivation of Ras signaling	Signaling	TPK	0	6	19	2

TWF1	YGR080W	Twinfilin, highly conserved actin monomer-sequestering protein involved in regulation of the cortical actin cytoskeleton, composed of two cofilin-like regions, localizes actin monomers to sites of rapid filament assembly	Other	-	0	2	3	0
TYE7	YOR344C	Serine-rich protein that contains a basic-helix-loop-helix (bHLH) DNA binding motif; binds E-boxes of glycolytic genes and contributes to their activation; may function as a transcriptional activator in Ty1-mediated gene expression	TF	-	0	9	6	0
UBC13	YDR092W	Ubiquitin-conjugating enzyme involved in the error-free DNA postreplication repair pathway; interacts with Mms2p to assemble ubiquitin chains at the Ub Lys-63 residue; DNA damage triggers redistribution from the cytoplasm to the nucleus	DNA Repair	-	30	4	2	0
UGA3	YDL170W	Transcriptional activator necessary for gamma-aminobutyrate (GABA)-dependent induction of GABA genes (such as UGA1, UGA2, UGA4); zinc-finger transcription factor of the Zn(2)-Cys(6) binuclear cluster domain type; localized to the nucleus	TF	-	0	1	1	0
UME1	YPL139C	Negative regulator of meiosis, required for repression of a subset of meiotic genes during vegetative growth, binding of histone deacetylase Rpd3p required for activity, contains a NEE box and a WD repeat motif; homologous with Wtm1p, Wtm2p	TF	RPD3L	0	9	15	1
UME6	YDR207C	Key transcriptional regulator of early meiotic genes, binds URS1 upstream regulatory sequence, couples metabolic responses to nutritional cues with initiation and progression of meiosis, forms complex with Ime1p, and also with Sin3p-Rpd3p	TF	-	19	47	48	31
UPC2	YDR213W	Sterol regulatory element binding protein, induces transcription of sterol transport and biosynthetic genes; involved in the anaerobic induction of DAN/TIR mannoproteins and seripauperins; binucleate zinc cluster protein; Ecm22p homolog	TF	-	0	2	39	18
VAC14	YLR386W	Protein involved in regulated synthesis of PtdIns(3,5)P(2), in control of trafficking of some proteins to the vacuole lumen via the MVB, and in maintenance of vacuole size and acidity; interacts with Fig4p; activator of Fab1p	Signaling	-	7	9	4	0
VHS1	YDR247W	Cytoplasmic serine/threonine protein kinase; identified as a high-copy suppressor of the synthetic lethality of a sis2 sit4 double mutant, suggesting a role in G1/S phase progression; homolog of Sks1p	Signaling	-	6	3	3	1
VIP1	YLR410W	Inositol hexakisphosphate (IP6) and inositol heptakisphosphate (IP7) kinase, probably involved in cortical actin cytoskeleton function; ortholog of <i>S. pombe</i> asp1+	Signaling	-	0	12	8	0
VPS71	YML041C	Nucleosome-binding component of the SWR1 complex, which exchanges histone variant H2AZ (Htz1p) for chromatin-bound histone H2A; required for vacuolar protein sorting	Chromatin	SWR1C	15	38	59	14
VPS72	YDR485C	Htz1p-binding component of the SWR1 complex, which exchanges histone variant H2AZ (Htz1p) for chromatin-bound histone H2A; required for vacuolar protein sorting	Chromatin	SWR1C	13	14	20	0

VPS75	YNL246W	NAP family histone chaperone; binds to histone H3-H4 tetramers and to histone acetyltransferase RTT109; possesses nucleosome assembly activity in vitro; proposed role in vacuolar protein sorting	Chromatin	-	12	4	4	0
WAR1	YML076C	Homodimeric Zn2Cys6 zinc finger transcription factor; binds to a weak acid response element to induce transcription of PDR12 and FUN34, encoding an acid transporter and a putative ammonia transporter, respectively	TF	-	0	3	2	2
WTM1	YOR230W	Transcriptional repressor involved in regulation of meiosis and silencing, required for nuclear localization of the ribonucleotide reductase small subunit Rnr2p and Rnr4p; contains WD repeats	TF	-	0	1	2	1
WTM2	YOR229W	Transcriptional repressor involved in regulation of meiosis and silencing; contains WD repeats	TF	-	0	1	7	0
WWM1	YFL010C	WW domain containing protein of unknown function; binds to Mca1p, a caspase-related protease that regulates H2O2-induced apoptosis; overexpression causes G1 phase growth arrest and clonal death that is suppressed by overexpression of MCA1	Other	-	9	0	0	0
XBP1	YIL101C	Transcriptional repressor that binds to promoter sequences of the cyclin genes, CYS3, and SMF2; expression is induced by stress or starvation during mitosis, and late in meiosis; member of the Swi4p/Mbp1p family; potential Cdc28p substrate	TF	-	0	4	5	5
YAK1	YJL141C	Serine-threonine protein kinase that is part of a glucose-sensing system involved in growth control in response to glucose availability; translocates from the cytoplasm to the nucleus and phosphorylates Pop2p in response to a glucose signal	Signaling	-	0	13	21	2
YAP1	YML007W	Basic leucine zipper (bZIP) transcription factor required for oxidative stress tolerance; mediates pleiotropic drug and metal resistance; localized to the nucleus in response to the presence of oxidants	TF	-	7	8	14	1
YAP3	YHL009C	Basic leucine zipper (bZIP) transcription factor	TF	-	0	14	10	2
YAP5	YIR018W	Basic leucine zipper (bZIP) transcription factor	TF	-	0	3	2	1
YAP6	YDR259C	Putative basic leucine zipper (bZIP) transcription factor; overexpression increases sodium and lithium tolerance	TF	-	2	2	2	2
YAP7	YOL028C	Putative basic leucine zipper (bZIP) transcription factor	TF	-	0	7	7	0
YBL054W	YBL054W		TF	-	8	3	2	0
YBR028C	YBR028C		Signaling	-	5	4	3	2
YBR239C	YBR239C		TF	-	0	0	1	3
YCK1	YHR135C	Palmitoylated, plasma membrane-bound casein kinase I isoform; shares redundant functions with Yck2p in morphogenesis, proper septin assembly, endocytic trafficking; provides an essential function overlapping with that of Yck2p	Signaling	YCK	0	3	1	0
YCK2	YNL154C	Palmitoylated, plasma membrane-bound casein kinase I isoform; shares redundant functions with Yck1p in morphogenesis, proper septin assembly, endocytic trafficking; provides an essential function overlapping with that of Yck1p	Signaling	YCK	2	3	4	0

YCK3	YER123W	Palmitoylated, vacuolar membrane-localized casein kinase I isoform; negatively regulates vacuole fusion during hypertonic stress via phosphorylation of the HOPS complex subunit, Vps41p; shares overlapping essential functions with Hrr25p	Signaling	-	0	6	15	3
YCR079W	YCR079W	Phosphoprotein phosphatase type 2C similar to mammalian PP1Ks; involved in mitophagy; localized to mitochondrial inner membrane space; null mutant is sensitive to rapamycin	Signaling	-	10	1	5	1
YCR095C	YCR095C	Cytoplasmic protein required for replication of Brome mosaic virus in <i>S. cerevisiae</i> , which is a model system for studying replication of positive-strand RNA viruses in their natural hosts	Signaling	OCA	0	7	5	2
YDL025C	YDL025C		Signaling	-	0	4	6	2
YDR026C	YDR026C		TF	-	0	4	3	0
YDR049W	YDR049W		TF	-	18	8	27	3
YDR067C	YDR067C	Cytoplasmic protein required for replication of Brome mosaic virus in <i>S. cerevisiae</i> , which is a model system for studying replication of positive-strand RNA viruses in their natural hosts	Signaling	OCA	10	7	5	0
YDR266C	YDR266C		TF	-	0	2	7	7
YER130C	YER130C		TF	-	0	1	2	4
YER184C	YER184C		TF	-	0	1	3	8
YFL052W	YFL052W		TF	-	2	5	2	0
YGK3	YOL128C	Protein kinase related to mammalian glycogen synthase kinases of the GSK-3 family; GSK-3 homologs (Mck1p, Rim11p, Mrk1p, Ygk3p) are involved in control of Msn2p-dependent transcription of stress responsive genes and in protein degradation	Signaling	-	0	3	3	1
YGL059W	YGL059W		Signaling	-	0	4	4	0
YGR067C	YGR067C		TF	-	0	3	3	0
YHP1	YDR451C	One of two homeobox transcriptional repressors (see also Yox1p), that bind to Mcm1p and to early cell cycle box (ECB) elements of cell cycle regulated genes, thereby restricting ECB-mediated transcription to the M/G1 interval	TF	-	2	1	1	1
YIL042C	YIL042C	Mitochondrial kinase, phosphorylates pyruvate dehydrogenase alpha subunit Pda1p	Signaling	-	4	3	5	2
YJL057C	YJL057C	Putative serine/threonine kinase; expression is induced during mild heat stress; deletion mutants are hypersensitive to copper sulphate and resistant to sorbate; interacts with an N-terminal fragment of Sst2p	Signaling	-	4	1	5	0
YJL206C	YJL206C		TF	-	0	1	3	0
YKL161C	YKL161C		Signaling	-	0	6	13	3
YKL171W	YKL171W		Signaling	-	0	0	0	0
YKL222C	YKL222C		TF	-	0	1	2	0

YKR064W	YKR064W	Zinc cluster protein of unknown function; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies	TF	-	2	2	4	2
YKU70	YMR284W	Subunit of the telomeric Ku complex (Yku70p-Yku80p), involved in telomere length maintenance, structure and telomere position effect; relocates to sites of double-strand cleavage to promote nonhomologous end joining during DSB repair	DNA Repair	-	14	5	3	0
YLR278C	YLR278C		TF	-	0	3	4	2
YML081W	YML081W		TF	-	0	4	2	0
YMR1	YJR110W	Phosphatidylinositol 3-phosphate [PI(3)P] phosphatase, regulates the localization and levels of PI(3)P; involved in cytoplasm to vacuole (CVT) transport; has similarity to the conserved myotubularin dual specificity phosphatase family	Signaling	-	0	1	2	0
YMR291W	YMR291W		Signaling	-	7	0	4	0
YNL056W	YNL056W	Putative protein with similarity to predicted tyrosine phosphatases Oca1p and Siw14p; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm; YNL056W is not an essential gene	Signaling	OCA	0	6	5	0
YNL217W	YNL217W		Signaling	-	0	3	4	0
YNR047W	YNR047W		Signaling	-	4	9	12	3
YNR063W	YNR063W		TF	-	0	2	3	2
YOX1	YML027W	Homeodomain-containing transcriptional repressor, binds to Mcm1p and to early cell cycle boxes (ECBs) in the promoters of cell cycle-regulated genes expressed in M/G1 phase; expression is cell cycle-regulated; potential Cdc28p substrate	TF	-	0	2	8	5
YPK1	YKL126W	Serine/threonine protein kinase required for receptor-mediated endocytosis; involved in sphingolipid-mediated and cell integrity signaling pathways; localized to the bud neck, cytosol and plasma membrane; homolog of mammalian kinase SGK	Signaling	-	0	1	1	1
YPK2	YMR104C	Protein kinase with similarity to serine/threonine protein kinase Ypk1p; functionally redundant with YPK1 at the genetic level; participates in a signaling pathway required for optimal cell wall integrity; homolog of mammalian kinase SGK	Signaling	-	0	6	7	0
YPL109C	YPL109C		Signaling	-	0	1	2	0
YPL141C	YPL141C		Signaling	-	0	0	0	0
YPL150W	YPL150W		Signaling	-	0	2	3	0
YPL230W	YPL230W		TF	-	5	7	0	10
YPL236C	YPL236C		Signaling	-	4	2	2	0
YPR022C	YPR022C		Other	-	5	2	3	0

YPR152C	YPR152C	Pre-mRNA splicing factor associated with the U2-U5-U6 snRNPs, the RES complex, and the Prp19-associated complex (NTC); null mutation displays synthetic genetic interactions with mutations affecting U2 snRNA and pre-mRNA splicing factors	Other	-	0	3	5	0
YPR196W	YPR196W		TF	-	0	2	1	0
YPS1	YLR120C	Aspartic protease, attached to the plasma membrane via a glycosylphosphatidylinositol (GPI) anchor	Other	-	0	5	5	5
YRR1	YOR162C	Zn2-Cys6 zinc-finger transcription factor that activates genes involved in multidrug resistance; paralog of Yrm1p, acting on an overlapping set of target genes	TF	-	0	2	3	0
YVH1	YIR026C	Protein phosphatase involved in vegetative growth at low temperatures, sporulation, and glycogen accumulation; transcription induced by low temperature and nitrogen starvation; member of the dual-specificity family of protein phosphatases	Signaling	-	0	1	11	1

Supplementary Table S3

Protein target	Name	Peptide target	log Fold-change	p-value
YJR060W	CBF1	R.DQGILLS*QESNDGNIDSALLSEGATLK	7.635	4.23E-04
YDR418W	RPL12B	K.IGPLGLS*PK	3.262	1.42E-04
YER088C	DOT6	K.RGS*FSGHS*MK	2.795	9.62E-03
YMR031C	YMR031C	K.TSGGGS*RTSSITS*SKK	2.718	2.88E-04
YAR009C	YAR009C	R.SPS*IDASPPENSSHNIVPIK	2.611	1.20E-03
YEL032W	MCM3	R.VRQPAS*NSGS*PIKSTPR,R.VRQPAS*NS*GSPIKSTPR	2.552	3.10E-03
YOR175C	YOR175C	K.DISASS*PNLGGILK	2.466	1.71E-03
YIL121W	QDR2	K.LALTRT*ES*VKPEPEITAPPHSR	2.416	3.92E-03
YER088C	DOT6	R.RSS*FAYPQQVAIT*TPSSPNS*SHVLLSSK,R.RSS*FAYPQQVAITT*TPSSPNS*SHVLLSSK	2.258	3.03E-03
YER032W	FIR1	R.QMLIDLQKS*PTNNNPR	2.183	5.62E-04
YER088C	DOT6	R.LNALSSDADMLS*PTHS*PQK	2.172	1.74E-04
YKR084C	HBS1	R.LPDWLDEEES*EGERNGEEANDEK	2.106	3.23E-04
YER088C	DOT6	R.RGS*LANWS*R	2.086	1.74E-04
YER088C	DOT6	K.SGSTTDDDKGS*DKEDVMGDGSNDDDEDNVDPLHR	2.034	1.74E-04
YDR303C	RSC3	R.KLS*EDGVTGDGKPIPESER	2.03	4.18E-03
YEL037C	RAD23	K.VTEPPIAPESATTPGRENST*EASPSTDASAAPAATAPEGSQPQEEQTATTER	1.982	1.34E-02
YCR034W	FEN1	K.NVPT*PS*PS*PKPQHR	1.912	4.95E-03
YKL052C	ASK1	K.GQADDNNEGPDEEEST*KEVPKPGTIIHFSTNR	1.901	4.49E-03
YER088C	DOT6	R.RGS*LANWSR	1.874	1.95E-04
YER063W	THO1	R.LIKDDEESKGESEVSPQEQNQEQGS*EPAAIEEPASQNITEK	1.869	3.33E-03
YER088C	DOT6	K.DVSPDPIFSPDPADDSNT*SDAGSR	1.811	3.97E-04
YER033C	ZRG8	K.STS*FDES*PKR	1.8	3.11E-03
YBL054W	YBL054W	R.RS*SFNSHAPTEPIS*R	1.795	2.98E-04
YER033C	ZRG8	R.NNS*DDETEHTSAIK	1.79	9.60E-03
YEL015W	EDC3	R.SNS*TSLPAANK	1.759	2.00E-04
YER169W	RPH1	R.ISS*FQEQPLNK	1.705	2.88E-04
YER088C	DOT6	K.SGSTTDDDKGS*DKEDVMGDGS*NDDDEDNVDPLHR	1.689	6.74E-03
YEL032W	MCM3	R.VRQPAS*NSGS*PIK	1.684	2.98E-04
YPR174C	YPR174C	R.AVNPLVTSS*PIHMS*PLQSR	1.64	5.77E-04
YPR111W	DBF20	R.ISLNHS*PK	1.639	2.72E-03
YER114C	BOI2	R.SAS*EAIKGETLK	1.615	1.74E-04
YHR132W-A	YHR132W-A	R.MS*SSSGGDSIS*R	1.611	4.35E-03
YER114C	BOI2	R.SSS*PEENPITSMPSEK	1.568	3.91E-04
YIL038C	NOT3	K.ETERS*PS*SSPIHNATKPEEAVK,K.ETERS*PSS*SPIHNATKPEEAVK	1.567	8.74E-04
YLR219W	MSC3	R.ANS*ITVK	1.556	1.74E-04

YER111C	SWI4	R.SQS*ISDEKEK	1.541	1.30E-02
YOR260W	GCD1	K.LGPQSMS*R	1.538	1.30E-02
YOL070C	YOL070C	R.ATLNTQRLS*AMIDSLNNEKDDR	1.534	3.27E-04
YGR008C	STF2	K.YFSHTGNYGES*PNHIK	-1.507	2.59E-03
YNL173C	MDG1	R.SIFSQEVVELPDS*EDETQQVNKTGK	-1.517	9.76E-04
YPL004C	LSP1	R.APTAAELQAPPPPSST*K	-1.521	1.15E-02
YKL062W	MSN4	R.RY*SEVVTSSFPSMTDSR	-1.538	4.96E-03
YDR171W	HSP42	K.KSS*S*FAHLQAPSPIPDPLQVSKPETR	-1.542	2.88E-04
YGR192C,YJR009C,YJL052W	TDH1, TDH2, TDH3	R.GGRTAS*GNIIPSSTGAAK	-1.543	3.59E-03
YPL127C	HHO1	K.KASS*PSSLTYK	-1.574	7.39E-04
YDL065C	PEX19	R.SANS*PLKHGNEEEELMK	-1.59	7.72E-03
YDL223C	HBT1	K.GYSNTDS*NSDRDVIPGSFR	-1.601	1.74E-04
YDL099W	YDL099W	K.NKNSSATGSIGSETPDLEGTPGEES*TQEETVK	-1.611	1.58E-03
YGL031C	RPL24A	R.S*LKPEVR	-1.621	1.74E-04
YDL110C	YDL110C	K.LEGADDRLEADD*DDLENIDSGDLALYKDSVR	-1.638	1.74E-04
YNL209W,YDL229W	SSB1, SSB2	K.SSNITISNAVGRLLS*EEIEK	-1.641	1.62E-03
YGL049C	TIF4632	R.S*NSRFNNHNQSNNSR	-1.643	2.05E-03
YDR515W	SLF1	K.SSS*PDSNTVIPVEELR	-1.655	3.65E-04
YLR335W	NUP2	R.VADAQIQRETYDS*NES*DDDVTPTSK	-1.726	1.40E-03
YJR104C	SOD1	K.FEQASESEPTTVSYEIAGNS*PNAER	-1.761	1.92E-03
YAR010C	YAR010C	R.AHNVSTS*NNS*PSTDNDSISK,R.AHNVST*SNNS*PSTDNDSISK	-1.802	2.26E-04
YMR105C	PGM2	K.CTGGIILTAS*HNPGGPENDMGIK	-1.883	1.74E-04
YLR429W	CRN1	K.SSDIDQVNNNAEDPSRDTSGWEEADDEPAPIKIETPVT*PTETKK	-1.886	3.23E-04
YOL109W	ZEO1	K.KQAS*AAVS*EKKETK	-1.939	4.43E-03
YDR043C	NRG1	R.NTLS*DEEDLEQRR	-1.944	5.15E-03
YKR004C	ECM9	K.T*FSDQSGISNENIYYMT*VGFLTTPENKTVYNVHE DLLK	-1.951	6.98E-03
YPL049C	DIG1	R.TSQPQQQS*PSLLQGEIR	-1.989	3.56E-04
YGR229C	SMI1	R.SQQGLSHVTSTGSS*SS*MER,R.SQQGLSHVTS*TGSSS*SMER	-2.113	2.16E-03
YHR027C	RPN1	K.QQTIDEQSQIS*PEK	-2.152	8.40E-04
YLR206W	ENT2	R.T*RSNPHDS*SPSYQDDLEKALEESR	-2.21	1.11E-02
YDR156W	RPA14	K.KETS*IGVSATGGKK	-2.224	2.56E-03
YHR097C	YHR097C	K.ANSS*TT*TLDAIKPNSK,K.ANSS*TTT*TLDAIKPNSK	-2.424	1.95E-03
YDR156W	RPA14	K.KETS*IGVSATGGKK	-2.466	3.56E-04
YLR335W	NUP2	R.ADGTGEAQVDNS*PTTESNSR	-2.646	1.74E-03
YER122C	GLO3	K.AISSDQLFGRGS*FDEAANR	-2.993	3.97E-04
YFL055W	AGP3	R.S*INLDEGRRKDMOADLS*DQESSLASSET*MK	-3.453	7.29E-04
YFL014W	HSP12	K.GVFQGVHDS*AEKGKDNAEGQGESLADQAR	-3.6	7.02E-05
YDL223C	HBT1	K.S*ISGGTFGFR	-3.976	5.00E-05
YFL014W	HSP12	K.GKDNAEGQGES*LADQAR	-4.026	5.74E-04
YDL223C	HBT1	K.SVQKQDEPLS*PR	-4.995	5.00E-05

YML100W	TSL1	R.SATRS*PSAFNR	-5.091	1.74E-04
YDL223C	HBT1	K.ASYGSGGNSQSQEYSS*DDNIDVNKNAK	-6.113	5.33E-04
YFL014W	HSP12	K.ASEALKPDS*QKS*YAEQGKEYITDKADK	-6.364	5.98E-03
YDL223C	HBT1	R.KYS*GNTATGPPQDTIKEIAQNVK	-6.474	7.72E-03
YDL223C	HBT1	R.KVSVGS*MGS*GK	-6.477	2.83E-03
YFL014W	HSP12	K.ASEALKPDS*QKSYAEQGK	-6.636	9.62E-04
YFL014W	HSP12	K.ASEALKPDS*QKS*YAEQGKEYITDK,K.ASEALKPDS QKS*Y*AEQGKEYITDK	-6.899	8.53E-03
YML013W	SEL1	K.WLKACIDEIQPFET*TGK	-6.916	8.53E-03
YPL124W	SPC29	R.MSS*PLHRLSPTGKS*DDR	-7.091	1.79E-03
YOR220W	YOR220W	R.NKPLLSINTDPGVTGVDSSSLNKGGSSLS*PDKSS*LE SPTMLK	-9.07	1.33E-04

Supplementary Table S4

GENE1	GENE2	PE-SCORE
HIR1	HIR3	2.788497
HIR1	HIR2	3.432783
HAP3	HAP2	4.752648
HAP3	HAP5	4.933407
RTG3	RTG1	6.053276
RXT2	RCO1	4.86063
RXT2	PHO23	10.430102
RXT2	RPD3	12.551748
RXT2	SIN3	11.509815
RXT2	UME1	12.615862
RXT2	CTI6	9.619161
RXT2	EAF3	4.755369
CDC28	CLB3	5.496195
CDC28	CLN1	2.706946
CDC28	CLN2	4.079194
SWC5	SWR1	9.827232
SWC5	VPS72	4.173873
SWC5	BDF1	5.770427
ISW1	RSC1	2.918411
ISW1	RSC2	5.641513
ISW1	SIN3	2.171429
DCC1	CTF8	5.081266
DCC1	CTF18	2.091372
YCR095C	SIW14	7.196557
YCR095C	YNL056W	2.563859
YCR095C	OCA1	6.554909
NHP10	IES3	10.586607
NHP10	ARP8	13.759448
MBP1	SWI6	9.264232
PPH21	PPH22	6.623274
PPH3	PSY2	17.755653
UME6	CTI6	3.034789
SWR1	VPS72	5.953967
SWR1	BDF1	5.107874
SWR1	VPS71	2.595262
ADA2	NUT1	3.735321
ADA2	YAP1	3.955575
ADA2	SSN3	2.526093
VPS72	VPS71	2.545141
EAF5	RCO1	2.016766

GENE1	GENE2	Number of citations of Physical interactions
CTK3	CTK1	2
PKH1	YPK1	2
RAD9	RAD9	5
ASF1	RAD53	7
SLT2	MSG5	2
SKN7	MBP1	2
IES3	ARP8	2
DCC1	CTF8	2
RPD3	CTI6	5
PHO4	PHO2	3
SIN3	RPD3	10
RXT2	PHO23	3
MRE11	RSC1	2
CDC28	CLB4	3
SNF1	SIP3	2
ASF1	HIR1	5
CBF1	CBF1	2
YPK1	YPK2	2
CDC28	SWE1	4
SWI4	SLT2	2
HOT1	CKB2	2
OPI1	INO2	3
HTZ1	VPS72	3
SIP4	SNF1	3
PGD1	NUT1	2
SIN3	EAF3	6
RPD3	RXT2	5
PUT3	PUT3	2
HIR1	HIR1	2
PPH21	PPH22	2
PHO4	PHO80	3
RAD5	RAD5	3
ASH1	PHO23	2
YNL056W	OCA1	4
PBS2	RCK2	3
SNF1	CAT8	2
RIM11	UME6	4
FUS3	TEC1	4
CKA1	CKA1	2
CYC8	RGT1	2

EAF5	EAF7	7.771636
EAF5	RPD3	2.199357
EAF5	UME1	2.328417
EAF5	EAF3	11.553041
RAD51	RAD52	2.074246
SWI4	SWI6	8.101305
CKB1	CKA1	21.419119
CKB1	HOT1	6.414988
CKB1	CKB2	21.225952
CKB1	CKA2	25.584132
PGD1	NUT1	8.278908
PGD1	YAP1	3.758778
PGD1	SSN3	7.15724
NUT1	YAP1	4.863761
NUT1	SSN8	3.196744
NUT1	SSN3	7.09654
HAP2	HAP5	5.650635
RTG2	RTT101	2.991104
RSC1	RSC2	13.993385
CTF8	CTF18	3.214206
CKA1	HOT1	4.693782
CKA1	CKB2	20.796937
CKA1	CKA2	26.065045
CKA1	CTI6	2.73757
XBP1	UME1	2.164067
CTK2	CTK1	6.867981
CTK2	CTK3	6.21172
RTT101	MMS1	2.322374
ASF1	RAD53	6.421096
PBS2	SSK2	2.443656
TPK1	TPK2	4.846008
HIR3	HIR2	4.670725
HIR3	RAD53	2.928104
YPK1	YPK2	2.145222
CTK1	CTK3	8.601688
TPK3	TPK2	2.578153
RTT109	VPS75	8.582446
IES3	ARP8	8.346366
HOG1	RCK2	2.461568
VAC14	FIG4	5.890958
YAP1	SSN3	4.963536
RCO1	PHO23	3.790978
RCO1	RPD3	16.328459
RCO1	SIN3	14.849308
RCO1	UME1	15.173956
RCO1	CTI6	2.12903
RCO1	EAF3	17.407629

TPK2	MGA1	2
HIR3	HIR2	2
TEC1	MSS11	2
SFL1	CYC8	2
IES3	NHP10	2
YCR095C	OCA1	3
RFX1	CYC8	2
RCO1	EAF3	5
RAD51	RAD51	6
CKB2	CKA1	3
CDC28	SWI6	3
HOG1	SKO1	2
NRG1	CYC8	2
FUS3	FUS3	2
RAD52	RAD52	2
SWR1	HTZ1	2
RXT2	UME1	3
HEX3	RAD52	2
TPK1	TPK3	2
ARG80	ARG81	2
SIW14	OCA1	2
TEC1	DIG1	2
PTC2	RAD53	2
RAD53	RAD9	15
WTM1	WTM1	2
RSC1	RSC2	3
INO4	INO2	6
SIN3	CTI6	6
FUS3	DIG1	5
CTF8	CTF18	2
SWI6	CLN2	2
RAD18	RAD18	2
MAC1	MAC1	3
PHO23	SIN3	3
SIN3	PHO23	5
RXT2	EAF3	2
CDC28	CLB1	3
RAD53	ASF1	8
MSN1	MSS11	3
CKA2	CKB1	3
HOG1	SMP1	2
SSK2	PBS2	4
UBC13	RAD5	4
SKN7	SKN7	3
PHO23	RPD3	4
SNF1	MSN2	2
CTK1	CTK3	6

HOT1	CKB2	6.41675
HOT1	CKA2	3.542335
CLN1	CLN2	2.495574
SIW14	YNL056W	3.093724
SIW14	OCA1	8.515399
YNL056W	OCA1	3.649896
PHO23	RPD3	11.235193
PHO23	SIN3	9.00103
PHO23	UME1	10.256805
PHO23	CTI6	7.624178
PHO23	EAF3	4.440526
EAF7	EAF3	5.743062
RPD3	SIN3	21.270967
RPD3	UME1	22.05868
RPD3	CTI6	12.012586
RPD3	EAF3	16.830296
SIN3	UME1	19.42699
SIN3	CTI6	13.154659
SIN3	EAF3	14.972455
CKB2	CKA2	22.725516
UME1	CTI6	12.049568
UME1	EAF3	14.977528

CDC28	CLN1	5
KSS1	DIG1	5
EAF5	EAF7	3
CKA1	HOT1	3
PPH3	PSY2	7
CLB5	CDC28	3
GAL4	ADA2	2
SIN3	RXT2	4
CDC28	ELM1	2
SIN3	RCO1	4
HOT1	CKA2	2
CKB1	CKA1	2
SUT1	CYC8	2
SDP1	SLT2	4
CDC28	SWI4	2
HAP2	HAP3	4
UME1	EAF3	3
CYC8	SET2	2
CYC8	RCS1	2
SSN3	SSN8	6
SLT2	MKK2	2
CDC28	CLN2	9
CKB1	CKB2	3
OCA1	SIW14	3
SLT2	SWI6	2
RPD3	CKA1	2
CDC28	SWI5	2
SWI5	PHO2	2
GAL4	SSN3	4
VPS71	SWR1	2
RXT2	CTI6	3
IME1	RIM11	3
EAF5	EAF3	3
RPD3	UME1	9
CTI6	UME1	3
SSN3	GAL4	3
SWI4	SWI6	9
IME1	UME6	3
UME1	RXT2	2
RAD5	RAD18	2
MBP1	SWI6	4
EAF3	RPD3	4
RAD18	RAD5	2
SWC5	BDF1	3
RXT2	SIN3	3
SSK22	PBS2	2
CKA2	CKB2	3

CTI6	SIN3	2
CLB2	SWI4	2
UME1	RPD3	3
YRR1	YRR1	2
CTI6	RPD3	3
CKB2	CKB1	4
RTT109	VPS75	3
CAT8	SIP4	2
GCN2	GCN2	5
CLB2	CDC28	10
TOR1	GLN3	2
SAE2	SAE2	2
IME2	IME1	2
SSN8	SSN3	6
MKK1	SLT2	2
INO2	INO4	3
MSG5	FUS3	3
VAC14	FIG4	2
GAL80	GAL80	3
BCK1	MKK1	2
SNF1	GLN3	2
RTG1	RTG3	3
TPK2	SFL1	3
RGT1	MTH1	3
CTK1	CTK2	5
UME6	IME1	2
RAD9	RAD53	5
KSS1	TEC1	2
ISW1	RSC2	3
CDC28	CLB3	4
EAF3	SIN3	3
RAD51	RAD52	14
SIN3	CKA1	2
RPD3	UME6	3
CLA4	SWE1	2
RTG3	RTG1	2
HTZ1	SWR1	6
MRE11	MRE11	3
MRE11	RSC2	2
HTZ1	BDF1	4
CKA1	CKB2	8
HOG1	RCK2	7
PTP2	SLT2	3
MSG5	SLT2	6
ASF1	HIR2	4
ARG81	ARG80	3
RAD17	RAD17	2

CKB1	HOT1	2
UME1	CTI6	3
RPD3	EAF3	5
CYC8	PGD1	2
SKO1	HOG1	2
HAP3	HAP5	4
RTT109	ASF1	2
CLN3	CDC28	2
TOS3	MIG1	2
PTP2	HOG1	5
INO4	PHO4	2
SWI4	CLN2	2
RIM11	IME1	5
DIG1	FUS3	3
CKB1	CKA2	3
ARG82	ARG80	3
SNF1	MIG3	2
CLB2	SWE1	2
RXT2	RPD3	3
RAD53	SWI4	3
TPK1	TPK2	3
RAD53	MRC1	2
PSY2	PPH3	6
PHO2	PHO4	6
SWR1	VPS72	5
CAT8	CAT8	2
PHO4	PHO4	3
PDR1	STB5	2
RPD3	PHO23	7
RCO1	RPD3	5
VHS1	SEF1	2
TPK2	TPK1	2
SWR1	BDF1	2
IRE1	PTC2	2
ASK10	SSN8	2
NHP10	RSC2	2
HOG1	HOT1	2
PSY2	RAD53	3
EAF3	UME1	4
MKK2	SLT2	3
MEC1	CLN1	2
SNF1	MIG1	6
RLM1	SLT2	2
GAL3	GAL80	8
EAF3	RCO1	3
SIN3	CKB1	2
RCK1	HOG1	2

DUN1	RAD53	2
MEC1	RAD53	4
RCO1	UME1	5
CKB2	HOT1	2
UME6	SIN3	4
SPT23	SPT23	2
RPD3	ASH1	2
SLT2	SWI4	3
CTK2	CTK1	5
YCR095C	SIW14	2
PHO2	SWI5	4
CTF18	CTF8	3
SWR1	VPS71	4
RPD3	SIN3	8
RAD5	UBC13	2
DIG1	KSS1	3
HTZ1	SWC5	2
RAD53	DUN1	4
RCK2	HOG1	5
SWI5	CLB2	2
RAD53	RAD53	3
CKB2	CKA2	6
WTM2	WTM2	3
HSL1	HSL1	3
INO4	TYE7	2
IRE1	IRE1	2
PHO80	PHO4	7
HEX3	SLX8	8
TPK2	TPK3	5
IME2	NDT80	5
RAD53	PTC2	3
EAF7	EAF3	3
ASF1	HIR3	3
WTM2	WTM1	3
SWC5	SWR1	3
CDC28	ASH1	2
RPD3	RPD3	2
TOR1	SLT2	2
UME1	SIN3	3
HIR2	HIR1	3
GAL80	GAL3	3
CDC28	CLN3	5
UME1	PHO23	2
HAP2	HAP5	7
CDC28	STB1	3
SWC5	VPS72	2
NHP10	IES3	2

CDC28	FKH2	3
HTZ1	VPS71	4
SWI6	SWI4	4
CLN2	CDC28	7
RCO1	SIN3	5
BAS1	PHO2	4
NHP10	ARP8	4
BCK1	SLT2	3
MEC1	CLN2	2
TPK1	CRZ1	3
CYC8	RTG3	2
SWE1	CLB2	2
SIN3	ISW1	2
CBF1	MET28	2
PHO23	UME1	2
SIN3	UME1	6
YNL056W	SIW14	2
RAD52	RAD51	8
VPS71	SWC5	2
INO2	OPI1	4
HIR1	HIR2	2
PHO80	VIP1	2
CKA2	CKA1	4
SWR1	SWC5	5
MIG1	SNF1	2
CLB3	CDC28	4
RCS1	RCS1	2
INO4	RTG3	2
CTI6	PHO23	2
SNF1	SIP4	3
CTI6	CYC8	2
CTK2	CTK3	6
ISW1	SIN3	2
UME1	RCO1	2
RAD53	SWI6	3
HOG1	PBS2	2
PBS2	PTC1	3
HOG1	HSL1	2
PIP2	OAF1	2
GAL80	GAL4	5
CKA1	CKB1	6
GAL4	GAL80	18
RPD3	RCO1	4
CKA1	CKA2	7
CDC28	CLB2	2
WTM1	WTM2	2
VPS72	HTZ1	2

CDC28	PHO2	2
SIN3	CKA2	2

Supplementary Table S5
Multi-gene modules identified in this study

Module ID	Genes	Name in Figure 5D
5	PHO80,VIP1	
7	ADA2,SSN3,PGD1,NUT1,YAP1	Mediator
13	DCC1,CTF18,CTF8	aRFC
21	YDR067C,YCR095C,OCA1,YNL056W,SIW14	OCA
38	TOS3,MIG1	
48	SMP1,HOG1	
53	HAC1,IRE1	HAC1/IRE1
63	GCN2,TOR1	
75	MKK1,ASK10	
83	SLX8,HEX3	
86	WTM2,WTM1	
93	RGT1,CYC8	
95	CKA1,CKB1,CKB2,CKA2,HOT1	CK2
98	TPK2,SFL1	
101	INO4,INO2	INO
111	MSS11,MSN1	
117	PPH22,PPH21	PP2A
122	MSN2,SNF1	
134	HAP5,HAP3,HAP2	HAP-C
135	SIP4,CAT8	
136	OAF1,PIP2	
141	PSY2,PPH3	PPH3-C
151	GAL80,GAL3	
179	MBP1,SWI6	MBF
184	ELM1,HSL1	Septin Checkpoint
191	RTT101,MMS1	RTT101-C
229	CTI6,PHO23,RPD3,UME6,SIN3	RPD3(L)
234	RCO1,SET2	
235	FAB1,SIT4	
244	MRE11,RSC2,RSC1	RSC
245	RAD5,RAD18	Post Replicative Repair
249	RAD52,RAD51	RAD52 Epistasis Group
256	EAF3,EAF5,EAF7	NuA4
258	SWE1,CLB2	
260	CLN2,CLN1	Cyclins
262	VPS75,RTT109	Rtt109-C
267	BCK1,MKK2,SLT2	MAPK
271	FIG4,VAC14	FIG4-C
282	CTK1,CTK2,CTK3	CTK-C
288	TPK1,TPK3,YBR028C	TPK-C
294	HIR3,HIR2,HIR1,ASF1	HIR-C

301	UME1,RXT2	
302	PHO2,BAS1	
303	TOF1,MRC1	Replication Pausing Checkpoint
310	HMS1,HMS2	HMS1/2
315	YCK1,MTH1,YCK2	YCK-C
331	VHS1,SEF1	
333	SWC5,VPS72,VPS71,SWR1,HTZ1	SWR-C
338	NHP10,IES3,ARP8	INO80
341	KSS1,TEC1,DIG1	MAPK_Growth
344	YPK2,YPK1,PKH2	YPK-C
364	PBS2,SSK2	
365	ARG80,ARG82	
392	PRK1,CDC28	
393	IME1,IME2	IME1/2
82	MEC1,TEL1,DUN1,RAD53	Damage Signaling

Supplementary Table S6
Module-Module interactions identified in this study

module ID	Genes	module ID	Genes	Number of Interactions	P-value	Genetic interaction bundle type
21	YDR067C,YCR095C,OCA1,YNL056W,SIW14	5	PHO80,VIP1	3	1.83E-05	Positive Untreated
101	INO4,INO2	229	CTI6,PHO23,RPD3,UME6,SIN3	3	1.83E-05	Positive Untreated
134	HAP5,HAP3,HAP2	229	CTI6,PHO23,RPD3,UME6,SIN3	3	6.81E-05	Positive Untreated
282	CTK1,CTK2,CTK3	38	TOS3,MIG1	2	0.000431644	Positive Untreated
134	HAP5,HAP3,HAP2	267	BCK1,MKK2,SLT2	2	0.00102486	Positive Untreated
117	PPH22,PPH21	333	SWC5,VPS72,VPS71,SWR1,HTZ1	2	0.00127649	Positive Untreated
179	MBP1,SWI6	7	ADA2,SSN3,PGD1,NUT1,YAP1	2	0.00127649	Positive Untreated
302	PHO2,BAS1	333	SWC5,VPS72,VPS71,SWR1,HTZ1	2	0.00127649	Positive Untreated
21	YDR067C,YCR095C,OCA1,YNL056W,SIW14	282	CTK1,CTK2,CTK3	2	0.00292565	Positive Untreated
21	YDR067C,YCR095C,OCA1,YNL056W,SIW14	244	MRE11,RSC2,RSC1	2	0.00292565	Positive Untreated
229	CTI6,PHO23,RPD3,UME6,SIN3	333	SWC5,VPS72,VPS71,SWR1,HTZ1	17	1.97E-23	Negative Untreated
282	CTK1,CTK2,CTK3	333	SWC5,VPS72,VPS71,SWR1,HTZ1	12	2.53E-18	Negative Untreated
301	UME1,RXT2	333	SWC5,VPS72,VPS71,SWR1,HTZ1	8	1.43E-12	Negative Untreated
234	RCO1,SET2	333	SWC5,VPS72,VPS71,SWR1,HTZ1	7	1.82E-10	Negative Untreated
229	CTI6,PHO23,RPD3,UME6,SIN3	282	CTK1,CTK2,CTK3	7	8.89E-09	Negative Untreated
13	DCC1,CTF18,CTF8	184	ELM1,HSL1	5	2.02E-08	Negative Untreated
282	CTK1,CTK2,CTK3	301	UME1,RXT2	5	2.02E-08	Negative Untreated
234	RCO1,SET2	83	SLX8,HEX3	4	1.81E-07	Negative Untreated
294	HIR3,HIR2,HIR1,ASF1	338	NHP10,IES3,ARP8	5	2.64E-06	Negative Untreated
282	CTK1,CTK2,CTK3	83	SLX8,HEX3	4	2.64E-06	Negative Untreated
13	DCC1,CTF18,CTF8	83	SLX8,HEX3	4	2.64E-06	Negative Untreated
256	EAF3,EAF5,EAF7	333	SWC5,VPS72,VPS71,SWR1,HTZ1	5	9.50E-06	Negative Untreated

267	BCK1,MKK2,SLT2	282	CTK1,CTK2,CTK3	4	2.11E-05	Negative Untreated
184	ELM1,HSL1	229	CTI6,PHO23,RPD3,UME6,SIN3	4	3.46E-05	Negative Untreated
179	MBP1,SWI6	184	ELM1,HSL1	3	3.48E-05	Negative Untreated
101	INO4,INO2	53	HAC1,IRE1	3	3.48E-05	Negative Untreated
282	CTK1,CTK2,CTK3	294	HIR3,HIR2,HIR1,ASF1	4	7.90E-05	Negative Untreated
301	UME1,RXT2	338	NHP10,IES3,ARP8	3	0.000168529	Negative Untreated
134	HAP5,HAP3,HAP2	260	CLN2,CLN1	3	0.000168529	Negative Untreated
282	CTK1,CTK2,CTK3	7	ADA2,SSN3,PGD1,NUT1,YAP1	4	0.000207325	Negative Untreated
229	CTI6,PHO23,RPD3,UME6,SIN3	267	BCK1,MKK2,SLT2	4	0.000207325	Negative Untreated
294	HIR3,HIR2,HIR1,ASF1	365	ARG80,ARG82	3	0.000457437	Negative Untreated
282	CTK1,CTK2,CTK3	338	NHP10,IES3,ARP8	3	0.000675588	Negative Untreated
302	PHO2,BAS1	63	GCN2,TOR1	2	0.00249468	Negative Untreated
5	PHO80,VIP1	53	HAC1,IRE1	2	0.00249468	Negative Untreated
184	ELM1,HSL1	260	CLN2,CLN1	2	0.00249468	Negative Untreated
184	ELM1,HSL1	258	SWE1,CLB2	2	0.00249468	Negative Untreated
184	ELM1,HSL1	191	RTT101,MMS1	2	0.00249468	Negative Untreated
229	CTI6,PHO23,RPD3,UME6,SIN3	338	NHP10,IES3,ARP8	3	0.00333519	Negative Untreated
244	MRE11,RSC2,RSC1	333	SWC5,VPS72,VPS71,SWR1,HTZ1	3	0.00333519	Negative Untreated
271	FIG4,VAC14	282	CTK1,CTK2,CTK3	2	0.00606685	Negative Untreated
267	BCK1,MKK2,SLT2	271	FIG4,VAC14	2	0.00606685	Negative Untreated
134	HAP5,HAP3,HAP2	234	RCO1,SET2	2	0.00606685	Negative Untreated
267	BCK1,MKK2,SLT2	5	PHO80,VIP1	2	0.00606685	Negative Untreated
244	MRE11,RSC2,RSC1	310	HMS1,HMS2	2	0.00606685	Negative Untreated
13	DCC1,CTF18,CTF8	303	TOF1,MRC1	2	0.00606685	Negative Untreated
267	BCK1,MKK2,SLT2	53	HAC1,IRE1	2	0.00606685	Negative Untreated
13	DCC1,CTF18,CTF8	249	RAD52,RAD51	2	0.00606685	Negative Untreated
249	RAD52,RAD51	82	MEC1,TEL1,DUN1,RAD53	8	3.65E-12	Conditional Positive
282	CTK1,CTK2,CTK3	333	SWC5,VPS72,VPS71,SWR1,HTZ1	9	5.54E-10	Conditional Positive
229	CTI6,PHO23,RPD3,UME6,SIN3	333	SWC5,VPS72,VPS71,SWR1,HTZ1	10	9.81E-09	Conditional Positive
13	DCC1,CTF18,CTF8	249	RAD52,RAD51	5	4.13E-07	Conditional Positive
282	CTK1,CTK2,CTK3	7	ADA2,SSN3,PGD1,NUT1,YAP1	7	4.83E-07	Conditional Positive

249	RAD52,RAD51	7	ADA2,SSN3,PGD1,NUT1,YAP1	6	4.87E-07	Conditional Positive
282	CTK1,CTK2,CTK3	294	HIR3,HIR2,HIR1,ASF1	6	2.01E-06	Conditional Positive
13	DCC1,CTF18,CTF8	294	HIR3,HIR2,HIR1,ASF1	6	2.01E-06	Conditional Positive
282	CTK1,CTK2,CTK3	301	UME1,RXT2	4	2.71E-05	Conditional Positive
249	RAD52,RAD51	282	CTK1,CTK2,CTK3	4	2.71E-05	Conditional Positive
229	CTI6,PHO23,RPD3,UME6,SI N3	282	CTK1,CTK2,CTK3	5	0.000156383	Conditional Positive
13	DCC1,CTF18,CTF8	7	ADA2,SSN3,PGD1,NUT1,YAP1	5	0.000156383	Conditional Positive
245	RAD5,RAD18	249	RAD52,RAD51	3	0.000200361	Conditional Positive
13	DCC1,CTF18,CTF8	282	CTK1,CTK2,CTK3	4	0.00020769	Conditional Positive
244	MRE11,RSC2,RSC1	282	CTK1,CTK2,CTK3	4	0.00020769	Conditional Positive
256	EAF3,EAF5,EAF7	282	CTK1,CTK2,CTK3	4	0.00020769	Conditional Positive
229	CTI6,PHO23,RPD3,UME6,SI N3	249	RAD52,RAD51	4	0.000335922	Conditional Positive
111	MSS11,MSN1	282	CTK1,CTK2,CTK3	3	0.000946862	Conditional Positive
282	CTK1,CTK2,CTK3	310	HMS1,HMS2	3	0.000946862	Conditional Positive
13	DCC1,CTF18,CTF8	141	PSY2,PPH3	3	0.000946862	Conditional Positive
249	RAD52,RAD51	267	BCK1,MKK2,SLT2	3	0.000946862	Conditional Positive
13	DCC1,CTF18,CTF8	333	SWC5,VPS72,VPS71,SWR1,HTZ1	4	0.00188054	Conditional Positive
229	CTI6,PHO23,RPD3,UME6,SI N3	7	ADA2,SSN3,PGD1,NUT1,YAP1	5	0.00196284	Conditional Positive
234	RCO1,SET2	294	HIR3,HIR2,HIR1,ASF1	3	0.00250635	Conditional Positive
249	RAD52,RAD51	294	HIR3,HIR2,HIR1,ASF1	3	0.00250635	Conditional Positive
21	YDR067C,YCR095C,OCA1,Y NL056W,SIW14	63	GCN2,TOR1	3	0.00507844	Conditional Positive
21	YDR067C,YCR095C,OCA1,Y NL056W,SIW14	301	UME1,RXT2	3	0.00507844	Conditional Positive
245	RAD5,RAD18	7	ADA2,SSN3,PGD1,NUT1,YAP1	3	0.00507844	Conditional Positive
301	UME1,RXT2	333	SWC5,VPS72,VPS71,SWR1,HTZ1	3	0.00507844	Conditional Positive
249	RAD52,RAD51	333	SWC5,VPS72,VPS71,SWR1,HTZ1	3	0.00507844	Conditional Positive
294	HIR3,HIR2,HIR1,ASF1	7	ADA2,SSN3,PGD1,NUT1,YAP1	4	0.00683625	Conditional Positive
229	CTI6,PHO23,RPD3,UME6,SI N3	294	HIR3,HIR2,HIR1,ASF1	4	0.00683625	Conditional Positive
111	MSS11,MSN1	249	RAD52,RAD51	2	0.00790452	Conditional Positive

184	ELM1,HSL1	260	CLN2,CLN1	2	0.00790452	Conditional Positive
245	RAD5,RAD18	75	MKK1,ASK10	2	0.00790452	Conditional Positive
249	RAD52,RAD51	310	HMS1,HMS2	2	0.00790452	Conditional Positive
141	PSY2,PPH3	245	RAD5,RAD18	2	0.00790452	Conditional Positive
141	PSY2,PPH3	249	RAD52,RAD51	2	0.00790452	Conditional Positive
245	RAD5,RAD18	53	HAC1,IRE1	2	0.00790452	Conditional Positive
249	RAD52,RAD51	98	TPK2,SFL1	2	0.00790452	Conditional Positive
122	MSN2,SNF1	260	CLN2,CLN1	2	0.00790452	Conditional Positive
260	CLN2,CLN1	53	HAC1,IRE1	2	0.00790452	Conditional Positive
191	RTT101,MMS1	249	RAD52,RAD51	2	0.00790452	Conditional Positive
13	DCC1,CTF18,CTF8	82	MEC1,TEL1,DUN1,RAD53	3	0.00880573	Conditional Positive
294	HIR3,HIR2,HIR1,ASF1	338	NHP10,IES3,ARP8	6	1.10E-06	Conditional Negative
267	BCK1,MKK2,SLT2	75	MKK1,ASK10	4	1.80E-05	Conditional Negative
38	TOS3,MIG1	63	GCN2,TOR1	3	0.000147434	Conditional Negative
184	ELM1,HSL1	338	NHP10,IES3,ARP8	3	0.000700645	Conditional Negative
294	HIR3,HIR2,HIR1,ASF1	75	MKK1,ASK10	3	0.00186493	Conditional Negative
134	HAP5,HAP3,HAP2	282	CTK1,CTK2,CTK3	3	0.00272764	Conditional Negative
282	CTK1,CTK2,CTK3	288	TPK1,TPK3,YBR028C	3	0.00272764	Conditional Negative
267	BCK1,MKK2,SLT2	288	TPK1,TPK3,YBR028C	3	0.00272764	Conditional Negative
117	PPH22,PPH21	7	ADA2,SSN3,PGD1,NUT1,YAP1	3	0.00379963	Conditional Negative
184	ELM1,HSL1	333	SWC5,VPS72,VPS71,SWR1,HTZ1	3	0.00379963	Conditional Negative
101	INO4,INO2	333	SWC5,VPS72,VPS71,SWR1,HTZ1	3	0.00379963	Conditional Negative
141	PSY2,PPH3	393	IME1,IME2	2	0.00646284	Conditional Negative
117	PPH22,PPH21	135	SIP4,CAT8	2	0.00646284	Conditional Negative
179	MBP1,SWI6	184	ELM1,HSL1	2	0.00646284	Conditional Negative
122	MSN2,SNF1	184	ELM1,HSL1	2	0.00646284	Conditional Negative
184	ELM1,HSL1	191	RTT101,MMS1	2	0.00646284	Conditional Negative
338	NHP10,IES3,ARP8	82	MEC1,TEL1,DUN1,RAD53	3	0.00662442	Conditional Negative
134	HAP5,HAP3,HAP2	294	HIR3,HIR2,HIR1,ASF1	3	0.00662442	Conditional Negative
344	YPK2,YPK1,PKH2	82	MEC1,TEL1,DUN1,RAD53	3	0.00662442	Conditional Negative
288	TPK1,TPK3,YBR028C	82	MEC1,TEL1,DUN1,RAD53	3	0.00662442	Conditional Negative
288	TPK1,TPK3,YBR028C	294	HIR3,HIR2,HIR1,ASF1	3	0.00662442	Conditional Negative
267	BCK1,MKK2,SLT2	82	MEC1,TEL1,DUN1,RAD53	3	0.00662442	Conditional Negative