# Dynamic reprogramming of transcription factors to and from the subtelomere

## *Supplementary Figures and Tables*

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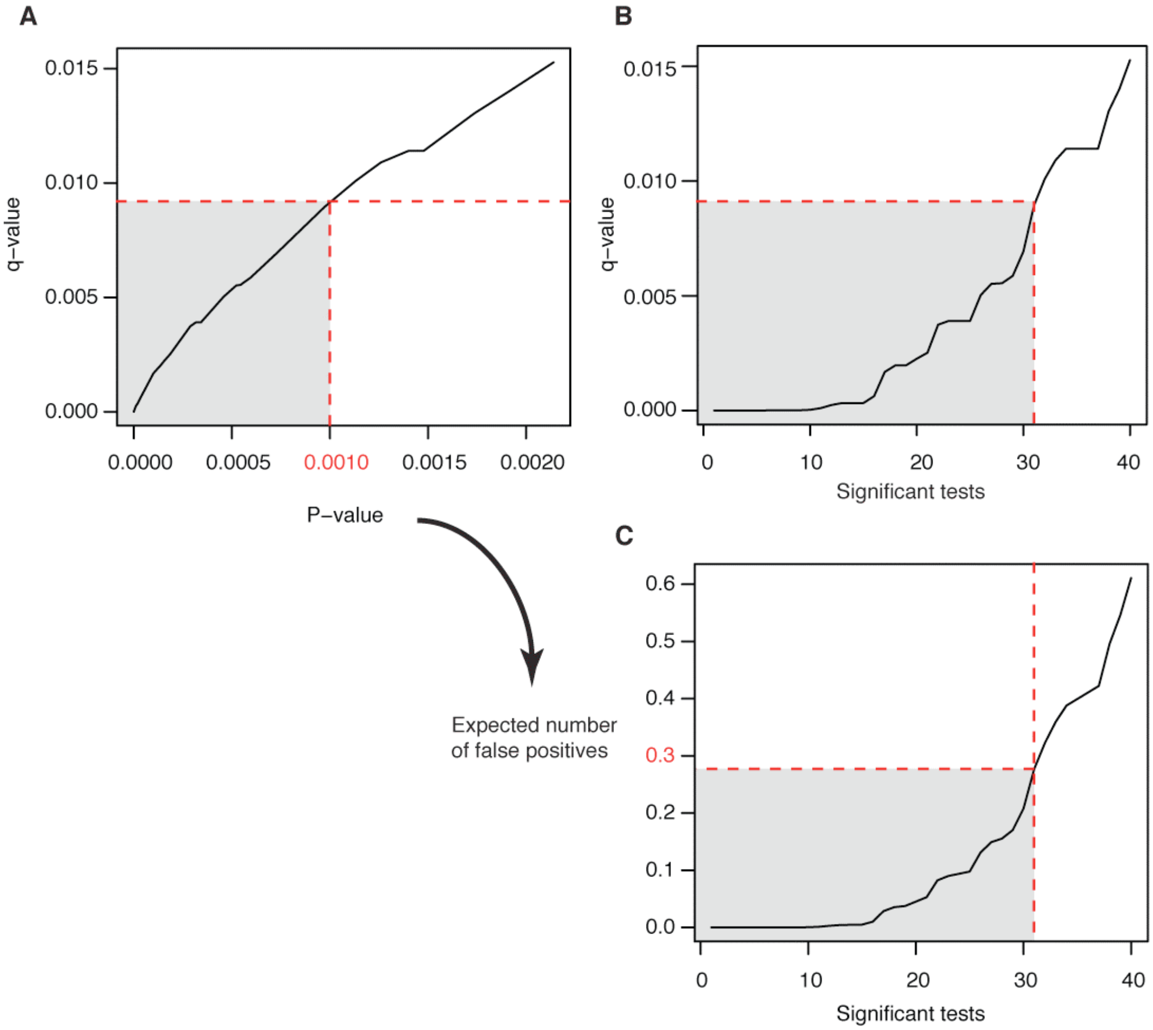
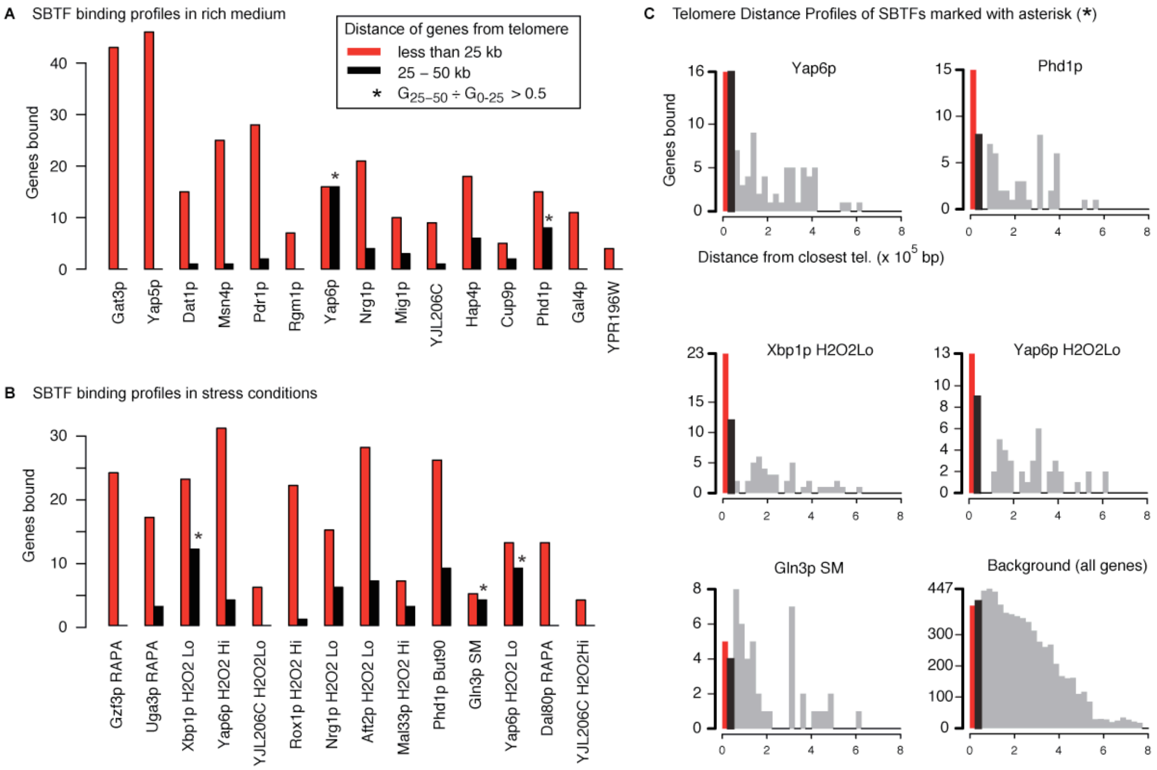
# Supplementary Figures



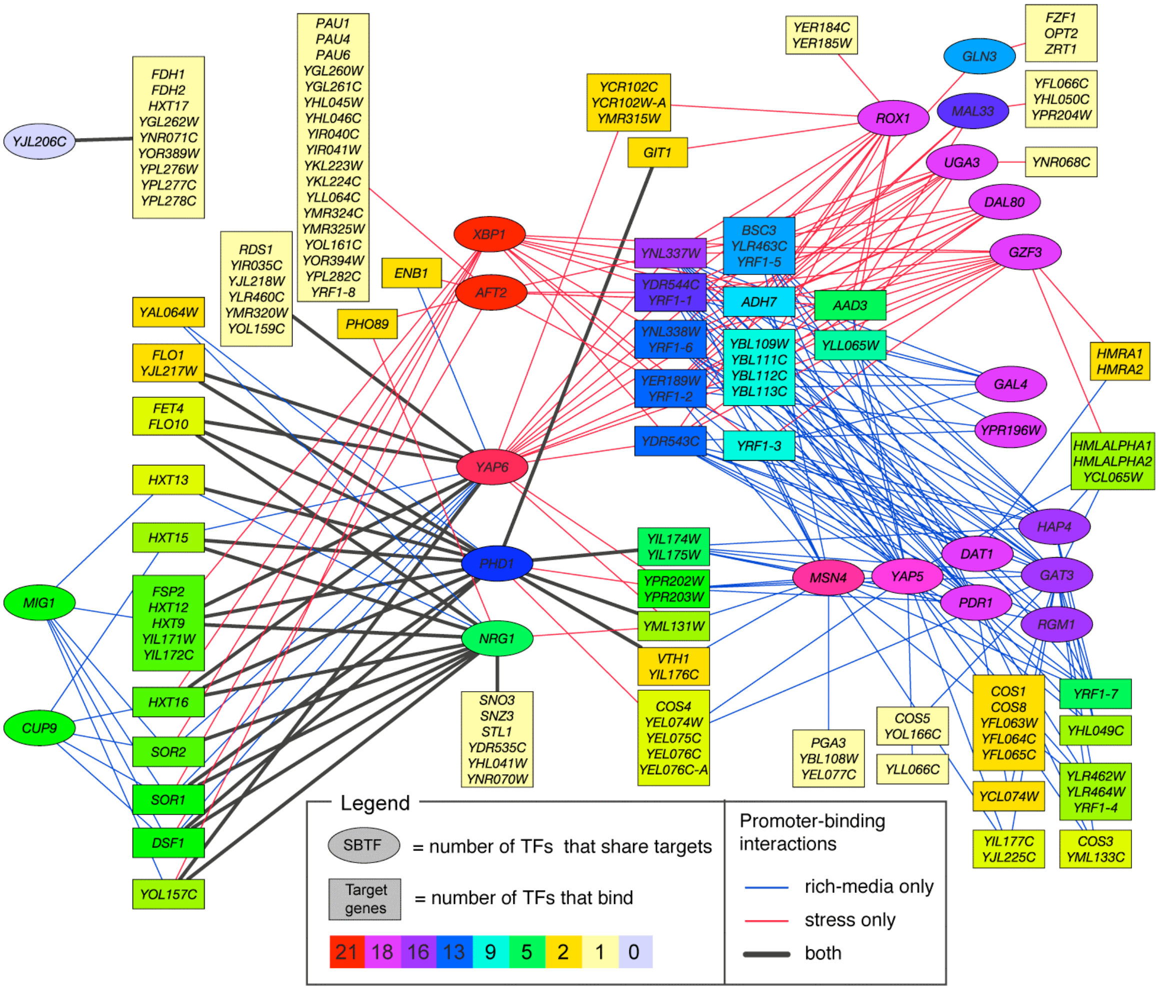
**Supplementary Figure 1. Estimating the error in identifying SBTFs.**

The Q-value software package (Storey et al. 2003) was used to account for multiple-hypothesis testing by estimating the false discovery rate for the telomere distance profile tests (see Figure 1 and text). **(A)** *P*-values plotted against their corresponding q-values. As indicated by the red dashed lines, the *P*-value threshold of 0.001 used in this study corresponds to a q-value (false discovery rate) of approximately 0.01, meaning that about 1% of the TF binding profiles with a significant subtelomeric preference are expected to be false positives. **(B)** At $P \leq 0.001$, 31 tests are considered significant. **(C)** Based on the q-value method, less than one (~0.3) of the 31 TF binding profiles with subtelomeric bias is expected to be a false positive.

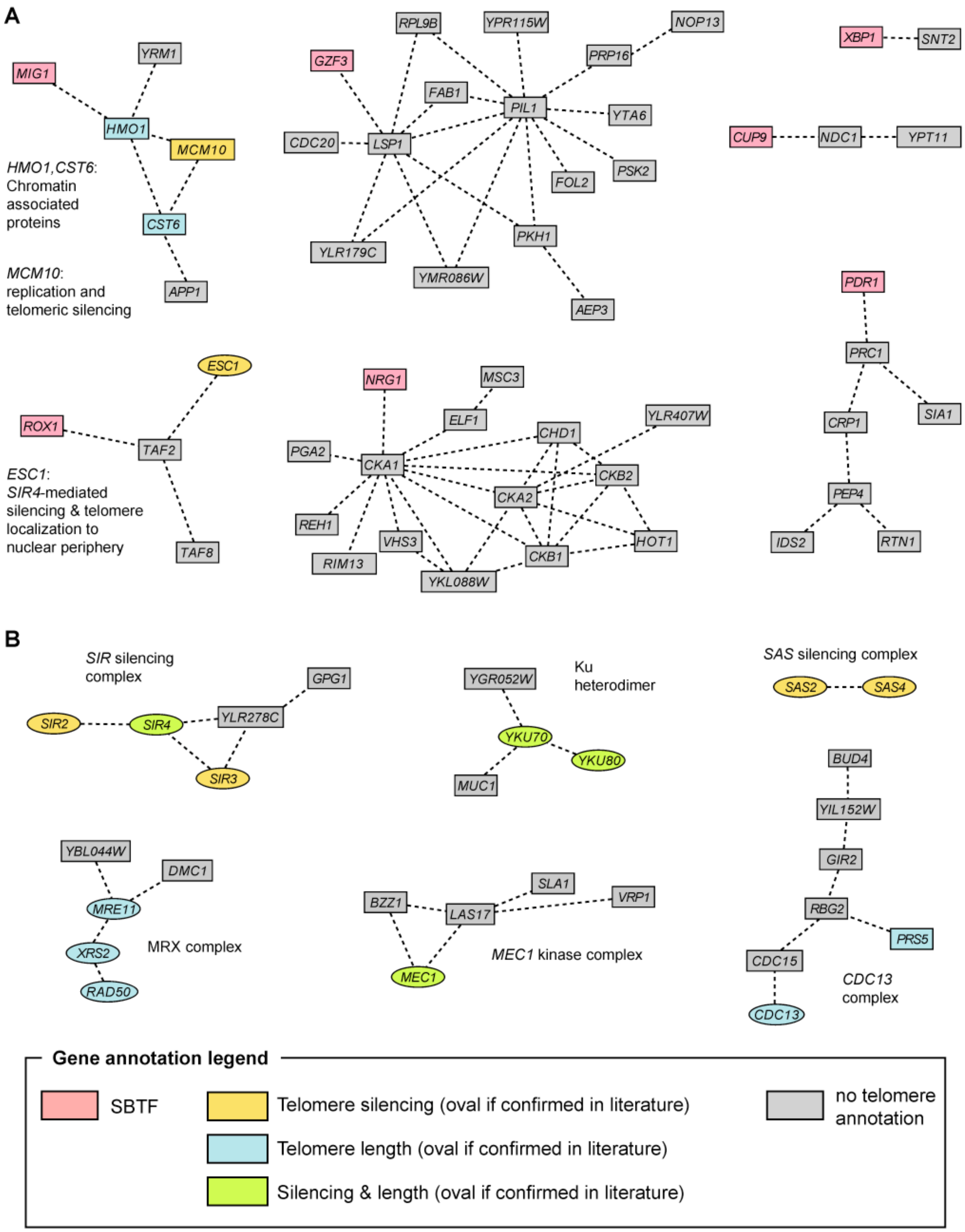


**Supplementary Figure 2. Analysis of negative control region 25-50 kb from telomere.**

Comparison of the number of subtelomeric genes bound (red bars) versus genes bound in the immediately adjacent 25 kb region (black bars; 25 – 50 kb from telomere). An asterisk (*) marks TFs for which the black bar is at least half the height of the red bar, indicating telomere-proximal binding that extends beyond our strict 25kb cutoff used to classify subtelomeric genes.

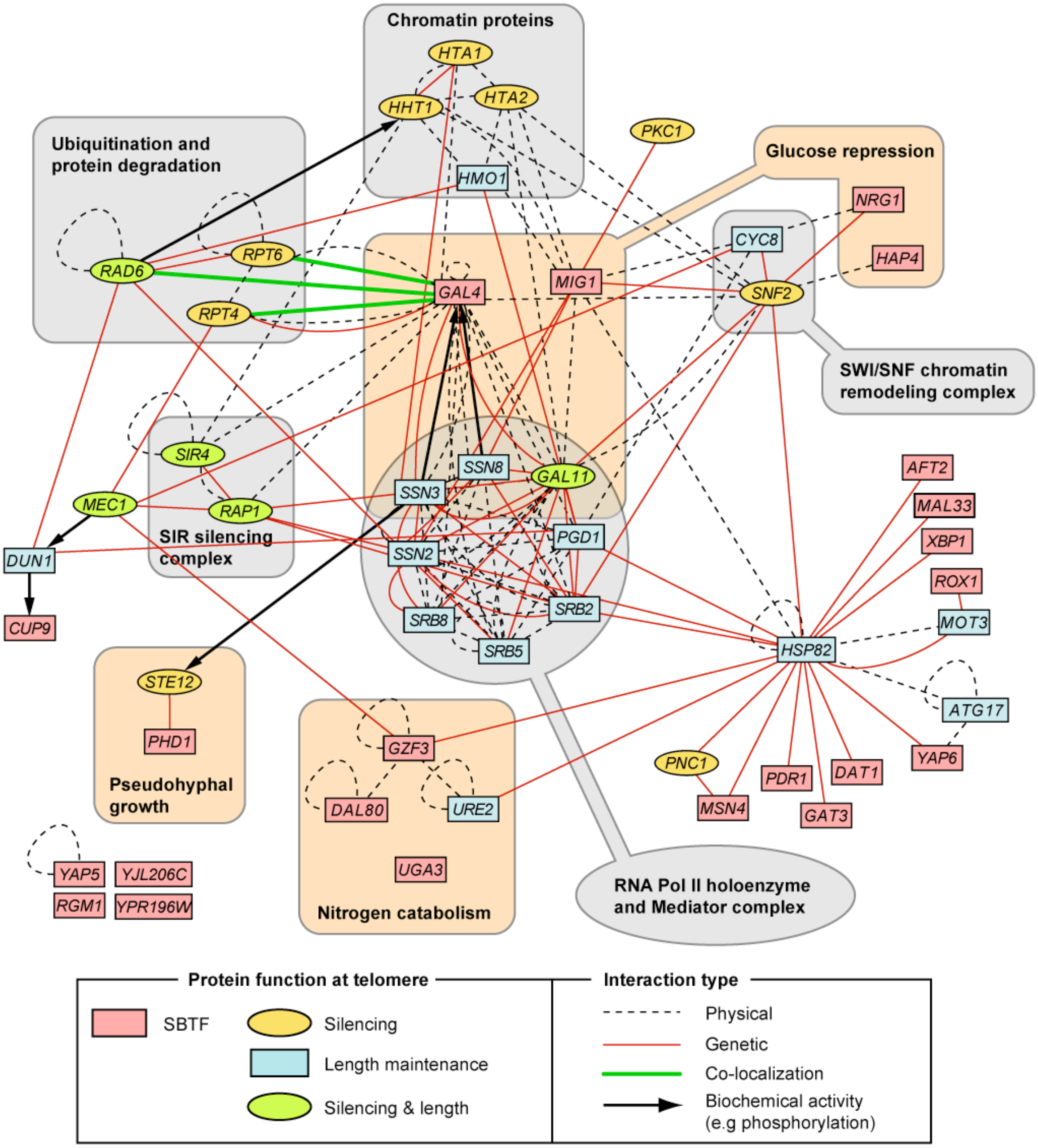


**Supplementary Figure 3. A map of the subtelomeric regulatory circuitry.** All TF-promoter binding interactions from significant SBTF binding profiles are visualized with Cytoscape (Shannon et al. 2003). See Legend for details.

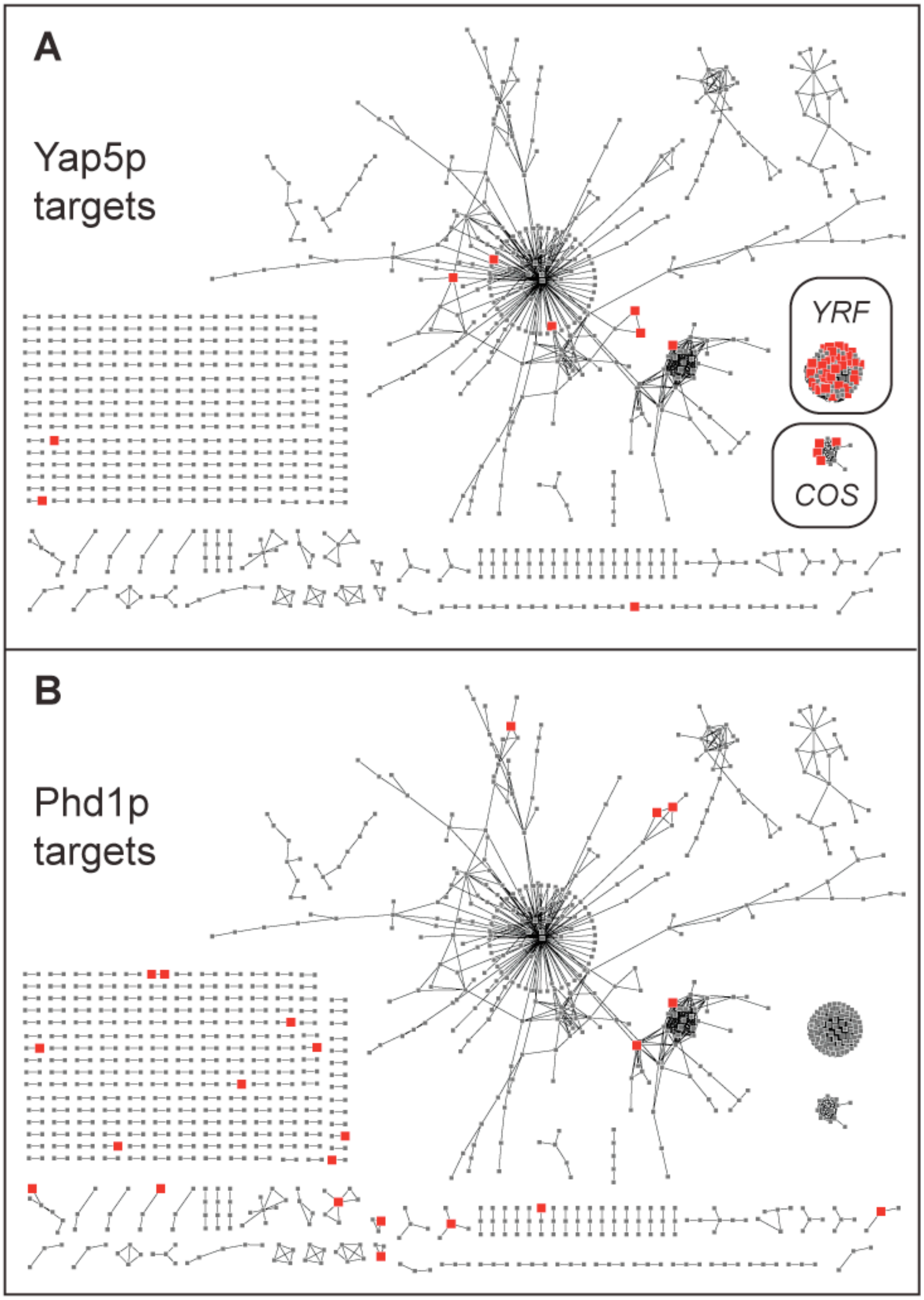


**Supplementary Figure 4. Analysis of protein complexes.**

**(A)** Protein complexes (Krogan et al. 2006) that contain SBTFs. **(B)** Examples of protein complexes identified in the same screen that contain telomere-related proteins identified in recent reviews of yeast telomeres (Lundblad 2006; Mondoux et al. 2006).

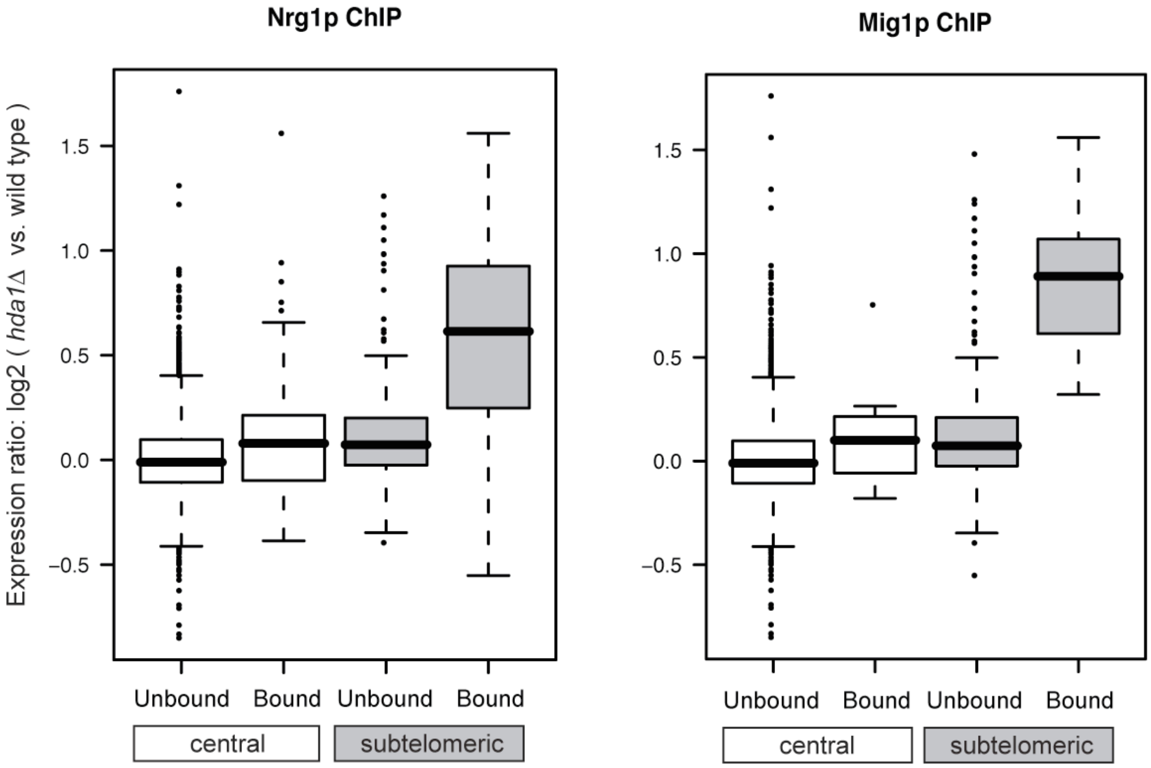


**Supplementary Figure 5. Interactions between SBTFs and telomere-related genes.** BioGRID (Stark et al. 2006) interactions that connect SBTFs to any telomere-related gene listed in Supplementary Table 1. Also shown are all interactions between these telomere-related genes. Genes that function at the telomere, but do not interact with a SBTF based on data from BioGRID, are not shown (e.g. *SIR2* or *YKU70*). Ovals indicate that a gene has been associated with the telomere in recent literature reviews (Lundblad 2006; Mondoux et al. 2006). Rectangles indicate annotation from the GO database or high-throughput experiments. Interaction types are described in detail in the Methods.

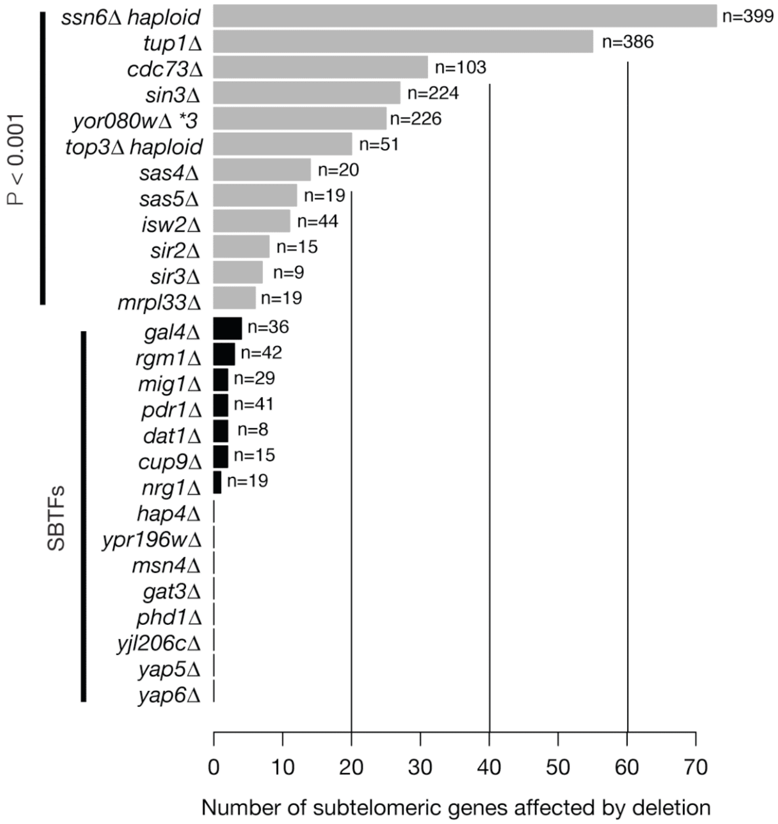


**Supplementary Figure 6. BLAST similarity is not a reliable indicator of microarray hybridization.**

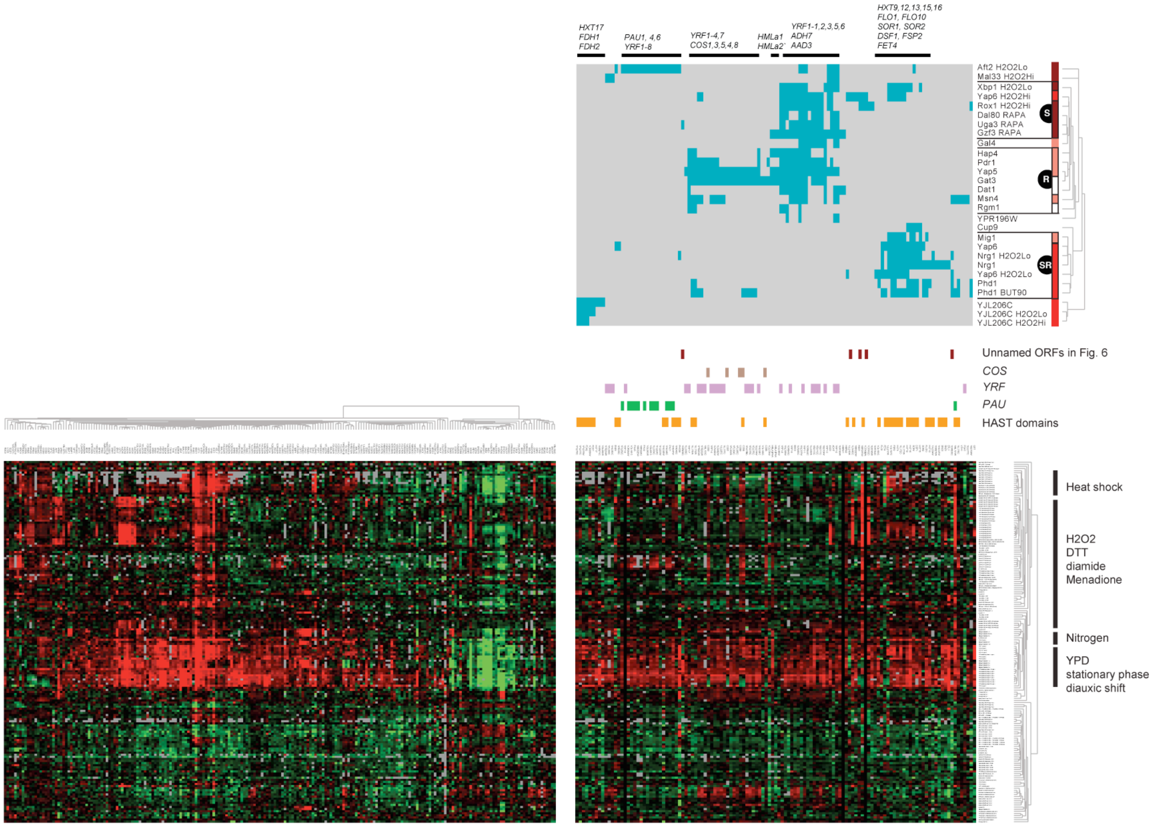
BLAST was used to exhaustively perform all pairwise comparisons of *S. cerevisiae* intergenic regions (E-value cutoff < 0.01). In the resulting promoter similarity network, edges connect intergenic regions (nodes) having DNA-level sequence similarity. **(A)** Visualization of the intergenic regions bound by Yap5p and **(B)** Phd1p. Red indicates bound intergenic regions. Instances of similar promoters that are not bound by the same TF (red nodes connected to grey) indicate that potential microarray cross-hybridization suggested by BLAST similarity is not observed.



**Supplementary Figure 7. Targets of Nrg1p and Mig1p are upregulated in *hda1Δ*.**
This figure accompanies Figure 4B of the main text.



**Supplementary Figure 8. Screening expression profiles of singe gene deletions.**
Gene expression profiles of single gene deletions (Hu et al. 2007; Hughes et al. 2000) were analyzed with the same Telomere Distance Profile analysis method used to identify SBTFs. The set of genes differentially expressed in each deletion mutant was identified using a *P*-value cutoff of 0.001, as described in the original publications. Bars show the number of subtelomeric genes affected by each TF deletion. Grey indicates deletions that affect an unexpectedly large number of subtelomeric genes (KS-test, $P<0.001$). Black bars show data for the 15 rich-media SBTFs**.** No deletions of the stress condition SBTFs were available in these data sets. Numbers next to each bar indicate the total number of genes differentially expressed in a deletion. Hughes *et al.* suggest that strain *yor080wΔ* may have contained a duplicated chromosome III (as indicated by the *3).



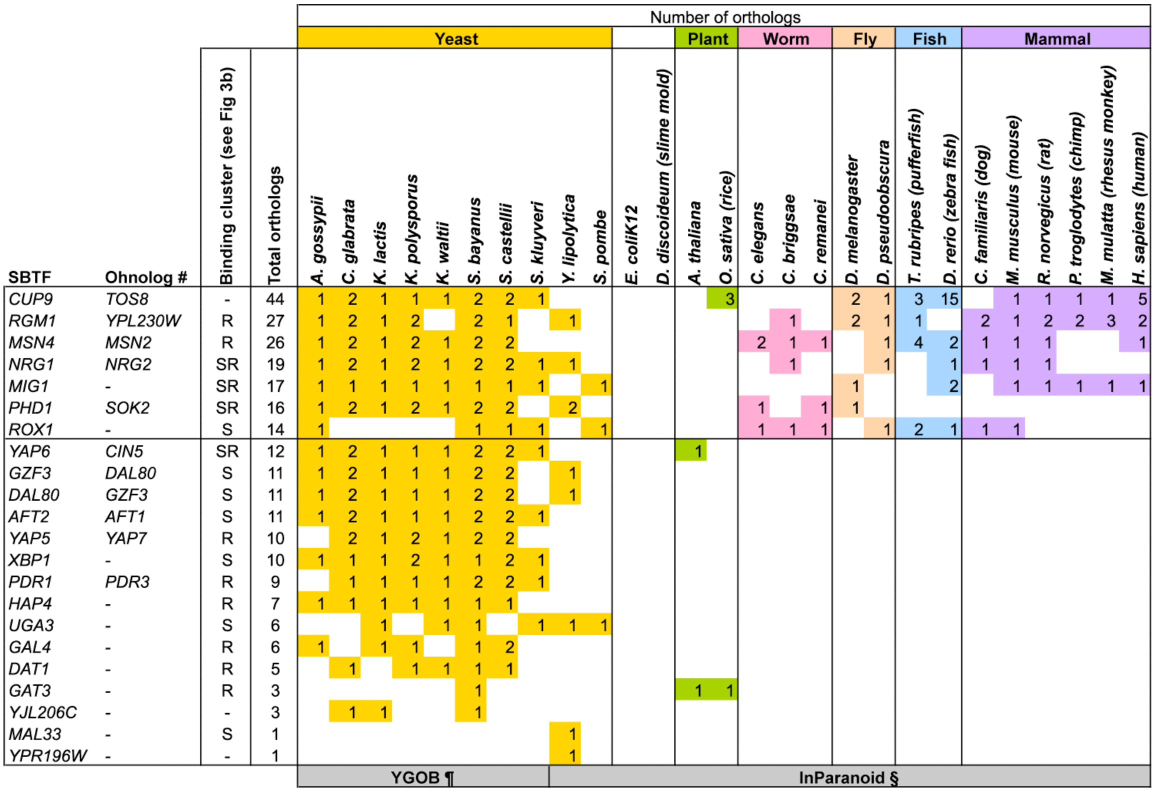
Subtelomeric genes not bound by SBTFs

Subtelomeric genes bound by SBTFs

**Supplementary Figure 9. Stress-induced expression of subtelomeric genes.**

Expression data are from Gasch and colleagues (Gasch et al. 2000). Subtelomeric genes (columns) are aligned with clustered binding patterns from Figure 3B. Unnamed stress responsive ORFs from Figure 5 (panels B and C) are indicated by maroon ticks and include *YNR068C*, *YML131W*, *YMR315W*, *YCR102C*, and *YLR460C*.

## Supplementary Figure 10. Orthologs of SBTFs in other species

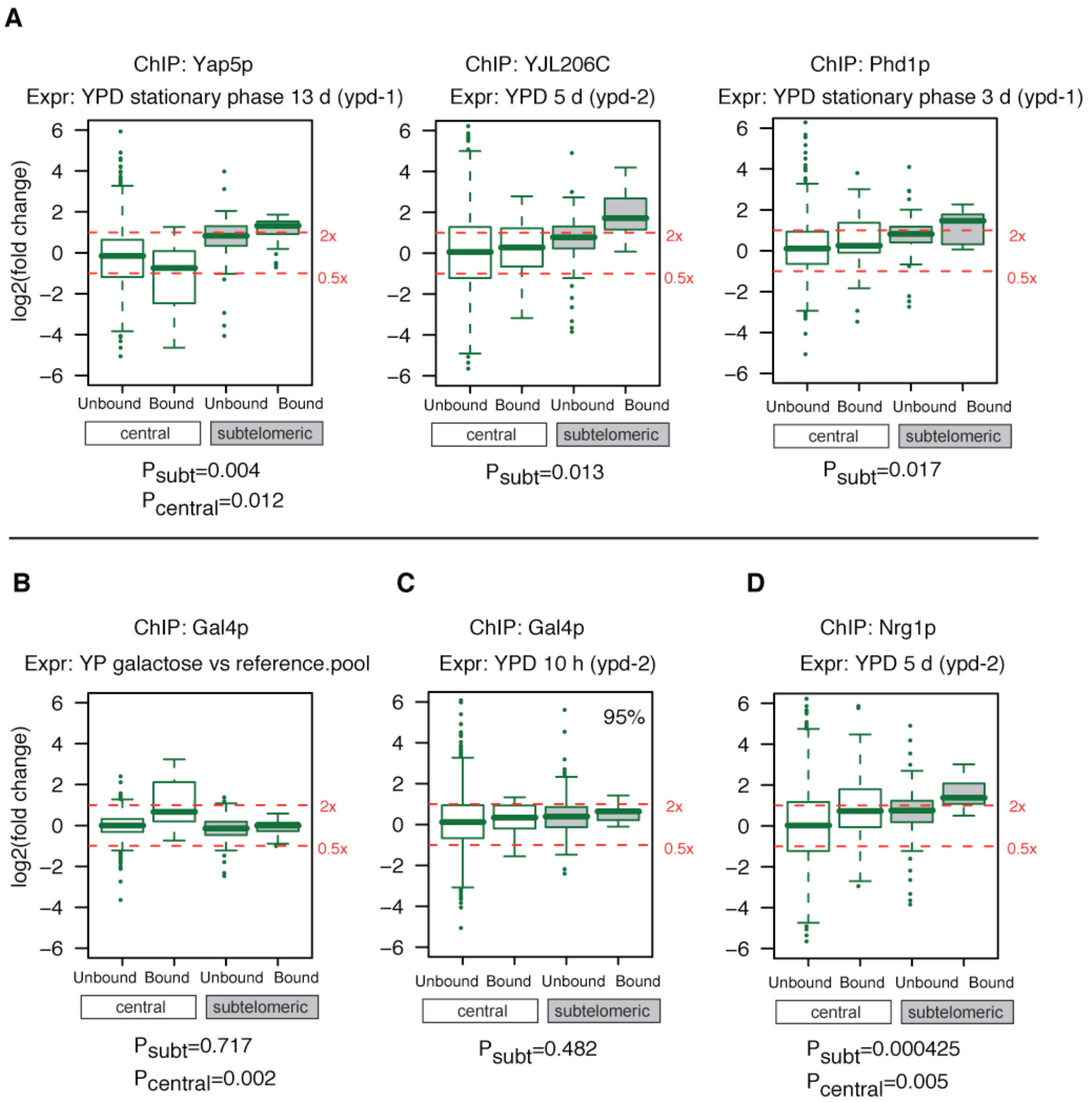


| | | | | Number of orthologs | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Yeast | | | | | | | | | | | | Plant | | Worm | | | Fly | | Fish | | Mammal | | | | | |
| SBTF | Ohnolog # | Binding cluster (see Fig 3b) | Total orthologs | *A. gossypii* | *C. glabrata* | *K. lactis* | *K. polysporus* | *K. waltii* | *S. bayanus* | *S. castellii* | *S. kluyveri* | *Y. lipolytica* | *S. pombe* | *E. coliK12* | *D. discoideum (slime mold)* | *A. thaliana* | *O. sativa (rice)* | *C. elegans* | *C. briggsae* | *C. remanei* | *D. melanogaster* | *D. pseudoobscura* | *T. rubripes (pufferfish)* | *D. rerio (zebra fish)* | *C. familiaris (dog)* | *M. musculus (mouse)* | *R. norvegicus (rat)* | *P. troglodytes (chimp)* | *M. mulatta (rhesus monkey)* | *H. sapiens (human)* |
| *CUP9* | *TOS8* | - | 44 | 1 | 2 | 1 | 1 | 1 | 2 | 2 | 1 | | | | | | 3 | | | | 2 | 1 | 3 | 15 | | 1 | 1 | 1 | 1 | 5 |
| *RGM1* | *YPL230W* | R | 27 | 1 | 2 | 1 | 2 | | 2 | 1 | | 1 | | | | | | | 1 | | 2 | 1 | 1 | | 2 | 1 | 2 | 2 | 3 | 2 |
| *MSN4* | *MSN2* | R | 26 | 1 | 2 | 1 | 2 | 1 | 2 | 2 | | | | | | | | 2 | 1 | 1 | | 1 | 4 | 2 | 1 | 1 | 1 | | | 1 |
| *NRG1* | *NRG2* | SR | 19 | 1 | 2 | 1 | 2 | 1 | 2 | 2 | 1 | 1 | | | | | | | 1 | | | 1 | | 1 | 1 | 1 | 1 | | | |
| *MIG1* | - | SR | 17 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | | 1 | | | | | | | | 1 | | | 2 | | 1 | 1 | 1 | 1 | 1 |
| *PHD1* | *SOK2* | SR | 16 | 1 | 2 | 1 | 2 | 1 | 2 | 2 | | 2 | | | | | | 1 | | 1 | 1 | | | | | | | | | |
| *ROX1* | - | S | 14 | 1 | | | | | 1 | 1 | 1 | | 1 | | | | | 1 | 1 | 1 | | 1 | 2 | 1 | 1 | 1 | | | | |
| *YAP6* | *CIN5* | SR | 12 | 1 | 2 | 1 | 1 | 1 | 2 | 2 | 1 | | | | | 1 | | | | | | | | | | | | | | |
| *GZF3* | *DAL80* | S | 11 | 1 | 2 | 1 | 1 | 1 | 2 | 2 | | 1 | | | | | | | | | | | | | | | | | | |
| *DAL80* | *GZF3* | S | 11 | 1 | 2 | 1 | 1 | 1 | 2 | 2 | | 1 | | | | | | | | | | | | | | | | | | |
| *AFT2* | *AFT1* | S | 11 | 1 | 2 | 1 | 1 | 1 | 2 | 2 | 1 | | | | | | | | | | | | | | | | | | | |
| *YAP5* | *YAP7* | R | 10 | | 2 | 1 | 2 | 1 | 2 | 2 | | | | | | | | | | | | | | | | | | | | |
| *XBP1* | - | S | 10 | 1 | 1 | 1 | 2 | 1 | 1 | 2 | 1 | | | | | | | | | | | | | | | | | | | |
| *PDR1* | *PDR3* | R | 9 | | 1 | 1 | 1 | 1 | 2 | 2 | 1 | | | | | | | | | | | | | | | | | | | |
| *HAP4* | - | R | 7 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | | | | | | | | | | | | | | | | | | | | |
| *UGA3* | - | S | 6 | | | 1 | | 1 | 1 | | 1 | 1 | 1 | | | | | | | | | | | | | | | | | |
| *GAL4* | - | R | 6 | 1 | | 1 | 1 | | 1 | 2 | | | | | | | | | | | | | | | | | | | | |
| *DAT1* | - | R | 5 | | 1 | | 1 | 1 | 1 | 1 | | | | | | | | | | | | | | | | | | | | |
| *GAT3* | - | R | 3 | | | | | | 1 | | | | | | | 1 | 1 | | | | | | | | | | | | | |
| *YJL206C* | - | - | 3 | | 1 | 1 | | | 1 | | | | | | | | | | | | | | | | | | | | | |
| *MAL33* | - | S | 1 | | | | | | | | | 1 | | | | | | | | | | | | | | | | | | |
| *YPR196W* | - | - | 1 | | | | | | | | | 1 | | | | | | | | | | | | | | | | | | |
| | | | | YGOB ¶ | | | | | | | | InParanoid § | | | | | | | | | | | | | | | | | | |

\# Ohnologs are defined to be paralogous genes (in this case in *S. cerevisiae*) that arose from a whole genome duplication event (Byrne et al. 2005)

¶ Ortholog data from the Yeast Gene Order Brower (Byrne et al. 2005)

§ Ortholog data from InParanoid (Remm et al. 2001) version 6.0



**Supplementary Figure 11. Representative results from global expression analysis.** Each box-plot summarizes gene expression data from one experimental condition (labeled “Expr”) for genes categorized according to one TF-promoter binding experiment (labeled “ChIP”). Red dotted lines indicate two-fold up or down regulation. Grey boxes show data for subtelomeric genes. The significance of global change of bound subtelomeric (or non-subtelomeric) genes versus unbound subtelomeric (or non-subtelomeric) genes is $P_{subt}$ (or $P_{central}$) (Kolmogorov-Smirnov *P*-value). Expression data are from (Gasch et al. 2000). **(A)** Examples of gene expression conditions in which the subtelomeric genes bound by a SBTF were significantly differentially expressed compared to the unbound subtelomeric genes. And in addition, the non-subtelomeric genes were not similarly expressed. **(B)** Positive control in which genes bound by Gal4p were, as expected, upregulated during growth in medium containing galactose. **(C)** Example in which neither the subtelomeric nor non-subtelomeric genes showed coherent global expression (~95% of matched ChIP-expression datasets tested). **(D)** Example of non-specific global expression: both subtelomeric and central genes were upregulated

# Supplementary Tables

## Supplementary Table 1. Telomere-related genes curated from the literature.

A complete table with more information on each gene is available as a separate Microsoft Excel file.

*ABF1*
*ADE12*
*ADO1*
*AFT2*
*AGP2*
*AHC2*
*APE3*
*APN1*
*ARD1*
*ARF1*
*ARG2*
*ARV1*
*ASC1*
*ASF1*
*ATC1*
*ATG11*
*ATG17*
*BCK1*
*BDF1*
*BEM2*
*BEM4*
*BRE1*
*BRE2*
*BRO1*
*BUD16*
*BUD21*
*BUD23*
*BUD30*
*BUD32*
*CAC1*
*CAC2*
*CAC3*
*CAX4*
*CBC2*
*CCW14*
*CDC13*
*CDC45*
*CDC46*
*CDC6*
*CDC7*
*CDC73*
*CDH1*
*CGI121*
*CHO2*
*CSM1*
*CSR2*
*CST6*
*CTF8*
*CTK1*
*CUP9*
*CYC8*
*DAL80*
*DAT1*
*DCC1*
*DEF1*
*DEP1*
*DIG1*
*DLS1*
*DNA2*
*DOA4*
*DOT1*
*DOT5*
*DOT6*
*DPB3*
*DPB4*
*DUN1*
*EAP1*
*EBS1*
*ELG1*
*EPL1*
*ERG2*
*ERJ5*
*ESC1*
*ESC8*
*EST1*
*EST2*
*EST3*
*EXO1*
*FMP26*
*FUS3*
*FYV12*
*FYV4*
*FYV6*
*GAL11*
*GAL4*
*GAT3*
*GBP2*
*GCV3*
*GLO4*
*GON7*
*GPB2*
*GTR1*
*GTR2*
*GUP1*
*GUP2*
*GZF3*
*HAP4*
*HAT1*
*HAT2*
*HCH1*
*HCM1*
*HCR1*
*HDA2*
*HEK1*
*HEK2*
*HFI1*
*HHF1*
*HHF2*
*HHT1*
*HHT2*
*HIF1*
*HIR1*
*HIR2*
*HIT1*
*HMO1*
*HPR1*
*HSC82*
*HSP104*
*HSP82*
*HST1*
*HST2*
*HST3*
*HST4*
*HTA1*
*HTA2*
*HTL1*
*HTZ1*
*HUR1*
*IES3*
*IFH1*
*IMG2*
*ISA1*
*ISW2*
*ITC1*
*KAE1*
*KEM1*
*KRE21*
*KRE28*
*LCD1*
*LDB19*
*LDB7*
*LEA1*
*LEO1*
*LRP1*
*LSM7*
*LST7*
*MAK10*
*MAK3*
*MAK31*
*MAL33*
*MCM10*
*MCM5*
*MDM10*
*MEC1*
*MEC3*
*MED1*
*MET18*
*MET7*
*MFT1*
*MIG1*
*MKK1*
*MLH1*
*MMM1*
*MMS19*
*MOT2*
*MOT3*
*MRC1*
*MRE11*
*MRM2*
*MRPL38*
*MRPL44*
*MRT4*
*MSN4*
*NAM7*
*NAT1*
*NAT3*
*NFI1*
*NMD2*
*NPL6*
*NPT1*
*NRG1*
*NSR1*
*NUP2*
*NUP60*
*NUT1*
*OGG1*
*OPI1*
*ORC2*
*ORC5*
*PAF1*
*PBP2*
*PCNA*
*PCP1*
*PDR1*
*PDX3*
*PEP3*
*PFD1*
*PGD1*
*PHD1*
*PHO80*
*PHO85*
*PHO87*
*PHO88*
*PIF1*
*PKC1*
*PKP1*
*PMT3*
*PNC1*
*POC4*
*POL1*
*POL12*
*POL2*
*POL30*
*POL32*
*PPE1*
*PRO1*
*PRS3*
*PRS5*
*PTC1*
*PXR1*
*RAD27*
*RAD5*
*RAD50*
*RAD51*
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*RAD59*
*RAD6*
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*RFA2*
*RFA3*
*RFM1*
*RGM1*
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*RNH35*
*RNR1*
*ROX1*
*RPA14*
*RPB4*
*RPB9*
*RPD3*
*RPL12B*
*RPL13B*
*RPL1B*
*RPL34B*
*RPN4*
*RPP1A*
*RPS10A*
*RPS11B*
*RPS14A*
*RPS16A*
*RPS16B*
*RPS17A*
*RPS17B*
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*RPS22A*
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*RPS23B*
*RPS27B*
*RPS28B*
*RPS30B*
*RPS4A*
*RPS4B*
*RPT4*
*RPT6*
*RRM3*
*RRP8*
*RSA1*
*RSC2*
*RTF1*
*RTT106*
*SAP30*
*SAS2*
*SAS3*
*SAS4*
*SAS5*
*SBA1*
*SCP160*
*SCS2*
*SCS22*
*SDC1*
*SEM1*
*SET1*
*SGS1*
*SHG1*
*SHP1*
*SIF2*
*SIN3*
*SIR1*
*SIR2*
*SIR3*
*SIR4*
*SIT4*
*SIW14*
*SLA2*
*SLI15*
*SLT2*
*SLX5*
*SLX8*
*SMI1*
*SNC2*
*SNF2*
*SNF7*
*SNF8*
*SOH1*
*SOL2*
*SPP1*
*SPS100*
*SPT21*
*SPT4*
*SRB2*
*SRB5*
*SRB8*
*SSE1*
*SSH1*
*SSN2*
*SSN3*
*SSN8*
*STE11*
*STE12*
*STE7*
*STM1*
*STN1*
*STO1*
*STP22*
*SUB2*
*SUM1*
*SUR4*
*SWA2*
*SWD1*
*SWD2*
*SWD3*
*TAT2*
*TEL1*
*TEL2*
*TEN1*
*THP2*
*TIF1*
*TLC1*
*TOM5*
*TOP3*
*TPD3*
*TRK1*
*UBP10*
*UGA3*
*UGO1*
*UPF1*
*UPF2*
*UPF3*
*URE2*
*VAM6*
*VAM7*
*VPS15*
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*WTM1*
*WTM2*
*WTM3*
*XBP1*
*XDJ1*
*XRS2*
*YAF9*
*YAP5*
*YAP6*
*YBR284W*
*YDJ1*
*YDL118W*
*YDR115W*
*YDR532C*
*YEL033W*
*YEL057C*
*YGL039W*
*YGR042W*
*YHL012W*
*YIL042C*
*YJL206C*
*YKU70*
*YKU80*
*YML035C-A*
*YMR031W-A*
*YMR269W*
*YOL138C*
*YOR008C-A*
*YOR1*
*YOR322C*
*YPL041C*
*YPL105C*
*YPL144W*
*YPL205C*
*YPR196W*
*YPT7*
*YRB2*
*YRF1-1*
*YRF1-2*
*YRF1-3*
*YRF1-4*
*YRF1-5*
*YRF1-6*
*YRF1-7*
*YSP3*
*YTA7*
*ZDS1*
*ZDS2*
*ZEO1*

**Supplementary Table 2. Top 30 TFs having the most physical interactions with proteins that play known roles at telomeres.**

| | | Number of interactions with proteins with known telomere functions | | |
|---|---|---|---|---|
| **TF (yellow = top 15%)** | **IsSBTF?** | **Directed (e.g phosphorylation)** | **Genetic** | **Physical** |
| Gal4p | 1 | 2 | 15 | 52 |
| Ste12p | 0 | 3 | 46 | 25 |
| Pho4p | 0 | 2 | 2 | 20 |
| Mig1p | 1 | 7 | 29 | 19 |
| Met18p | 0 | 0 | 91 | 18 |
| Ume1p | 0 | 5 | 46 | 18 |
| Dig1p | 0 | 2 | 9 | 15 |
| Wtm1p | 0 | 1 | 3 | 14 |
| Hap4p | 1 | 0 | 2 | 14 |
| Hir1p | 0 | 0 | 90 | 13 |
| Kre33p | 0 | 0 | 0 | 13 |
| Rap1p | 0 | 0 | 68 | 12 |
| Hir2p | 0 | 0 | 93 | 11 |
| Mot2p | 0 | 0 | 66 | 11 |
| Abf1p | 0 | 1 | 18 | 11 |
| Yap1p | 0 | 0 | 13 | 11 |
| Ifh1p | 0 | 2 | 3 | 11 |
| Gzf3p | 1 | 6 | 3 | 11 |
| Wtm2p | 0 | 1 | 3 | 11 |
| Sum1p | 0 | 0 | 34 | 10 |
| Pdr1p | 1 | 1 | 10 | 9 |
| Cst6p | 0 | 1 | 5 | 9 |
| Dal80p | 1 | 0 | 2 | 8 |
| Yap6p | 1 | 7 | 1 | 8 |
| Rpn4p | 0 | 3 | 277 | 7 |
| Ume6p | 0 | 0 | 35 | 7 |
| Snf1p | 0 | 12 | 25 | 7 |
| Rco1p | 0 | 0 | 15 | 6 |
| Opi1p | 0 | 5 | 9 | 6 |

## Supplementary Table 3. Correlation of binding profiles with genomic features.

**Bonferroni corrected log10 P-values**

| | Non-ORF features annotated in SGD | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **SBTF** | **ARS** | **X_element_combinatorial_repeats** | **Y'_element** | **long_terminal_repeat** | **multigene locus** | **pseudogene** | **retrotransposon** | **tRNA** | **telomeric_repeat** | **transposable_element_gene** |
| Gal4p | 1.16 | 1.80 | 0.27 | 2.16 | 0.69 | 1.70 | 1.99 | 1.70 | 0.76 | 2.10 |
| Gat3p | 1.99 | 2.29 | -0.82 | 1.98 | 2.04 | 2.10 | 2.29 | 2.29 | 1.16 | 1.80 |
| Phd1p | 0.63 | 1.90 | 1.81 | 2.18 | 1.66 | 2.11 | 1.82 | 2.05 | 1.90 | 2.00 |
| Pdr1p | 1.17 | 2.00 | -0.37 | 2.21 | 1.83 | 1.84 | 2.19 | 1.20 | 1.49 | 1.91 |
| Yap5p | 2.16 | 2.24 | -3.80 | 2.17 | 2.09 | 2.16 | 2.26 | 1.55 | 0.27 | 1.76 |
| Dat1p | 1.62 | 1.73 | 1.01 | 2.27 | 1.84 | 2.25 | 1.95 | 1.82 | 1.12 | 2.07 |
| Cup9p | 1.15 | 1.72 | 1.98 | 1.35 | 2.05 | 1.94 | 2.10 | 2.10 | 2.00 | 2.17 |
| Msn4p | 1.48 | 2.06 | -3.33 | 1.86 | 2.23 | 2.25 | 1.73 | 2.15 | -1.53 | 1.94 |
| Hap4p | 1.00 | 1.57 | 0.29 | 1.97 | 2.21 | 1.24 | 1.98 | 1.87 | 2.17 | 2.02 |
| Rgm1p | 0.81 | 1.93 | 0.95 | 1.93 | 2.00 | 0.94 | 2.06 | 2.06 | 2.16 | 2.14 |
| Mig1p | 1.87 | 2.16 | 2.23 | 1.46 | 1.89 | 2.26 | 1.99 | 1.99 | 2.24 | 2.10 |
| YJL206C | 0.81 | 1.93 | 2.24 | 1.93 | 1.72 | 2.06 | 2.06 | 2.06 | 2.16 | 2.14 |
| Nrg1p | 1.76 | 2.00 | 2.01 | 2.09 | 1.44 | 1.80 | 1.67 | 1.67 | 1.58 | 1.91 |
| YPR196W | 2.04 | 2.00 | 1.26 | 1.91 | 2.05 | 1.94 | 2.10 | 2.10 | 2.00 | 2.17 |
| Yap6p | 2.14 | 2.24 | 1.52 | 1.97 | 1.72 | 2.02 | 1.87 | 1.87 | 1.99 | 2.02 |

🟦 Cells marked in blue are significant at $P < 0.05$

**Pearson correlation**

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Gal4p | -0.32 | 0.18 | 0.45 | 0.06 | 0.39 | -0.21 | -0.12 | 0.21 | -0.38 | -0.09 |
| Gat3p | -0.13 | 0.00 | 0.56 | -0.13 | -0.11 | 0.09 | 0.00 | 0.00 | -0.32 | -0.18 |
| Phd1p | 0.40 | -0.15 | -0.18 | -0.05 | -0.22 | 0.08 | -0.17 | 0.10 | 0.15 | -0.12 |
| Pdr1p | -0.32 | 0.12 | 0.52 | 0.04 | 0.17 | 0.17 | 0.05 | 0.31 | -0.25 | -0.15 |
| Yap5p | -0.06 | 0.02 | 0.75 | -0.06 | 0.09 | 0.06 | -0.02 | 0.24 | -0.45 | -0.19 |
| Dat1p | -0.23 | 0.20 | 0.35 | -0.01 | -0.17 | -0.02 | -0.14 | 0.18 | -0.33 | -0.10 |
| Cup9p | 0.32 | -0.20 | -0.13 | -0.28 | -0.10 | -0.14 | -0.08 | -0.08 | -0.12 | -0.06 |
| Msn4p | -0.26 | -0.10 | 0.73 | -0.16 | -0.03 | 0.02 | -0.20 | 0.07 | -0.62 | -0.14 |
| Hap4p | -0.35 | 0.24 | 0.45 | -0.13 | 0.04 | 0.31 | 0.13 | -0.16 | -0.06 | -0.11 |
| Rgm1p | -0.38 | 0.14 | 0.36 | -0.14 | -0.12 | 0.36 | -0.10 | -0.10 | -0.06 | -0.07 |
| Mig1p | 0.16 | -0.06 | -0.03 | -0.26 | -0.15 | 0.01 | -0.12 | -0.12 | 0.03 | -0.09 |
| YJL206C | -0.38 | 0.14 | -0.02 | -0.14 | 0.20 | 0.10 | -0.10 | -0.10 | -0.06 | -0.07 |
| Nrg1p | 0.19 | 0.12 | -0.12 | -0.09 | -0.27 | -0.18 | -0.21 | -0.21 | 0.23 | -0.15 |
| YPR196W | -0.11 | 0.12 | 0.30 | 0.15 | -0.10 | -0.14 | -0.08 | -0.08 | -0.12 | -0.06 |
| Yap6p | 0.07 | 0.03 | -0.25 | -0.13 | -0.20 | 0.11 | -0.16 | -0.16 | 0.12 | -0.11 |

**Supplementary Table 4. TDP analyses of TF targets filtered by BLAST similarity.**

| TF | TDP P-value | TDP P-value (adjusted) | Is SBTF? (adjusted) | Subtelomeric genes (adjusted) # | Subtelomeric remaining (post-adjust) |
|---|---|---|---|---|---|
| Gat3p | 4.00E-26 | 0.002978 | TRUE* | 9 | 21 % |
| Yap5p | 3.80E-19 | 0.002783 | TRUE* | 9 | 20 % |
| Gzf3p RAPA | 5.62E-11 | 0.02473 | | 8 | 33 % |
| Dat1p | 1.04E-08 | 0.037682 | | 3 | 20 % |
| Uga3p RAPA | 2.15E-08 | 0.015293 | | 3 | 18 % |
| Xbp1p H2O2Lo | 3.63E-08 | 0.002377 | TRUE* | 9 | 39 % |
| Msn4p | 3.70E-08 | 0.411555 | | 6 | 24 % |
| Yap6p H2O2Hi | 8.77E-08 | 0.081569 | | 12 | 39 % |
| Pdr1p | 2.45E-07 | 0.028278 | | 6 | 21 % |
| YJL206C H2O2Lo | 1.00E-06 | 7.00E-05 | TRUE | 3 | 50 % |
| Rox1p H2O2Hi | 4.00E-06 | 0.131499 | | 9 | 41 % |
| Rgm1p | 1.00E-05 | 0.01489 | | 3 | 43 % |
| Nrg1p | 1.50E-05 | 0.000126 | TRUE | 16 | 76 % |
| Yap6p | 1.50E-05 | 0.000371 | TRUE | 11 | 69 % |
| Nrg1p H2O2L | 1.60E-05 | 0.000558 | TRUE | 10 | 67 % |
| Mig1p | 3.30E-05 | 0.002256 | TRUE* | 6 | 60 % |
| YJL206C | 9.70E-05 | 0.000889 | TRUE | 6 | 67 % |
| Hap4p | 0.000122 | 0.014725 | | 6 | 33 % |
| Aft2p H2O2Lo | 0.000123 | 0.736544 | | 7 | 25 % |
| Mal33p H2O2Hi | 0.000146 | 0.000916 | TRUE | 3 | 43 % |
| Phd1p BUT90 | 0.000171 | 0.01278 | | 18 | 69 % |
| Cup9p | 0.000276 | 0.001456 | TRUE* | 2 | 40 % |
| Phd1p | 0.000311 | 0.000945 | TRUE | 13 | 87 % |
| Gal4p | 0.000336 | 0.769441 | | 1 | 9 % |
| YPR196W | 0.000456 | 0.145988 | | 1 | 25 % |
| Gln3p SM | 0.000507 | 0.00084 | TRUE | 4 | 80 % |
| Yap6p H2O2Lo | 0.000562 | 0.002402 | TRUE* | 11 | 85 % |
| Dal80p RAPA | 0.000718 | 0.827761 | | 2 | 15 % |
| YJL206C H2O2Hi | 0.000953 | 0.000953 | TRUE | 4 | 100 % |

* = $P < 0.005$; otherwise $P < 0.001$

# Adjusted = Unadjusted - Nodes(CoverGraph) + ConnectedComponents (CoverGraph)

Detailed methods supporting Supplementary Table 4

1. Download intergenic sequences from SGD (http://downloads.yeastgenome.org/sequence/genomic_sequence/intergenic/).

2. Compare sequences using BLAST version 2.2.6
    a. Prepare sequences for BLAST analysis using `formatdb`
    b. Perform all pairwise comparisons using `blastall` (E-value $< 0.01$)
    c. Merge multiple BLAST hits found between two regions using previously published methods (Guan et al. 2007; Kellis et al. 2004) that used a weighted scoring scheme that accounts for both percent identify and the number of matching bases.
    d. Output network of merged BLAST hits (visualized in Supplementary Figure 6)

3. Collapse SBTF targets that are connected in the BLAST network
    a. For each SBTF
        i. Compute the *CoverGraph*, meaning:
            1. Map subtelomeric SBTF targets onto nodes in network
            2. An edge is *Covered* if both endpoints are subtelomeric targets
            3. *CoverGraph* is the subgraph of all *Covered* edges
        ii. Count number of connected components in *CoverGraph*
        iii. Compute adjusted number of subtelomeric targets bound (reported in Supplementary Table 4)
            1. Adjusted = (# subtelomeric targets) – (# nodes in *CoverGraph*) + (# connected components)
        iv. Adjust set of subtelomeric targets by replacing all of the targets in one connected component with one member of that component.

4. Repeat Telomere Distance Profile analysis using adjusted set of subtelomeric targets. Report *P*-value in Supplementary Table 4.

# Supplementary Table 5. SBTF tagets found in HAST domains

## AFT2_H2O2Lo_hast (9)

| | | |
|---|---|---|
| YEL070W | DSF1 | Deletion suppressor of mpt5 mutation |
| YOL158C | ENB1<br>arn4 | Endosomal ferric enterobactin transporter, expressed under conditions of iron deprivation; member of the major facilitator superfamily; expression is regulated by Rcs1p and affected by chloroquine treatment |
| YOR383C | FIT3 | Mannoprotein that is incorporated into the cell wall via a glycosylphosphatidylinositol (GPI) anchor, involved in the retention of siderophore-iron in the cell wall |
| YOR384W | FRE5 | Putative ferric reductase with similarity to Fre2p; expression induced by low iron levels; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies |
| YBR296C | PHO89<br>itn1 | Na+/Pi cotransporter, active in early growth phase; similar to phosphate transporters of Neurospora crassa; transcription regulated by inorganic phosphate concentrations and Pho4p |
| YHL045W | YHL045W | Putative protein of unknown function; not an essential gene |
| YHL046C | YHL046C | Putative protein of unknown function; not an essential gene |
| YIR040C | YIR040C | Hypothetical protein |
| YIR041W | YIR041W | Hypothetical protein |

## CUP9_hast (3)

| | | |
|---|---|---|
| YEL070W | DSF1 | Deletion suppressor of mpt5 mutation |
| YJR158W | HXT16 | Protein of unknown function with similarity to hexose transporter family members, expression is repressed by high levels of glucose |
| YJR159W | SOR1<br>sdh1 | Sorbitol dehydrogenase; expression is induced in the presence of sorbitol |

## GAT3_hast (4)

| | | |
|---|---|---|
| YFL062W | COS4 | Protein of unknown function, member of the DUP380 subfamily of conserved, often subtelomerically-encoded proteins |
| YJR161C | COS5 | Protein of unknown function, member the DUP380 subfamily of conserved, often subtelomerically-encoded proteins |

| | | |
|---|---|---|
| YIL174W | YIL174W | Hypothetical protein |
| YIL175W | YIL175W | Hypothetical protein |

## HAP4_hast (4)

| | | |
|---|---|---|
| YPR191W | QCR2<br>ucr2<br>cor2 | Subunit 2 of the ubiquinol cytochrome-c reductase complex, which is a component of the mitochondrial inner membrane electron transport chain; transcription is regulated by Hap1p, Hap2p/Hap3p, and heme |
| YPR190C | RPC82<br>rpc3 | RNA polymerase III subunit C82 |
| YIL174W | YIL174W | Hypothetical protein |
| YIL175W | YIL175W | Hypothetical protein |

## MAL33_H2O2Hi_hast (1)

| | | |
|---|---|---|
| YAL062W | GDH3<br>fun51 | NADP(+)-dependent glutamate dehydrogenase, synthesizes glutamate from ammonia and alpha-ketoglutarate; rate of alpha-ketoglutarate utilization differs from Gdh1p; expression regulated by nitrogen and carbon sources |

## MIG1_hast (10)

| | | |
|---|---|---|
| YEL070W | DSF1 | Deletion suppressor of mpt5 mutation |
| YJL221C | FSP2 | Protein of unknown function, expression is induced during nitrogen limitation |
| YOL156W | HXT11<br>lgt3 | Putative hexose transporter that is nearly identical to Hxt9p, has similarity to major facilitator superfamily (MFS) transporters and is involved in pleiotropic drug resistance |
| YIL170W | HXT12 | Possible pseudogene in strain S288C; YIL170W/HXT12 and the adjacent ORF, YIL171W, together encode a non-functional member of the hexose transporter family |
| YEL069C | HXT13 | Hexose transporter, induced in the presence of non-fermentable carbon sources, induced by low levels of glucose, repressed by high levels of glucose |
| YJL219W | HXT9 | Putative hexose transporter that is nearly identical to Hxt11p, has similarity to major facilitator superfamily (MFS) transporters, expression of HXT9 is regulated by transcription factors Pdr1p and Pdr3p |
| YJR159W | SOR1<br>sdh1 | Sorbitol dehydrogenase; expression is induced in the presence of sorbitol |

| | | |
|---|---|---|
| YIL172C | YIL172C | Putative protein of unknown function with similarity to glucosidases; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm |
| YJL216C | YJL216C | Protein of unknown function, similar to alpha-D-glucosidases; transcriptionally activated by both Pdr8p and Yrm1p, along with transporters and other genes involved in the pleiotropic drug resistance (PDR) phenomenon |
| YOL157C | YOL157C | Putative protein of unknown function |

**MSN4_hast (4)**

| | | |
|---|---|---|
| YIL173W | VTH1 | Putative membrane glycoprotein with strong similarity to Vth2p and Pep1p/Vps10p, may be involved in vacuolar protein sorting |
| YIL174W | YIL174W | Hypothetical protein |
| YIL175W | YIL175W | Hypothetical protein |
| YIL176C | YIL176C | Hypothetical protein |

**NRG1_H2O2Lo_hast (12)**

| | | |
|---|---|---|
| YEL070W | DSF1 | Deletion suppressor of mpt5 mutation |
| YMR319C | FET4 | Low-affinity Fe(II) transporter of the plasma membrane |
| YAL063C | FLO9 | Lectin-like protein with similarity to Flo1p, thought to be expressed and involved in flocculation |
| YJL221C | FSP2 | Protein of unknown function, expression is induced during nitrogen limitation |
| YOL156W | HXT11<br>lgt3 | Putative hexose transporter that is nearly identical to Hxt9p, has similarity to major facilitator superfamily (MFS) transporters and is involved in pleiotropic drug resistance |
| YIL170W | HXT12 | Possible pseudogene in strain S288C; YIL170W/HXT12 and the adjacent ORF, YIL171W, together encode a non-functional member of the hexose transporter family |
| YJR158W | HXT16 | Protein of unknown function with similarity to hexose transporter family members, expression is repressed by high levels of glucose |
| YJL219W | HXT9 | Putative hexose transporter that is nearly identical to Hxt11p, has similarity to major facilitator superfamily (MFS) transporters, expression of HXT9 is regulated by transcription factors Pdr1p and Pdr3p |

| | | |
|---|---|---|
| YBR296C | PHO89<br>itn1 | Na+/Pi cotransporter, active in early growth phase; similar to phosphate transporters of Neurospora crassa; transcription regulated by inorganic phosphate concentrations and Pho4p |
| YJR159W | SOR1<br>sdh1 | Sorbitol dehydrogenase; expression is induced in the presence of sorbitol |
| YIL172C | YIL172C | Putative protein of unknown function with similarity to glucosidases; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm |
| YOL157C | YOL157C | Putative protein of unknown function |

## NRG1_hast (17)

| | | |
|---|---|---|
| YEL070W | DSF1 | Deletion suppressor of mpt5 mutation |
| YMR319C | FET4 | Low-affinity Fe(II) transporter of the plasma membrane |
| YKR102W | FLO10 | Lectin-like protein with similarity to Flo1p, thought to be involved in flocculation |
| YJL221C | FSP2 | Protein of unknown function, expression is induced during nitrogen limitation |
| YOL156W | HXT11<br>lgt3 | Putative hexose transporter that is nearly identical to Hxt9p, has similarity to major facilitator superfamily (MFS) transporters and is involved in pleiotropic drug resistance |
| YIL170W | HXT12 | Possible pseudogene in strain S288C; YIL170W/HXT12 and the adjacent ORF, YIL171W, together encode a non-functional member of the hexose transporter family |
| YEL069C | HXT13 | Hexose transporter, induced in the presence of non-fermentable carbon sources, induced by low levels of glucose, repressed by high levels of glucose |
| YJR158W | HXT16 | Protein of unknown function with similarity to hexose transporter family members, expression is repressed by high levels of glucose |
| YJL219W | HXT9 | Putative hexose transporter that is nearly identical to Hxt11p, has similarity to major facilitator superfamily (MFS) transporters, expression of HXT9 is regulated by transcription factors Pdr1p and Pdr3p |
| YFL060C | SNO3 | Protein of unknown function, nearly identical to Sno2p; expression is induced before the diauxic shift and also in the absence of thiamin |
| YFL059W | SNZ3 | Member of a stationary phase-induced gene family; transcription of SNZ2 is induced prior to diauxic shift, and also in the absence of thiamin in a Thi2p-dependent |

| | | |
|---|---|---|
| | | manner; forms a coregulated gene pair with SNO3 |
| YJR159W | SOR1<br>sdh1 | Sorbitol dehydrogenase; expression is induced in the presence of sorbitol |
| YAL064W | YAL064W | Protein of unknown function; may interact with ribosomes, based on co-purification experiments |
| YHL041W | YHL041W | Hypothetical protein |
| YIL172C | YIL172C | Putative protein of unknown function with similarity to glucosidases; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm |
| YJL216C | YJL216C | Protein of unknown function, similar to alpha-D-glucosidases; transcriptionally activated by both Pdr8p and Yrm1p, along with transporters and other genes involved in the pleiotropic drug resistance (PDR) phenomenon |
| YOL157C | YOL157C | Putative protein of unknown function |

### PDR1_hast (3)

| | | |
|---|---|---|
| YOR381W | FRE3 | Ferric reductase, reduces siderophore-bound iron prior to uptake by transporters; expression induced by low iron levels |
| YIL174W | YIL174W | Hypothetical protein |
| YIL175W | YIL175W | Hypothetical protein |

### PHD1_BUT90_hast (17)

| | | |
|---|---|---|
| YFL062W | COS4 | Protein of unknown function, member of the DUP380 subfamily of conserved, often subtelomerically-encoded proteins |
| YEL070W | DSF1 | Deletion suppressor of mpt5 mutation |
| YMR319C | FET4 | Low-affinity Fe(II) transporter of the plasma membrane |
| YKR102W | FLO10 | Lectin-like protein with similarity to Flo1p, thought to be involved in flocculation |
| YAL063C | FLO9 | Lectin-like protein with similarity to Flo1p, thought to be expressed and involved in flocculation |
| YJL221C | FSP2 | Protein of unknown function, expression is induced during nitrogen limitation |
| YIL170W | HXT12 | Possible pseudogene in strain S288C; YIL170W/HXT12 and the adjacent ORF, YIL171W, together encode a non-functional member of the hexose transporter family |

| | | |
|---|---|---|
| YEL069C | HXT13 | Hexose transporter, induced in the presence of non-fermentable carbon sources, induced by low levels of glucose, repressed by high levels of glucose |
| YJR158W | HXT16 | Protein of unknown function with similarity to hexose transporter family members, expression is repressed by high levels of glucose |
| YJL219W | HXT9 | Putative hexose transporter that is nearly identical to Hxt11p, has similarity to major facilitator superfamily (MFS) transporters, expression of HXT9 is regulated by transcription factors Pdr1p and Pdr3p |
| YJR159W | SOR1<br>sdh1 | Sorbitol dehydrogenase; expression is induced in the presence of sorbitol |
| YIL173W | VTH1 | Putative membrane glycoprotein with strong similarity to Vth2p and Pep1p/Vps10p, may be involved in vacuolar protein sorting |
| YIL172C | YIL172C | Putative protein of unknown function with similarity to glucosidases; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm |
| YIL174W | YIL174W | Hypothetical protein |
| YIL175W | YIL175W | Hypothetical protein |
| YIL176C | YIL176C | Hypothetical protein |
| YJL217W | YJL217W | Cytoplasmic protein of unknown function; expression induced by calcium shortage and via the copper sensing transciption factor Mac1p during conditons of copper deficiency; mRNA is cell cycle regulated, peaking in G1 phase |

## **PHD1_hast (14)**

| | | |
|---|---|---|
| YEL070W | DSF1 | Deletion suppressor of mpt5 mutation |
| YKR102W | FLO10 | Lectin-like protein with similarity to Flo1p, thought to be involved in flocculation |
| YAL063C | FLO9 | Lectin-like protein with similarity to Flo1p, thought to be expressed and involved in flocculation |
| YJL221C | FSP2 | Protein of unknown function, expression is induced during nitrogen limitation |
| YEL066W | HPA3 | D-Amino acid N-acetyltransferase, catalyzes N-acetylation of D-amino acids through ordered bi-bi mechanism in which acetyl-CoA is first substrate bound and CoA is last product liberated; similar to Hpa2p, acetylates histones weakly in vitro |

| | | |
|---|---|---|
| YEL069C | HXT13 | Hexose transporter, induced in the presence of non-fermentable carbon sources, induced by low levels of glucose, repressed by high levels of glucose |
| YJR158W | HXT16 | Protein of unknown function with similarity to hexose transporter family members, expression is repressed by high levels of glucose |
| YJL219W | HXT9 | Putative hexose transporter that is nearly identical to Hxt11p, has similarity to major facilitator superfamily (MFS) transporters, expression of HXT9 is regulated by transcription factors Pdr1p and Pdr3p |
| YJR159W | SOR1<br>sdh1 | Sorbitol dehydrogenase; expression is induced in the presence of sorbitol |
| YIL173W | VTH1 | Putative membrane glycoprotein with strong similarity to Vth2p and Pep1p/Vps10p, may be involved in vacuolar protein sorting |
| YAL064W | YAL064W | Protein of unknown function; may interact with ribosomes, based on co-purification experiments |
| YEL068C | YEL068C | Hypothetical protein |
| YIL174W | YIL174W | Hypothetical protein |
| YIL175W | YIL175W | Hypothetical protein |

### RGM1_hast (2)

| | | |
|---|---|---|
| YIL174W | YIL174W | Hypothetical protein |
| YIL175W | YIL175W | Hypothetical protein |

### ROX1_H2O2Hi_hast (1)

| | | |
|---|---|---|
| YMR315W | YMR315W | Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus; YMR315W is not an essential gene |

### UGA3_RAPA_hast (1)

| | | |
|---|---|---|
| YJR149W | YJR149W | Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm |

### XBP1_H2O2Lo_hast (9)

| | | |
|---|---|---|
| YJL221C | FSP2 | Protein of unknown function, expression is induced during nitrogen limitation |

|  |  |  |
|---|---|---|
| YOL156W | HXT11<br>lgt3 | Putative hexose transporter that is nearly identical to Hxt9p, has similarity to major facilitator superfamily (MFS) transporters and is involved in pleiotropic drug resistance |
| YIL170W | HXT12 | Possible pseudogene in strain S288C; YIL170W/HXT12 and the adjacent ORF, YIL171W, together encode a non-functional member of the hexose transporter family |
| YJR158W | HXT16 | Protein of unknown function with similarity to hexose transporter family members, expression is repressed by high levels of glucose |
| YJL219W | HXT9 | Putative hexose transporter that is nearly identical to Hxt11p, has similarity to major facilitator superfamily (MFS) transporters, expression of HXT9 is regulated by transcription factors Pdr1p and Pdr3p |
| YJR159W | SOR1<br>sdh1 | Sorbitol dehydrogenase; expression is induced in the presence of sorbitol |
| YIL172C | YIL172C | Putative protein of unknown function with similarity to glucosidases; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm |
| YJL213W | YJL213W | Protein of unknown function that may interact with ribosomes; periodically expressed during the yeast metabolic cycle; phosphorylated in vitro by the mitotic exit network (MEN) kinase complex, Dbf2p/Mob1p |
| YOL157C | YOL157C | Putative protein of unknown function |

**YAP5_hast (3)**

|  |  |  |
|---|---|---|
| YFL062W | COS4 | Protein of unknown function, member of the DUP380 subfamily of conserved, often subtelomerically-encoded proteins |
| YIL174W | YIL174W | Hypothetical protein |
| YIL175W | YIL175W | Hypothetical protein |

**YAP6_H2O2Hi_hast (10)**

|  |  |  |
|---|---|---|
| YAL063C | FLO9 | Lectin-like protein with similarity to Flo1p, thought to be expressed and involved in flocculation |
| YJL221C | FSP2 | Protein of unknown function, expression is induced during nitrogen limitation |
| YOL156W | HXT11<br>lgt3 | Putative hexose transporter that is nearly identical to Hxt9p, has similarity to major facilitator superfamily (MFS) transporters and is involved in pleiotropic drug |

| | | |
|---|---|---|
| | | resistance |
| YIL170W | HXT12 | Possible pseudogene in strain S288C; YIL170W/HXT12 and the adjacent ORF, YIL171W, together encode a non-functional member of the hexose transporter family |
| YJL219W | HXT9 | Putative hexose transporter that is nearly identical to Hxt11p, has similarity to major facilitator superfamily (MFS) transporters, expression of HXT9 is regulated by transcription factors Pdr1p and Pdr3p |
| YIL172C | YIL172C | Putative protein of unknown function with similarity to glucosidases; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm |
| YJL218W | YJL218W | Putative protein of unknown function, similar to bacterial galactoside O-acetyltransferases; induced by oleate in an OAF1/PIP2-dependent manner; promoter contains an oleate response element consensus sequence; non-essential gene |
| YMR315W | YMR315W | Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus; YMR315W is not an essential gene |
| YMR320W | YMR320W | Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data |
| YOL157C | YOL157C | Putative protein of unknown function |

**YAP6_H2O2Lo_hast (13)**

| | | |
|---|---|---|
| YMR319C | FET4 | Low-affinity Fe(II) transporter of the plasma membrane |
| YAL063C | FLO9 | Lectin-like protein with similarity to Flo1p, thought to be expressed and involved in flocculation |
| YJL221C | FSP2 | Protein of unknown function, expression is induced during nitrogen limitation |
| YOL156W | HXT11<br>lgt3 | Putative hexose transporter that is nearly identical to Hxt9p, has similarity to major facilitator superfamily (MFS) transporters and is involved in pleiotropic drug resistance |
| YIL170W | HXT12 | Possible pseudogene in strain S288C; YIL170W/HXT12 and the adjacent ORF, YIL171W, together encode a non-functional member of the hexose transporter family |
| YJR158W | HXT16 | Protein of unknown function with similarity to hexose transporter family members, expression is repressed by high levels of glucose |
| YJL219W | HXT9 | Putative hexose transporter that is nearly identical to |

| | | |
|---|---|---|
| | | Hxt11p, has similarity to major facilitator superfamily (MFS) transporters, expression of HXT9 is regulated by transcription factors Pdr1p and Pdr3p |
| YIL172C | YIL172C | Putative protein of unknown function with similarity to glucosidases; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm |
| YJL216C | YJL216C | Protein of unknown function, similar to alpha-D-glucosidases; transcriptionally activated by both Pdr8p and Yrm1p, along with transporters and other genes involved in the pleiotropic drug resistance (PDR) phenomenon |
| YJL217W | YJL217W | Cytoplasmic protein of unknown function; expression induced by calcium shortage and via the copper sensing transciption factor Mac1p during conditons of copper deficiency; mRNA is cell cycle regulated, peaking in G1 phase |
| YJL218W | YJL218W | Putative protein of unknown function, similar to bacterial galactoside O-acetyltransferases; induced by oleate in an OAF1/PIP2-dependent manner; promoter contains an oleate response element consensus sequence; non-essential gene |
| YOL157C | YOL157C | Putative protein of unknown function |
| YOL159C | YOL159C | Hypothetical protein |

### YAP6_hast (18)

| | | |
|---|---|---|
| YLL052C | AQY2 | Water channel that mediates the transport of water across cell membranes, only expressed in proliferating cells, controlled by osmotic signals, may be involved in freeze tolerance; disrupted by a stop codon in many S. cerevisiae strains |
| YEL070W | DSF1 | Deletion suppressor of mpt5 mutation |
| YOL158C | ENB1<br>arn4 | Endosomal ferric enterobactin transporter, expressed under conditions of iron deprivation; member of the major facilitator superfamily; expression is regulated by Rcs1p and affected by chloroquine treatment |
| YMR319C | FET4 | Low-affinity Fe(II) transporter of the plasma membrane |
| YKR102W | FLO10 | Lectin-like protein with similarity to Flo1p, thought to be involved in flocculation |
| YJL221C | FSP2 | Protein of unknown function, expression is induced during nitrogen limitation |
| YOL151W | GRE2 | NADPH-dependent methylglyoxal reductase (D-lactaldehyde dehydrogenase); stress induced (osmotic, ionic, |

| | | |
|---|---|---|
| | | oxidative, heat shock and heavy metals); regulated by the HOG pathway |
| YOL156W | HXT11<br>lgt3 | Putative hexose transporter that is nearly identical to Hxt9p, has similarity to major facilitator superfamily (MFS) transporters and is involved in pleiotropic drug resistance |
| YIL170W | HXT12 | Possible pseudogene in strain S288C; YIL170W/HXT12 and the adjacent ORF, YIL171W, together encode a non-functional member of the hexose transporter family |
| YJR158W | HXT16 | Protein of unknown function with similarity to hexose transporter family members, expression is repressed by high levels of glucose |
| YJL219W | HXT9 | Putative hexose transporter that is nearly identical to Hxt11p, has similarity to major facilitator superfamily (MFS) transporters, expression of HXT9 is regulated by transcription factors Pdr1p and Pdr3p |
| YJR159W | SOR1<br>sdh1 | Sorbitol dehydrogenase; expression is induced in the presence of sorbitol |
| YIL172C | YIL172C | Putative protein of unknown function with similarity to glucosidases; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm |
| YIR035C | YIR035C | Putative cytoplasmic protein of unknown function |
| YJL216C | YJL216C | Protein of unknown function, similar to alpha-D-glucosidases; transcriptionally activated by both Pdr8p and Yrm1p, along with transporters and other genes involved in the pleiotropic drug resistance (PDR) phenomenon |
| YJL217W | YJL217W | Cytoplasmic protein of unknown function; expression induced by calcium shortage and via the copper sensing transciption factor Mac1p during conditons of copper deficiency; mRNA is cell cycle regulated, peaking in G1 phase |
| YLL053C | YLL053C | Putative protein; in the Sigma 1278B strain background YLL053C is contiguous with AQY2 which encodes an aquaporin |
| YOL157C | YOL157C | Putative protein of unknown function |

### YJL206C_H2O2Hi_hast (4)

| | | |
|---|---|---|
| YPL275W | FDH2 | NAD(+)-dependent formate dehydrogenase, may protect cells from exogenous formate; YPL275W and YPL276W comprise a continuous open reading frame in some S. cerevisiae strains but not in the genomic reference strain S288C |

| | | |
|---|---|---|
| YPL276W | YPL276W<br>fdh2 | NAD(+)-dependent formate dehydrogenase, may protect cells from exogenous formate; YPL275W and YPL276W comprise a continuous open reading frame in some S. cerevisiae strains but not in the genomic reference strain S288C |
| YPL277C | YPL277C | Hypothetical protein |
| YPL278C | YPL278C | Hypothetical protein |

### YJL206C_H2O2Lo_hast (6)

| | | |
|---|---|---|
| YOR388C | FDH1 | NAD(+)-dependent formate dehydrogenase, may protect cells from exogenous formate |
| YPL275W | FDH2 | NAD(+)-dependent formate dehydrogenase, may protect cells from exogenous formate; YPL275W and YPL276W comprise a continuous open reading frame in some S. cerevisiae strains but not in the genomic reference strain S288C |
| YOR389W | YOR389W | Hypothetical protein |
| YPL276W | YPL276W<br>fdh2 | NAD(+)-dependent formate dehydrogenase, may protect cells from exogenous formate; YPL275W and YPL276W comprise a continuous open reading frame in some S. cerevisiae strains but not in the genomic reference strain S288C |
| YPL277C | YPL277C | Hypothetical protein |
| YPL278C | YPL278C | Hypothetical protein |

### YJL206C_hast (6)

| | | |
|---|---|---|
| YOR388C | FDH1 | NAD(+)-dependent formate dehydrogenase, may protect cells from exogenous formate |
| YPL275W | FDH2 | NAD(+)-dependent formate dehydrogenase, may protect cells from exogenous formate; YPL275W and YPL276W comprise a continuous open reading frame in some S. cerevisiae strains but not in the genomic reference strain S288C |
| YOR389W | YOR389W | Hypothetical protein |
| YPL276W | YPL276W<br>fdh2 | NAD(+)-dependent formate dehydrogenase, may protect cells from exogenous formate; YPL275W and YPL276W comprise a continuous open reading frame in some S. cerevisiae strains but not in the genomic reference strain S288C |
| YPL277C | YPL277C | Hypothetical protein |
| YPL278C | YPL278C | Hypothetical protein |

# Supplementary Table 6. Promoters bound by Phd1p and Yap6p

Subtelomeric ORFs are underlined

| ORF | Name | SGD annotation |
|---|---|---|
| YER045C | ACA1 | Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, may regulate transcription of genes involved in utilization of non-optimal carbon sources |
| YEL070W | DSF1 | Deletion suppressor of mpt5 mutation |
| YKR102W | FLO10 | Lectin-like protein with similarity to Flo1p, thought to be involved in flocculation |
| YJL221C | FSP2 | Protein of unknown function, expression is induced during nitrogen limitation |
| YMR136W | GAT2 | Protein containing GATA family zinc finger motifs; similar to Gln3p and Dal80p; expression repressed by leucine |
| YMR135C | GID8<br>dcr1 | Protein of unknown function, involved in proteasome-dependent catabolite inactivation of fructose-1,6-bisphosphatase; contains LisH and CTLH domains, like Vid30p; dosage-dependent regulator of START |
| YDL245C | HXT15 | Protein of unknown function with similarity to hexose transporter family members, expression is induced by low levels of glucose and repressed by high levels of glucose |
| YJR158W | HXT16 | Protein of unknown function with similarity to hexose transporter family members, expression is repressed by high levels of glucose |
| YJL219W | HXT9 | Putative hexose transporter that is nearly identical to Hxt11p, has similarity to major facilitator superfamily (MFS) transporters, expression of HXT9 is regulated by transcription factors Pdr1p and Pdr3p |
| YJR094C | IME1 | 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 |
| YBL030C | PET9<br>op1<br>anc2<br>aac2 | Major ADP/ATP carrier of the mitochondrial inner membrane, exchanges cytosolic ADP for mitochondrially synthesized ATP; required for viability in many common lab strains carrying a mutation in the polymorphic SAL1 gene |
| YNL178W | RPS3<br>suf14 | Protein component of the small (40S) ribosomal subunit, has apurinic/apyrimidinic (AP) endonuclease activity; essential for viability; has similarity to E. coli S3 and rat S3 ribosomal proteins |

| | | |
|---|---|---|
| YIL099W | SGA1 | Intracellular sporulation-specific glucoamylase involved in glycogen degradation; induced during starvation of a/a diploids late in sporulation, but dispensable for sporulation |
| YJR159W | SOR1<br>sdh1 | Sorbitol dehydrogenase; expression is induced in the presence of sorbitol |
| YMR017W | SPO20<br>dbi9 | Meiosis-specific subunit of the t-SNARE complex, required for prospore membrane formation during sporulation; similar to but not functionally redundant with Sec9p; SNAP-25 homolog |
| YEL040W | UTR2<br>crh2 | Cell wall protein that functions in the transfer of chitin to beta(1-6)glucan; putative chitin transglycosidase; glycosylphosphatidylinositol (GPI)-anchored protein localized to the bud neck; has a role in cell wall maintenance |
| YBL029W | YBL029W | Non-essential protein of unknown function |
| YEL007W | YEL007W<br>tos9 | Putative protein with sequence similarity to S. pombe gti1+ (gluconate transport inducer 1) |
| YIR020C | YIR020C | Hypothetical protein |
| YIR020W-B | | Dubious ORF |
| YPR013C | YPR013C | Putative zinc finger protein; YPR013C is not an essential gene |

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