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Supplementary Materials for

Histone exchange is associated with activator function at transcribed promoters and with repression at histone loci

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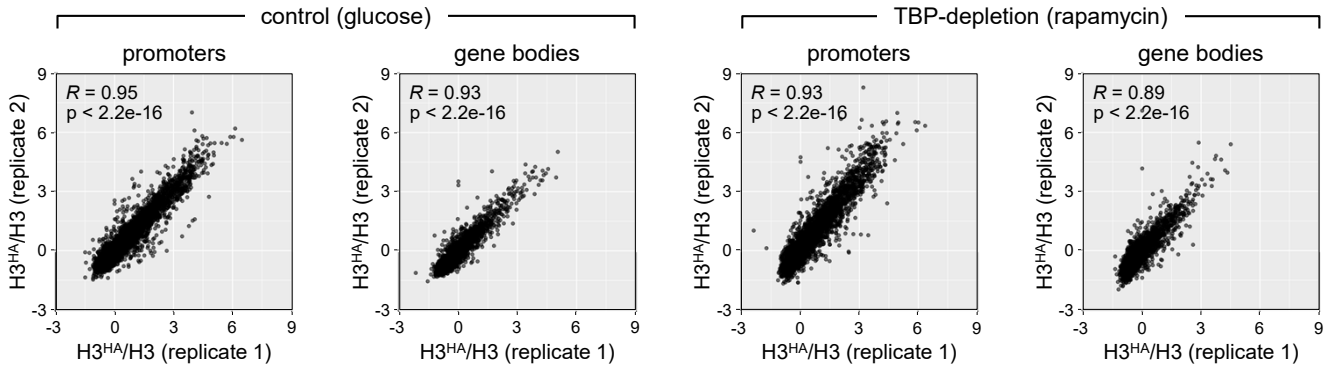
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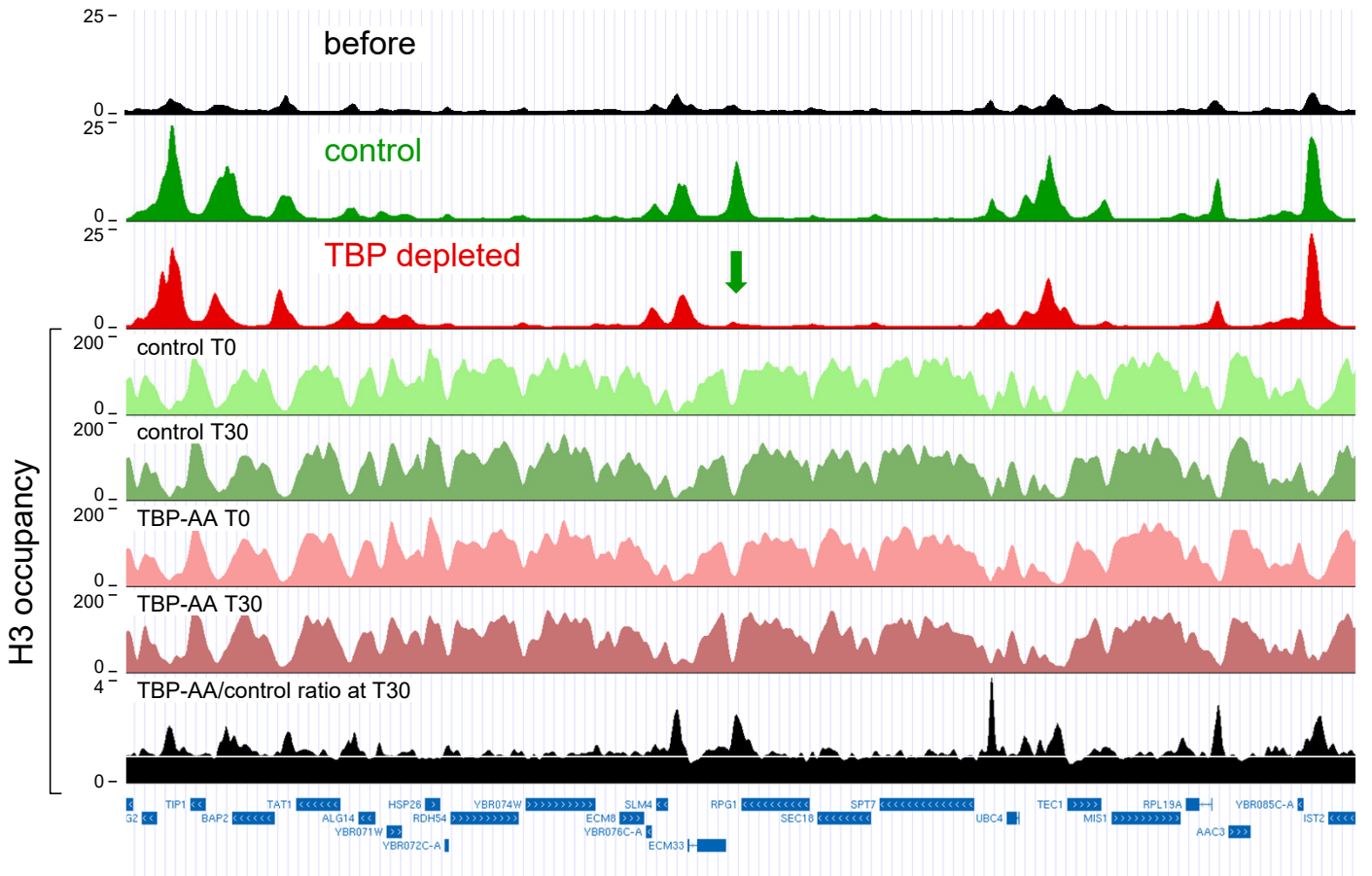
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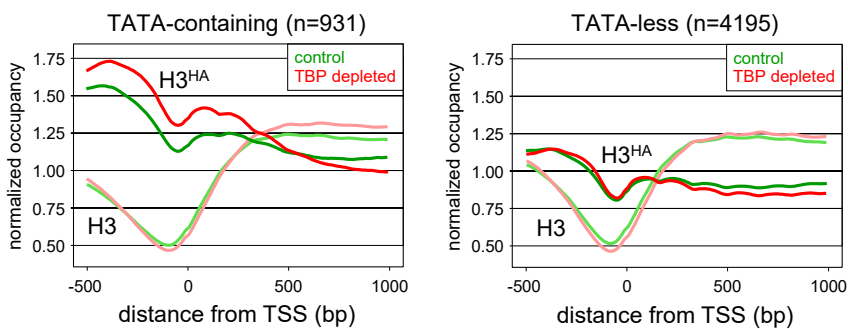
A



B



C



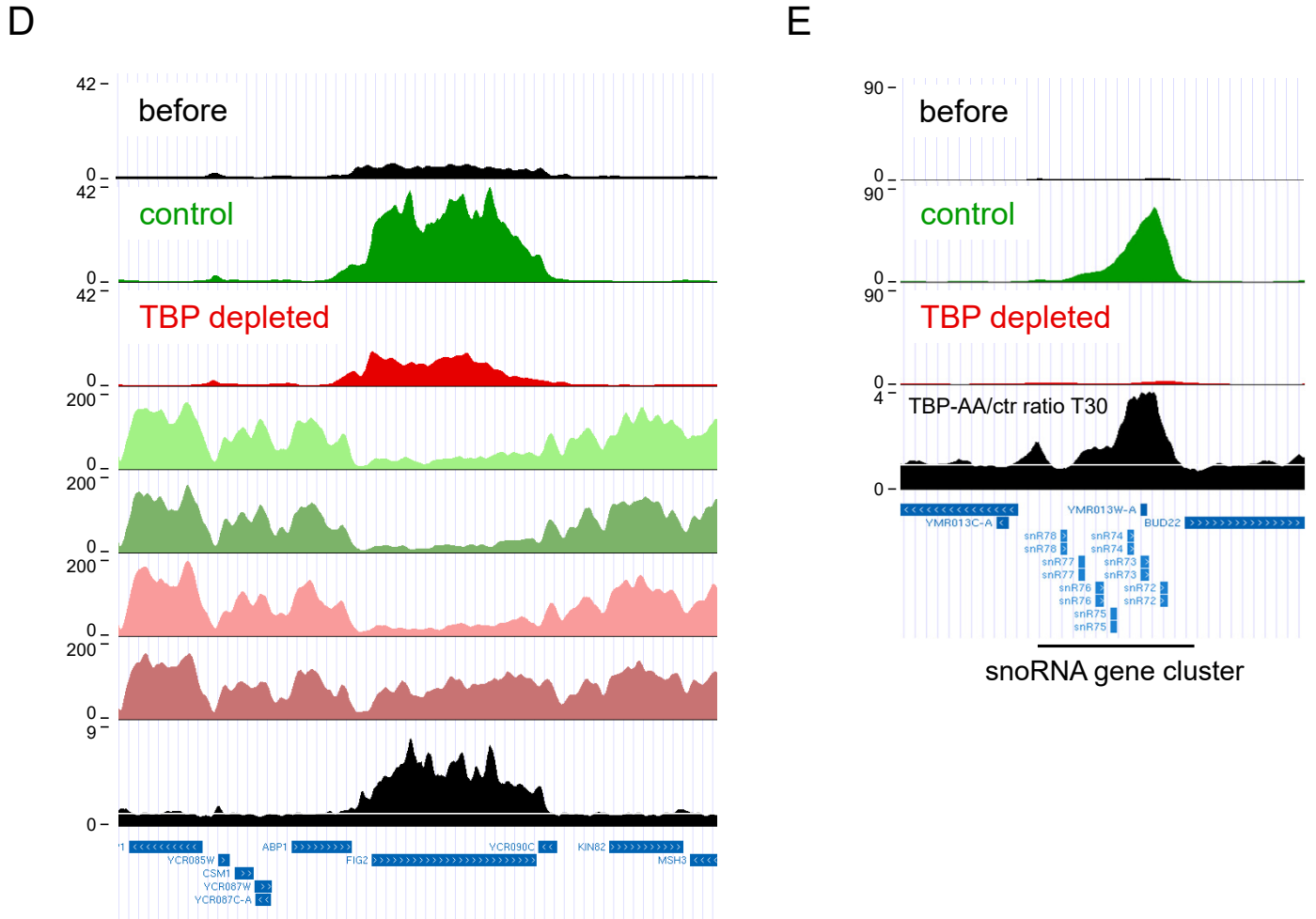


Fig. S1. Histone exchange and nucleosome occupancy in the absence of TBP. Related to Fig. 1.

(A) Comparison of the H3^{HA} enrichment over promoters (-500 to TSS) and gene bodies (TSS to +1000 bp) shows good reproducibility between two independent biological ChIP-Seq replicates. R values were calculated using the `stat_cor` function of the `ggpubr` package (57).

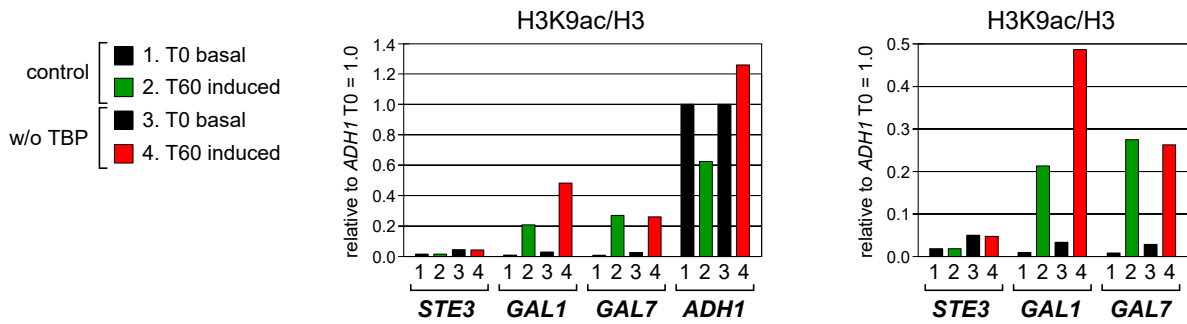
(B) Genome browser view of a region in chromosome II (365,000-425,000) showing TBP-dependent H3^{HA} incorporation between two genes (*ECM33* and *RPG1*; see arrow) oriented in a tail-to-tail fashion. Shown on top is a T0 time point control (before) when H3^{HA} is expressed at low levels prior to galactose induction. Shown below is H3 occupancy at T0 and T30 under control or TBP-depletion (TBP-AA) conditions as indicated. Regions of high histone exchange often show increased nucleosome occupancy upon TBP depletion (lower panel with white bar set to 1.0).

(C) Replicate of Fig. 1C.

(D) The *FIG2* gene is one of the very few RNA pol II genes showing high histone turnover over the gene body. Another example is *YHR020W*. Note that depletion of TBP results in a marked increase in nucleosome occupancy. Data are presented as in (C).

(E) High TBP-dependent histone turnover over a snoRNA gene cluster. Note that an increase in H3 occupancy following TBP depletion occurs in the absence of H3^{HA} incorporation, thus pointing to two independent events. The increase in histone occupancy must be rapid, occurring prior to the onset of H3^{HA} expression.

A



B

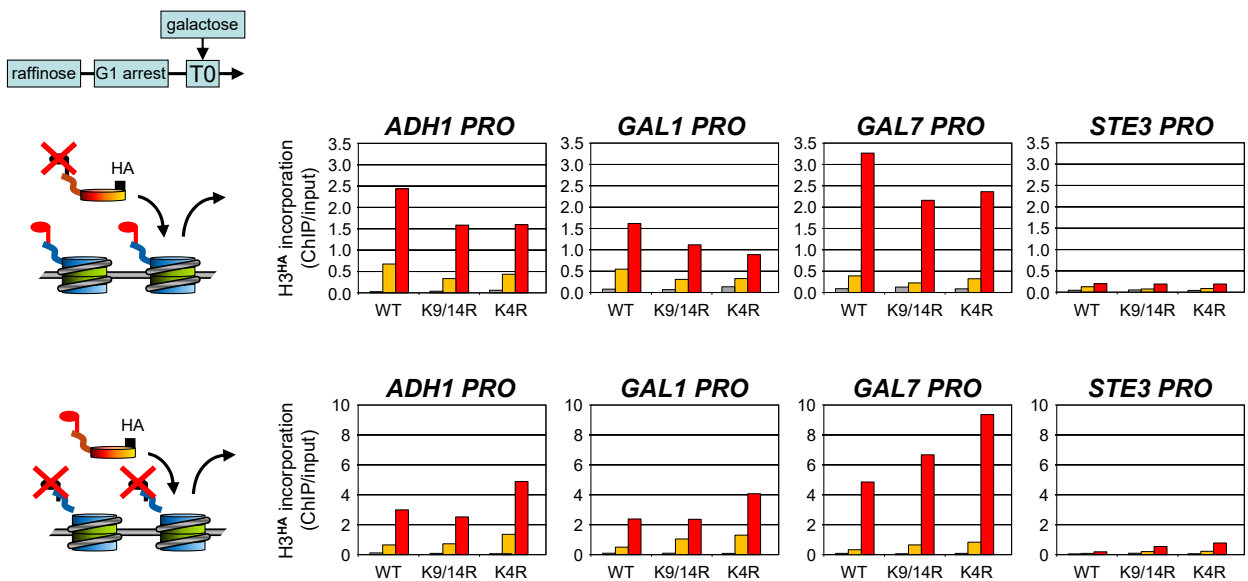


Fig. S2. Histone exchange and modifications at *GAL* genes. Related to Fig. 2.

(A) Galactose activation of the *GAL* genes is associated with increased H3K9/14ac at the promoter independently of TBP. Shown are the ChIP signals for H3K9/14ac normalized to H3 occupancy just prior to (T0) and at 60 min (T60) after galactose induction under control or TBP-depletion conditions. Right panel: without *ADH1*.

(B) Histone exchange at the active *GAL* promoters occurs independently of H3K4me and H3K9/14ac. Upper panels: incorporation of HA-tagged histone H3 K4R and K9/14R modification mutants in a wild-type chromatin background. Lower panel: incorporation of wild-type H3 in a chromatin containing the H3 modification mutants. Shown are the amounts of tagged histones detected just prior to (gray bars) and at 30 min (orange bars) and 60 min (red bars) after galactose induction of H3^{HA}. Data for the control *ADH1* and *STE3* gene promoters are from (41).

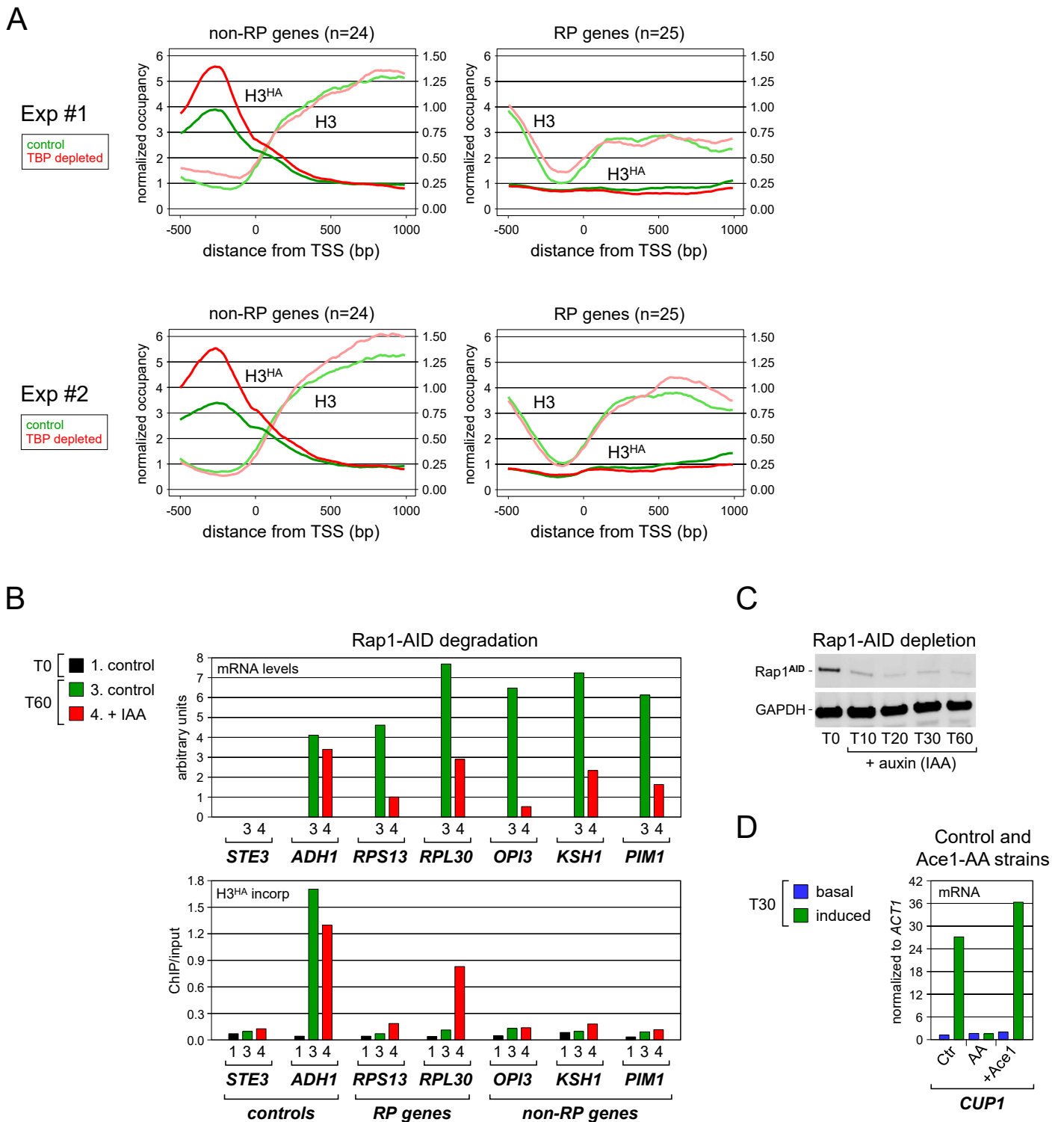


Fig. S3. Lack of histone exchange at Rap1-dependent RP and non-RP gene promoters. Related to Fig. 5.

(A) Low histone exchange at RP gene promoters in the presence or absence of TBP. Metagenome analysis of the average H3^{HA} incorporation and H3 occupancy under control (green) or TBP-depletion (red) conditions; left panels show a selected set of non-RP genes with high turnover at their promoters, right panels show RP genes (gene lists can be found in Table S4). The results are

presented as in Fig. 1C. The scale for H3 occupancy is on the right axis. Note that H3 levels are similar at both sets of promoters, indicating that the difference in HA^{H3} incorporation between these gene sets is not simply a result of H3 occupancy differences. Also see Fig. 1C.

(B) Same experiment as in Fig. 5C but including three Rap1-regulated non-RP genes. The genes were selected based on ChIP-Seq (58) and RNA-Seq (59) studies. The OPI3 mRNA signal, and the KSH1 and PIM1 mRNA signals were multiplied, respectively, by 8 and 100 to facilitate comparison.

(C) Time course analysis of auxin-mediated degradation of Rap1 fused to AID. Rap1-AID was detected using anti-Rap1 antibodies.

(D) Control experiment for Fig. 5E showing that anchor-away of Ace1 (AA) in the parental strain abrogates copper-mediated activation of *CUP1* and that normal activation is restored upon ectopic expression of Ace1 (+Ace1).

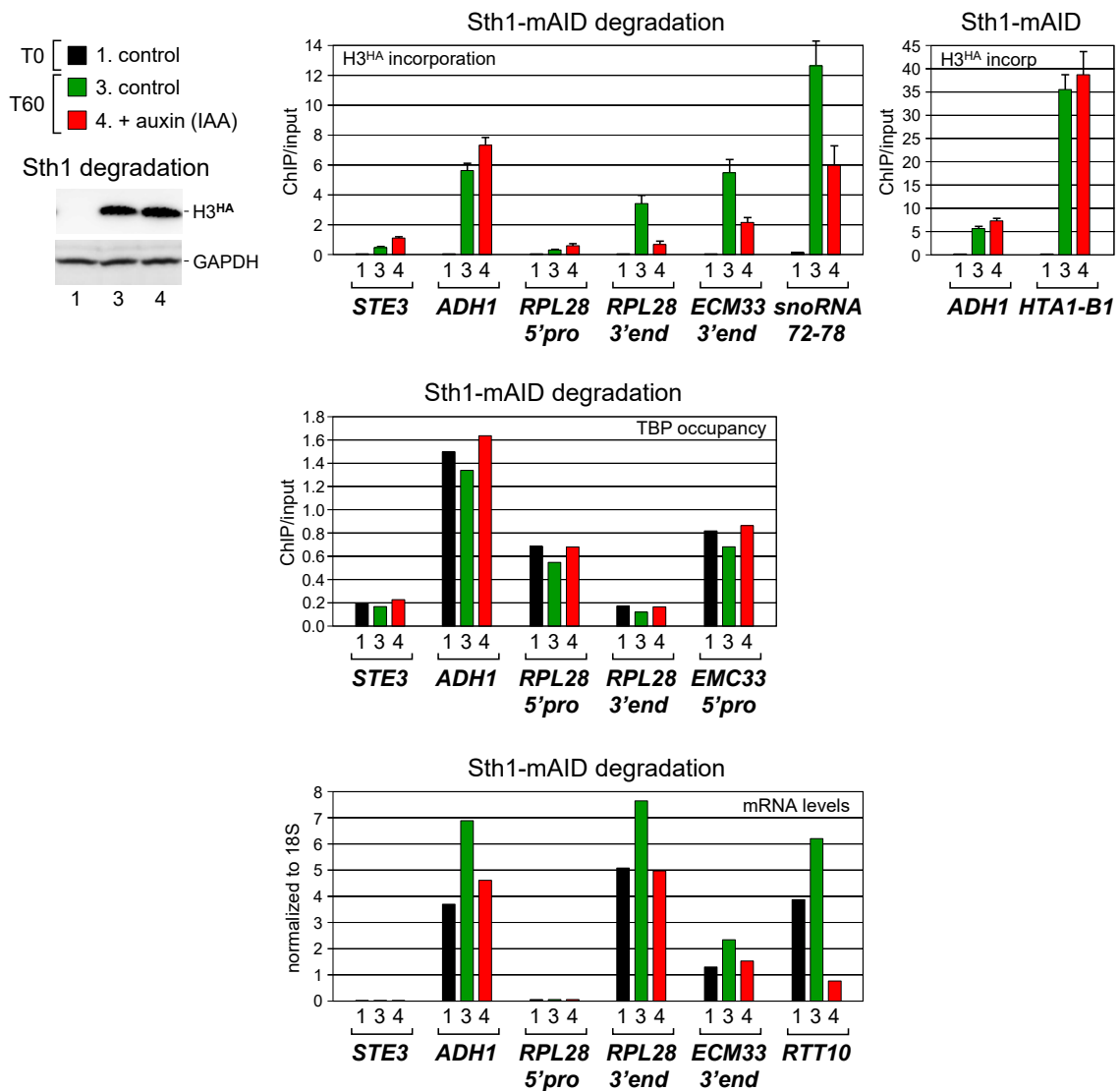


Fig. S4. Histone exchange in the absence of RSC. Related to Fig. 6.

Upper panels: Yeast cells expressing the essential RSC complex subunit Sth1 fused to mini-AID (mAID) were arrested in G1 by alpha factor. Auxin (IAA) was added or not 30 min prior to galactose activation of H3^{HA} to induce degradation of Sth1-mAID. H3^{HA} incorporation was measured at the indicated gene promoters and 3' ends as before. Shown are the mean and SD of triplicate cultures. On the left is the sample color code and a Western blot analysis for H3^{HA} expression. See fig. S5 for experimental details. *RPL28* (Fig. 1A) and *ECM33* (fig. S1B) are two genes showing TBP-dependent histone exchange at their 3' ends.

Middle and lower panels: TBP occupancy and mRNA levels for the indicated genes were monitored by RT-qPCR and quantitative ChIP under the same experimental conditions as above. Expression of *RTT10* is dependent on RSC (35) and serves as a control for auxin-induced degradation of Sth1. Note that HIR-mediated H3^{HA} incorporation at the histone *HTA1-HTB1* locus is unaffected by inactivation of RSC.

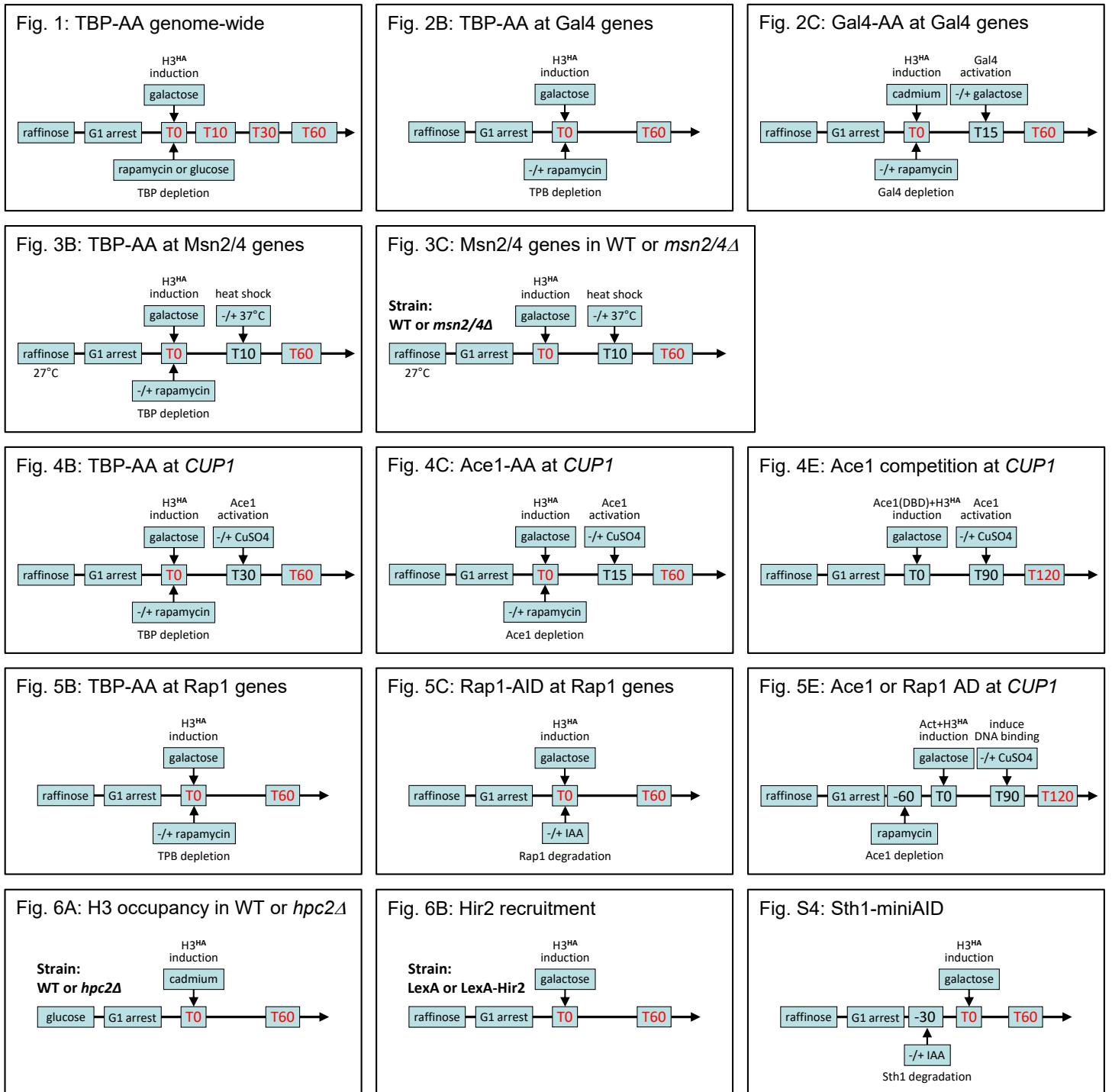


Fig. S5. Experimental schemes.

Schematic diagram illustrating the experiments presented in the indicated figures. Measurements were made at the time points indicated in red.

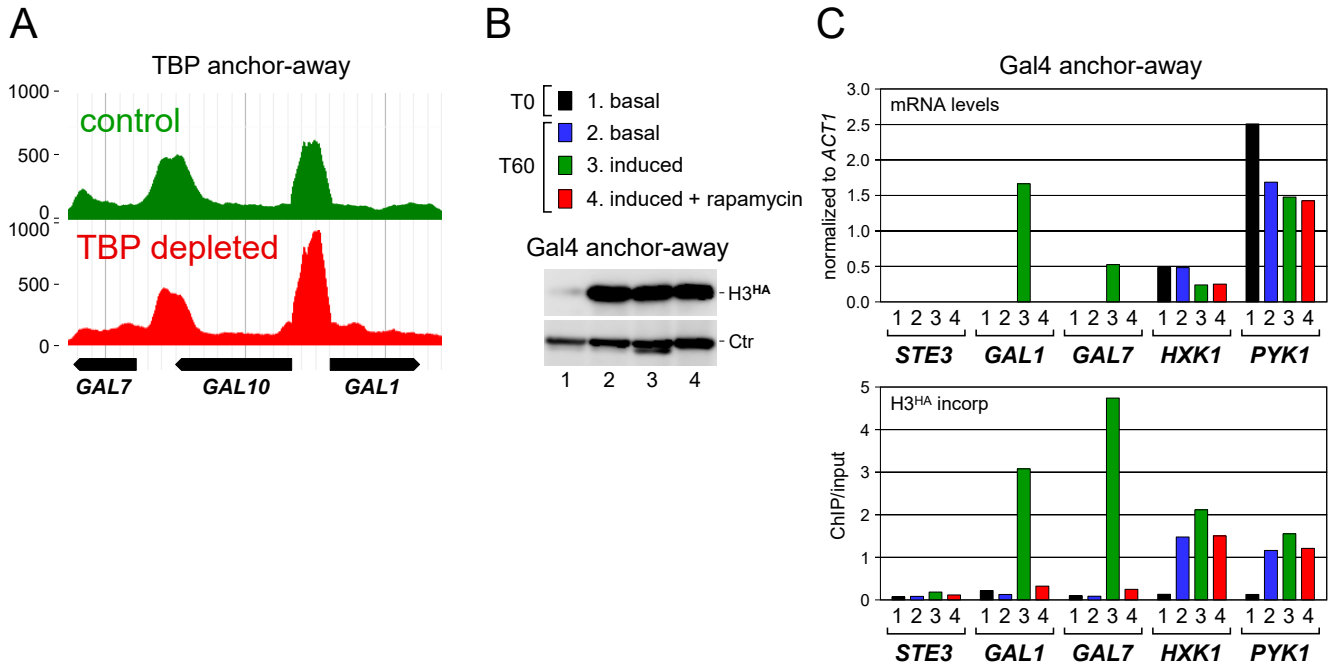


Fig. S6. Independent biological replicate of Fig. 2.

Same experiments as in Fig. 2 except that (A) shows a genome browser view of H3^{HA} incorporation at the *GAL* gene cluster. The data are presented as in Fig. 1B but without normalization to H3 occupancy. Shown in (B) is the sample color code and a Western blot analysis for H3^{HA} expression in the Gal4 anchor-away experiment presented in (C). Ctr: cross-reactive band that serves as loading control.

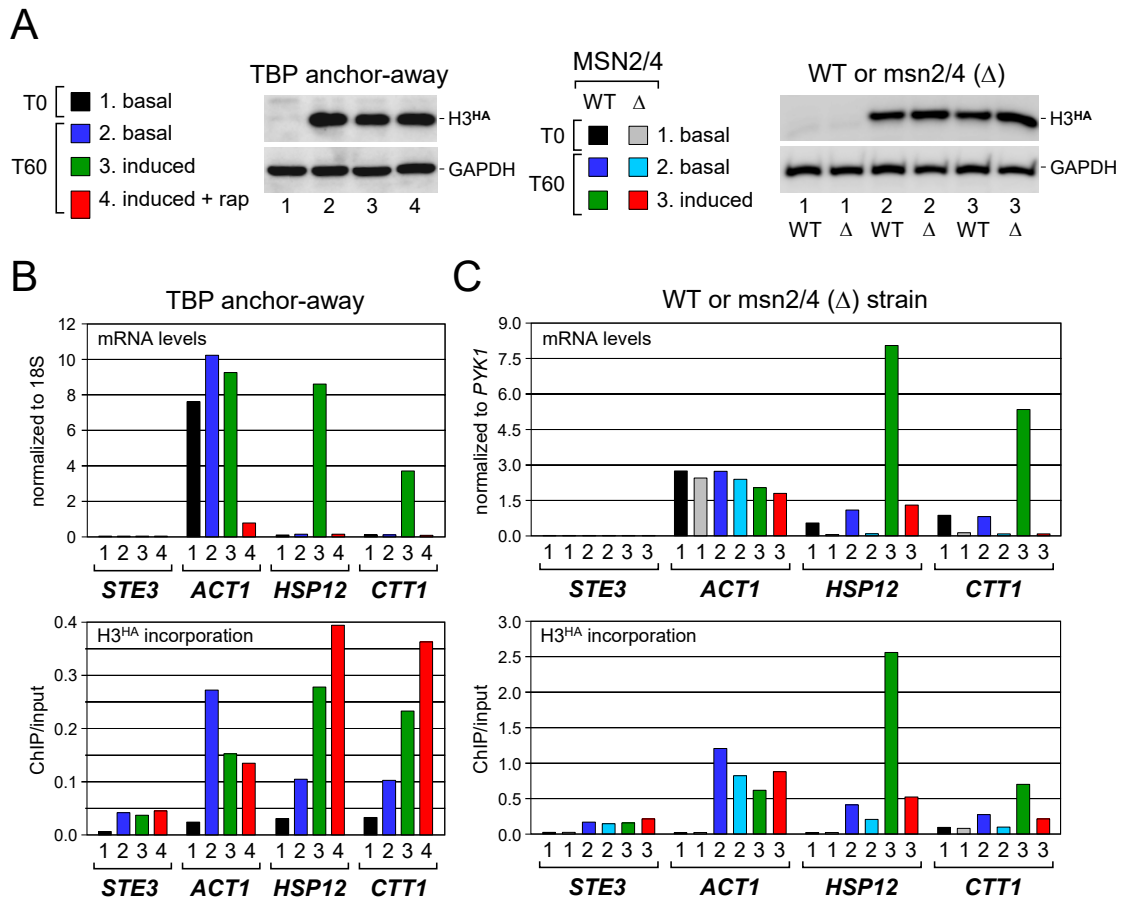


Fig. S7. Independent biological replicate of Fig. 3.

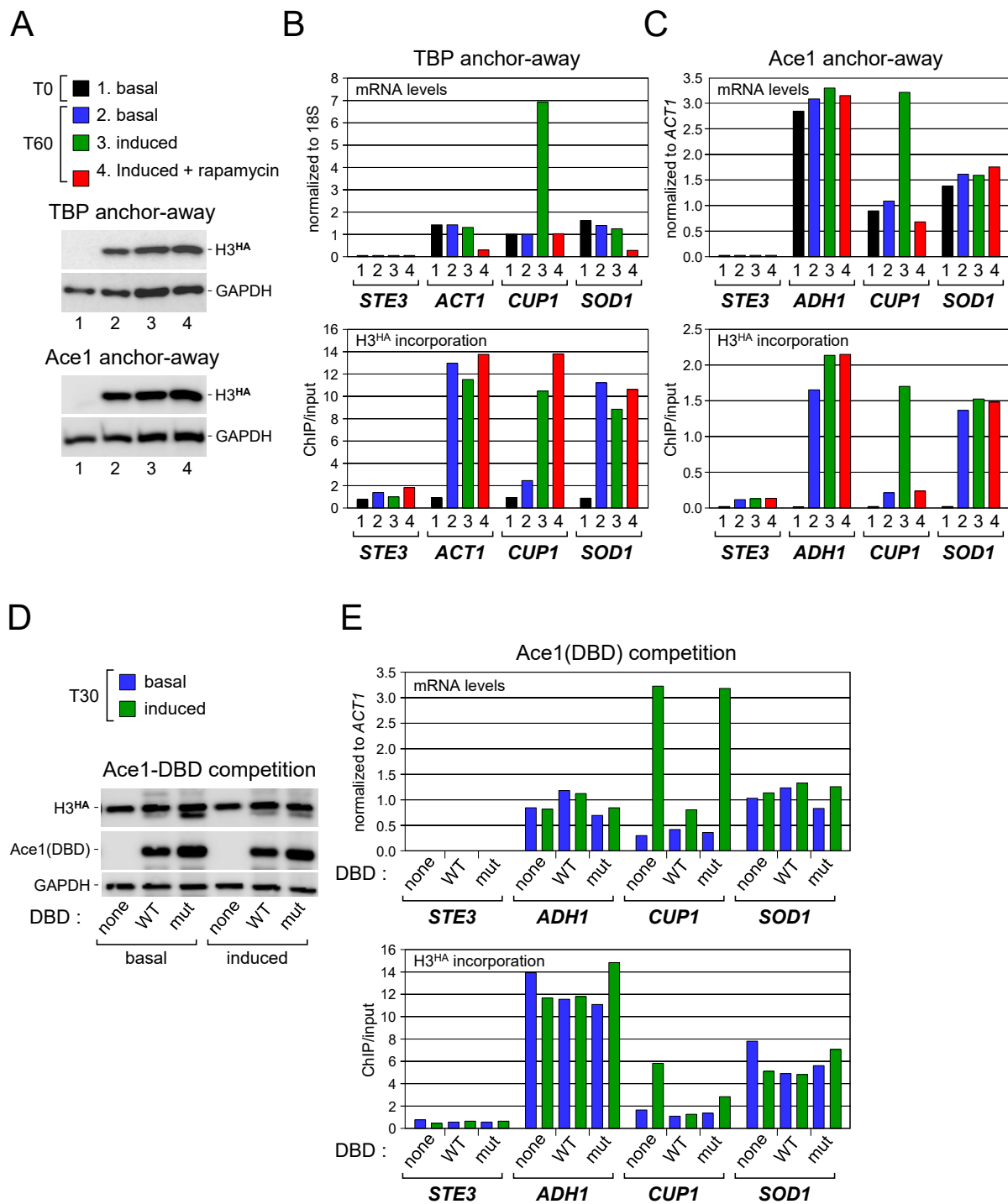


Fig. S8. Independent biological replicate of Fig. 4.

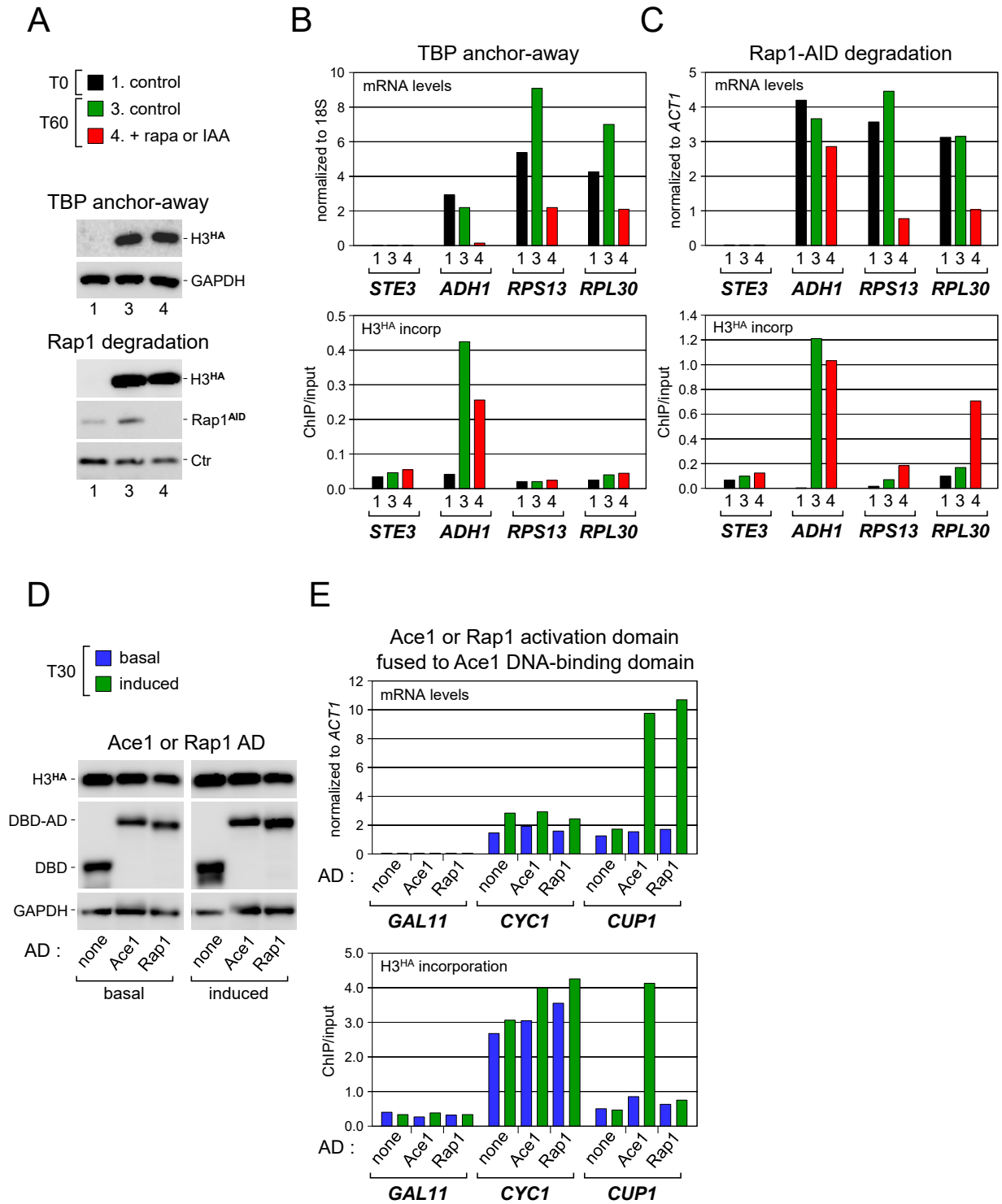
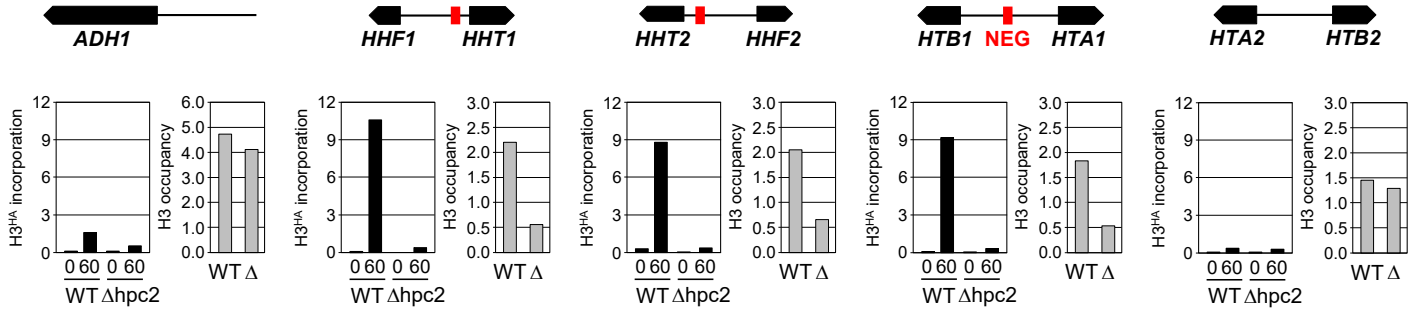


Fig. S9. Independent biological replicate of Fig. 5.

A



B

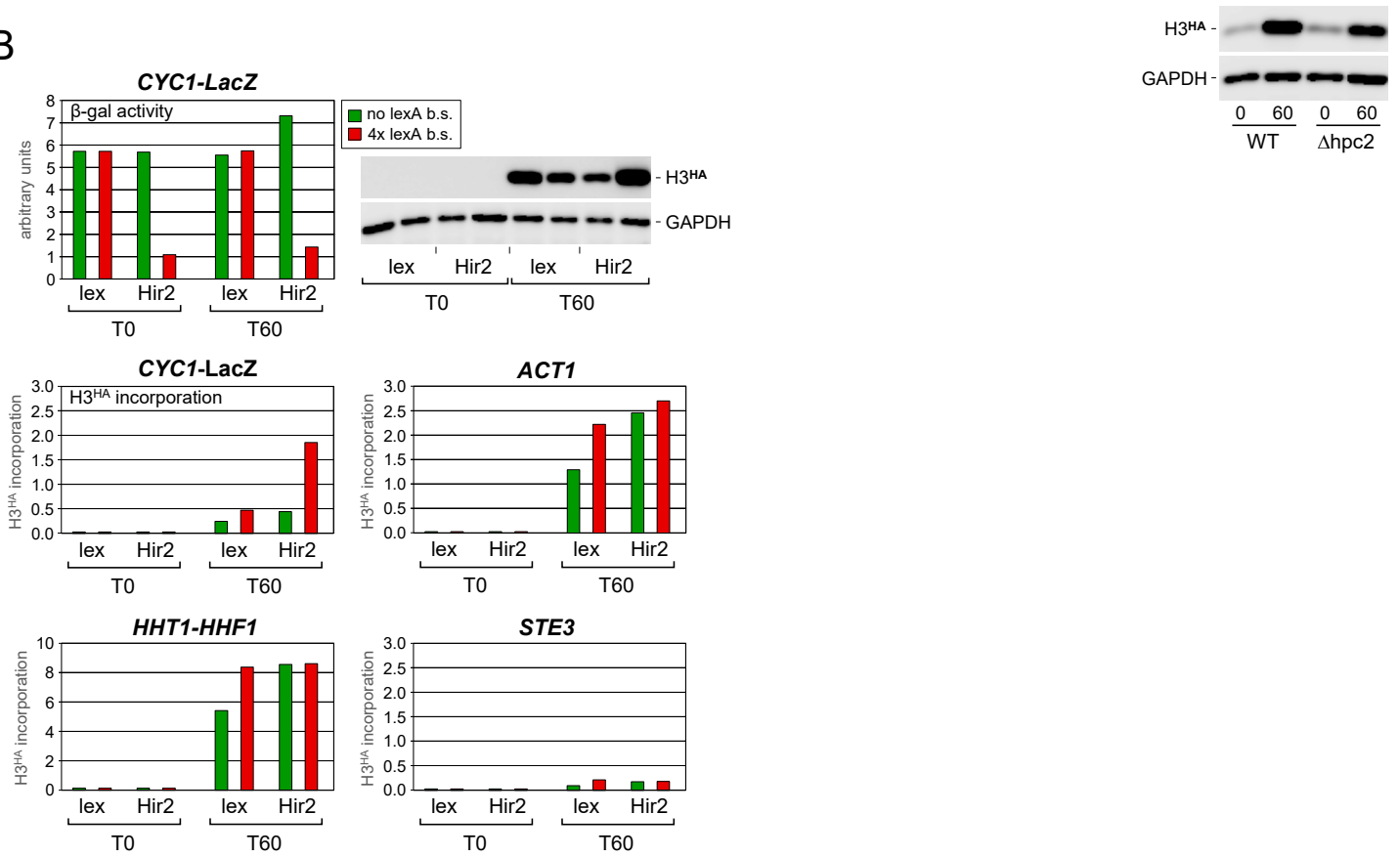


Fig. S10. Independent biological replicate of Fig. 6.

Supplementary Table S1

Yeast strains

Strain	Relevant genotype	Figure	Source
HHY221	<i>MATa, tor1-1, fpr1::loxP-LEU2-loxP, RPL13A-2×FKBP12::loxP, ade2-1, trp1-1, his3-11, ura3</i>		(17)
HH4	HHY221; <i>bar1::URA3</i>		(10)
SKY50	HH4; <i>GAL4-FRB-HISM3, pRS314-GAL1pro-H3.HA</i>	2C	This study
SKY15	HH4; <i>ACE1-FRB-HISM3</i>		This study
SKY23	HH4; <i>ACE1-FRB-HISM3, pRS314-GAL1pro-H3.HA</i>	4A, 4C	This study
HHY154	<i>MATα, ade2-1, ura3-1, tor1-1, fpr1::NAT, TBP1-FRB::KAN, RPL13A-2×FKBP12::TRP1</i>		(17)
YG19	HHY154; <i>MATa, bar1::URA3</i>		(10)
SKY12	YG19; <i>pRSADE-GAL1pro-H3.HA</i>	1A-1C, 2A, 2B, 3A, 3B, 4A, 4B, 5A, 5B, 6A, S1, S2A, S2B, S3A	This study
YG31	YG19; <i>hpc2::LEU2</i>		This study
SKY54	YG31; <i>pRSADE-MET3pro-H3.HA</i>	6A	This study
W303-1A	<i>MATa, leu2-3,112, his3-11,15 ura3-1, ade2-1, trp1-1, can1-100</i>		(25)
Wmsn2- msn4	W303-1A; <i>msn2-Δ3::HIS3, msn4-1::TRP1</i>		(25)
SKY65	W303-1A; <i>bar1::KANMX3, pRSADE-GAL1pro-H3.HA</i>	3A, 3C	This study
SKY66	Wmsn2- <i>msn4</i> ; <i>bar1::KANMX3, pRSADE-GAL1pro-H3.HA</i>	3A, 3C	This study

RH932.5A	<i>MATa, trp1, bar1-1</i>		Howard Riezman
SKY84	RH932.5A; <i>pBTM116-HIR2 + pAJ1+ pRSADE-GAL1pro-H3.HA</i>	6B	This study
SKY86	RH932.5A; <i>pBTM116-HIR2 + pJK1621+ pRSADE-GAL1pro-H3.HA</i>	6B	This study
SKY88	RH932.5A; <i>pBTM116 + pAJ1+ pRSADE-GAL1pro-H3.HA</i>	6B	This study
SKY89	RH932.5A; <i>pBTM116 + pJK1621+ pRSADE-GAL1pro-H3.HA</i>	6B	This study
SKY56	RH932.5A; <i>pRS314-GAL1pro-H3.HA + p793</i>	4D, 4E	This study
SKY57	RH932.5A; <i>pRS314-GAL1pro-H3.HA + p1883</i>	4D, 4E	This study
SKY58	RH932.5A; <i>pRS314-GAL1pro-H3.HA + p1885</i>	4D, 4E	This study
YJB25	<i>MATa, HIS3, ADE2, pRS306Padh1.OsTIR1, pRAP1-AID-LEU2</i>		(58)
SKY44	YJB25; <i>bar1::KANMX3, pRS314-GAL1pro-H3.HA</i>	5A, 5C, S3B	This study
SKY113	SKY15; <i>ura3::KANMX3</i>		This study
SKY114	SKY113; <i>pRS314-GAL1pro-H3.HA + p793</i>	5D, 5E, S3C	This study
SKY115	SKY113; <i>pRS314-GAL1pro-H3.HA + p1883</i>	5D, 5E	This study
SKY116	SKY113; <i>pRS314-GAL1pro-H3.HA + p1883-ACE1(AD)</i>	5D, 5E, S3C	This study
SKY117	SKY113; <i>pRS314-GAL1pro-H3.HA + p1883-RAP1(AD)</i>	5D, 5E	This study
SKY164	<i>MATa, HIS3, ADE2, pRS306Padh1.OsTIR1, STH1-miniAID-KANMX3, bar1::HYGB</i>		gift from David Shore
SKY165	SKY164; <i>pRSADE-GAL1pro-H3.HA</i>	S4	This study

Supplementary Table S2

Plasmids

Plasmid name	Description	Marker	Source
	pRS314-GAL1pro-H3.HA	TRP1	(10)
	pRSADE-GAL1pro-H3.HA	ADE2	(10)
	pRSADE-MET3pro-H3.HA	ADE2	This study
p793 (GFP-pYeF2)	pYeF2-GAL1pro-GFP	URA3	(28)
p1883	pYeF2-GAL1pro-Ace1(DBD:WT).GFP	URA3	(28)
p1885	pYeF2-GAL1pro-Ace1(DBD:G37Q).GFP	URA3	(28)
p1883-ACE1(AD)	pYeF2-GAL1pro-Ace1(DBD:WT).Ace1(AD).GFP	URA3	This study
p1883-RAP1(AD)	pYeF2-GAL1pro-Ace1(DBD:WT).Rap1(AD).GFP	URA3	This study
pBTM116	pBTM116-ADH1pro-LexA	TRP1	(36)
pBTM116-HIR2	pBTM116-ADH1pro-LexA.HIR2	TRP1	(36)
pAJ1	pAJ1-CYC1pro-LACZ reporter without LexA-binding sites	URA3	(36, 60)
pJK1621	pAJ1-CYC1pro-LACZ reporter carrying four LexA-binding sites upstream of the <i>CYC1</i> UAS elements	URA3	(36, 60)

Supplemental Table S3

Cloning PCR amplification primers

Name	Description	Sequence	Comments
MS2293	ClaI RAP1 AD Fw	CC <u>ATCGAT</u> gcAATTATAGTTCTCAAAGAAATG TTCAGCC	Cla1 site underlined; used to generate p1883-RAP1(AD). The bases in lower case have been added to keep the reading frame open
MS2294	ClaI RAP1 AD Rev	CC <u>ATCGAT</u> tTGGTGGAAAGCTTATGGTATCAGG	Cla1 site underlined; same
MS2295	ClaI ACE1 AD Fw	CC <u>ATCGAT</u> gcCTGGACGTTCTTTTGGGCC	Cla1 site underlined; used to generate p1883-ACE1(AD). The bases in lower case have been added to keep the reading frame open
MS2296	ClaI ACE1 AD Rev	CC <u>ATCGAT</u> tTTGTGAATGTGAGTTATGCGAAG	Cla1 site underlined; same
MS1730	KpnI MET3pro Fw	CGCGGT <u>ACCAAT</u> GAAAACACAGAAGTA	Kpn1 site underlined; used to generate pRSADE-MET3pro-H3.HA
MS1734	MscI MET3pro Rev	GCGT <u>GGCCATACT</u> TTTATTCTTGTTATTA	Msc1 site underlined; same

ChIP qPCR primers

Name	Description	Sequence	Comments
MS819	ACT1 PRO Fw	GCGCTAGAACATAACCAGAATC	
MS820	ACT1 PRO Rev	TCTTCCTTCCCCTTTCTACTC	
MS291	ADH1 PRO Fw	CACGCACACTACTCTCTAATGAG	
MS290	ADH1 PRO Rev	CTGGGATAGACATTGTATATGAG	
MS2056	CTT1 PRO Fw	ATGAGTACGTCGCCGATC	
MS2057	CTT1 PRO Rev	GTCCAGGCTACGTCGAAT	
MS1922	CUP1 PRO Fw	ACTTCACCACCCTTTATTTTC	

MS1923	CUP1 PRO Rev	CTGACAATCCATATTGCGTT	
MS1141	CYC1 PRO Fw	GATGGCCAGGCAACTTTA	
MS1142	CYC1 PRO Rev	ATGCTGCAAAGGTCTCTAA	
MS2054	CYC1-LACZ PRO Fw	TGTGCGACGACACATGATC	Hybridizes to the CYC1 core promoter
MS2055	CYC1-LACZ PRO Rev	GTGAGACGGGCAACAGCCAA	Hybridizes at the junction between CYC1 and the LacZ ORF
MS2698	EMC33 PRO Fw	CGTTCATTTCGCTTCTACAC	
MS2699	EMC33 PRO Rev	GCAGTAGCAGTCAAAGCG	
MS2694	EMC33 3'-end Fw	GAACGGTGCCACATCTAC	
MS2695	EMC33 3'-end Rev	GAGCAGCACCCCTTAGACT	
MS699	GAL1 PRO Fw	GCTGCATAACCACTTTAAC	
MS700	GAL1 PRO Rev	CTTTGCGCTAGAATTGAAC	
MS705	GAL7 PRO Fw	CTTGGACCCGTAAGTTTCAC	
MS706	GAL7 PRO Rev	TGCTGGTTACGAAGCAAGAC	
MS1041	GAL11 PRO Fw	GCTGGTTCCACAAAGAAG	
MS1042	GAL11 PRO Rev	ACGGCACTATACGAAACG	
MS1599	HHF1-HHT1 URR Fw	ACCGTATTCGCGGGCATTTCG	To amplify the regulatory region between HHF1 and HHT1
MS1600	HHF1-HHT1 URR Rev	ATAATGTATGGGACAATGCG	Same
MS1601	HHF2-HHT2 URR Fw	ACATTGGGGCATAATGAACGC	To amplify the regulatory region between HHF2 and HHT2
MS1602	HHF2-HHT2 URR Rev	TCTGGTCTGGTCTGCATTTTCG	Same
MS1595	HTA1-HTB1 URR Fw	TCTTGATTTTAAATCCATCG	To amplify the regulatory region between HTA1 and HTB1
MS1596	HTA1-HTB1 URR Rev	ATAGCTTCGCACAGTGAGGC	Same
MS1905	HTA2-HTB2 URR Fw	CACCGCTTTATTAGGCGAAG	To amplify the regulatory region between HTA2 and HTB2
MS1906	HTA2-HTB2 URR Rev	TTATGGCCCCCAGGTTAATG	Same
MS2596	HSP12 PRO Fw	TGCGTTCTACTTCCTCAATTGC	
MS2597	HSP12 PRO Rev	GCGTCAGACATTGTTGTATTTAGTTTTT	
MS1344	HXK1 PRO Fw	TGAGTATTGCAAGCCACA	
MS1345	HXK1 PRO Rev	CTTCTGTTTCCTCCTTTTC	

MS2682	KSH1 PRO Fw	GTCGGCAGATTTCTCACC	
MS2683	KSH1 PRO Rev	CAGGTGGGTTTATGCAGTG	
MS2678	OPI3 PRO Fw	TGATGACCAGGGTAGGTG	
MS2679	OPI3 PRO Rev	CAGTGGTCATTGCAGTGG	
MS2700	PIM1 PRO Fw	ATTGCAGCAACGACAAGC	
MS2701	PIM1 PRO Rev	AGACCCTTAGCACAGTGG	
MS835	PYK1 PRO Fw	CCCCTTTCAAAGTTATTCTCTACTC	
MS836	PYK1 PRO Rev	GAACCAGCAACAACGTTTAATG	
MS2208	RPL28 PRO Fw	CAGGGACCCACACATTAC	
MS2209	RPL28 PRO Rev	GGAGAAAGCAAACGCCAT	
MS2210	RPL28 3'-end Fw	TGGACATTGATCCCAGAAG	Used to amplify the 3' end of the RPL28 open reading frame
MS2211	RPL28 3'-end Rev	CTTCAGCCAACTTGGAGA	Same
MS2236	RPL30 PRO Fw	TTCTGGATAGGACGCCAAC	
MS2237	RPL30 PRO Rev	GATCCTTACTGCGGTGCTA	
MS2228	RPS13 PRO Fw	ACCACCCATAAACCATAAAGT	
MS2229	RPS13 PRO Rev	GTACAGAAGTGAAATCTCATTC	
MS1924	SOD1 PRO Fw	GCCGCTTACTGGAAGTAC	
MS1925	SOD1 PRO Rev	ACAGCTAAACATTTGCCC	
MS588	STE3 PRO Fw	CAAAGCCCTATTATTGCTGAC	
MS589	STE3 PRO Rev	TCTCCACAATTTGGGCAGAAG	
MS2646	snoRNA72-78 Fw	TTACAGACGGTCAACTGC	
MS2647	snoRNA72-78 Rev	GAGTCGTCCAAATAGTCAGC	

Expression analysis qPCR primers

Name	Description	Sequence	Comments
MS825	ACT1 ORF Fw	GTCCAAGGCGACGTAACATAG	
MS826	ACT1 ORF Rev	GCCGGTAGAGATTTGACTGAC	

MS315	ADH1 ORF Fw	TAGGTTCTTTGGCTGTTCAATACG	
MS316	ADH1 ORF Rev	CGGAAACGGAAACGTTGATGACACCG	
MS2151	CTT1 ORF Fw	TGCCACGCTTGTAAGATC	
MS2152	CTT1 ORF Rev	CAAGGAACTCCCAAGCATT	
MS1898	CUP1 ORF Fw	GAAGGTCATGAGTGCCAATG	
MS1899	CUP1 ORF Rev	CATTTGTCGTCGCTGTTACAC	
MS2076	CYC1 ORF Fw	CTCTGGTCAAGCTGAAGG	
MS2077	CYC1 ORF Rev	CACCAAAGGCCATCTTGG	
MS701	GAL1 ORF Fw	GGGCCCCAAATGGCAACATAG	
MS702	GAL1 ORF Rev	GCCCAATGCTGGTTTAGAGAC	
MS737	GAL7 ORF Fw	CTCTTTGAGGCTCACCTAAC	
MS738	GAL7 ORF Rev	GCTCCTTTGAATGCGACTG	
MS1043	GAL11 ORF Fw	GAAAGTGGCACCTATTCC	
MS1044	GAL11 ORF Rev	CTTCGCAGCTTCCATATC	
MS2002	HSP12 ORF Fw	AGCTTTGAAGCCAGACTCTCA	
MS406	HSP12 ORF Rev	CAGAGTCGTGGACACCTTGGGA	
MS903	HXK1 ORF Fw	TGTAGCAATGGGACGACATC	
MS904	HXK1 ORF Rev	AACACCAAGGACACCTTACC	
MS2666	KSH1 ORF Fw	TTCGTTCTCTTCTGCAAGTG	
MS2667	KSH1 ORF Rev	GACTGGCCCTTTCACCAA	
MS2600	OPI3 ORF Fw	TGGGTGTGGCTCTCTTTG	
MS2601	OPI3 ORF Rev	GACAAAGTGAACCCTGG	
MS2702	PIM1 ORF Fw	AGGCGTCTATCCACTTGC	
MS2703	PIM1 ORF Rev	CTCAACCCACCGATACGT	
MS839	PYK1 ORF Fw	CCAAGGGTCCAGAAATCAG	
MS840	PYK1 ORF Rev	CTTGTCATCGGTGGTGAAG	
MS2238	RPL30 ORF Fw	TTGCCGCTAACACTCCAG	
MS2239	RPL30 ORF Rev	CAGAGTCACCAGCTTCCA	
MS2230	RPS13 ORF Fw	GGTTTGGCTCCAGAAATCC	
MS2231	RPS13 ORF Rev	GGTGGTAAGACAGCAACAG	

MS2692	RTT10 ORF Fw	CGCGCTTGGGAAATTACC	
MS2693	RTT10 ORF Rev	CCAACACCTCCGATCAGT	
MS1902	SOD1 ORF Fw	ACCTCCGTTGTAGGCAGAAG	
MS1903	SOD1 ORF Rev	CGGCATTACCAGTCTTCAA	
MS591	STE3 ORF Fw	CGTCAAGGACCTTGTGATTAGC	
MS590	STE3 ORF Rev	GCGCCACAAATGACCATATAAGC	
MS1237	18S RNA Fw	CCTGAGAAACGGCTACCACATC	
MS1238	18S RNA Rev	ATTGTCACTACCTCCCTGAATTAGGA	

Supplemental Table S4

List of non-RP and RP genes used for fig. S3A

	non-RP genes	RP genes		non-RP genes	RP genes
1	YAL040C	YBL087C	14	YKL189W	YKL180W
2	YBL029W	YBR181C	15	YLR023C	YKR057W
3	YBL042C	YBR189W	16	YLR354C	YKR094C
4	YBR114W	YDR012W	17	YML008C	YLR029C
5	YDR085C	YDR064W	18	YMR017W	YLR287C-A
6	YEL036C	YDR500C	19	YMR065W	YLR441C
7	YER045C	YER056C-A	20	YMR205C	YML026C
8	YER056C	YER102W	21	YOR274W	YMR194W
9	YER132C	YFL034C-A	22	YOR303W	YMR230W
10	YHR007C	YGL147C	23	YPL048W	YOL120C
11	YHR162W	YGR085C	24	YPL137C	YOR167C
12	YIL099W	YHL033C	25		YPL198W
13	YJR104C	YJR094W-A			

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