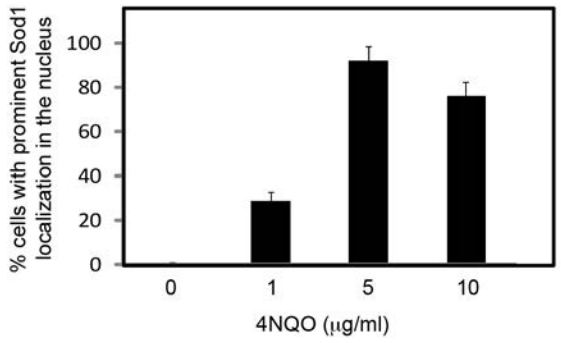
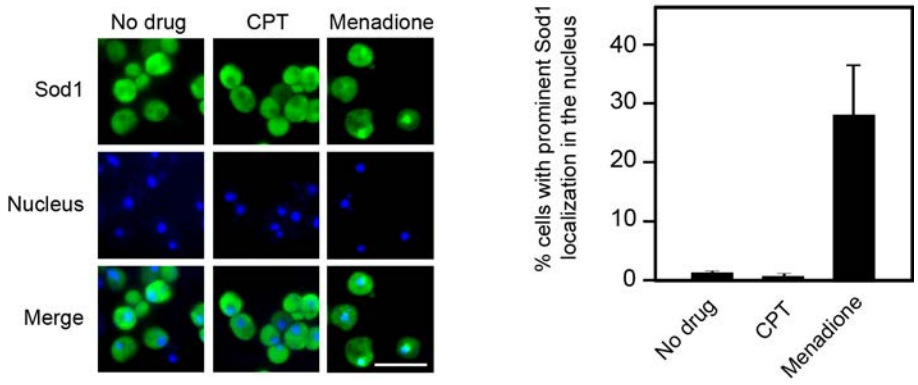
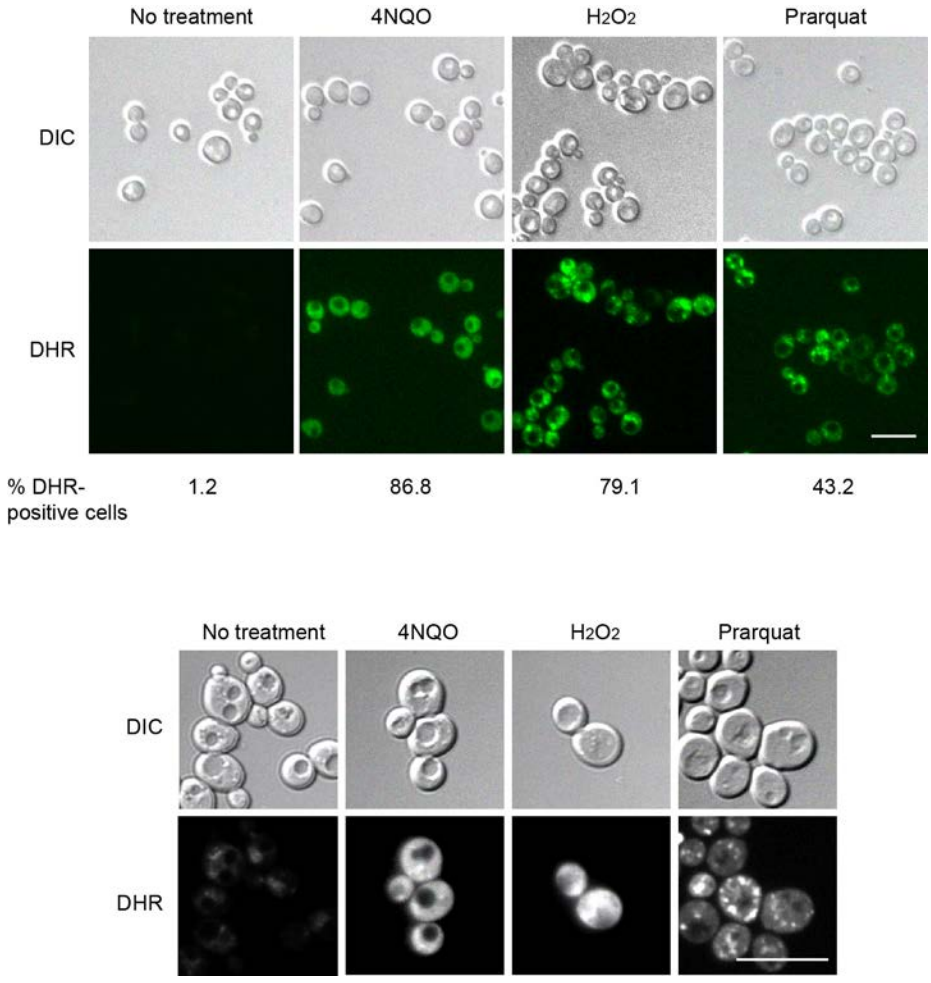


Supplementary Figure 1. ROS induces rapid Sod1 nuclear localization in a dosage-dependent manner. WT yeast cells (SZy1051) were treated with 4NQO at different concentrations for 30 min and analyzed for Sod1-Myc9 localization by IF. The nucleus was stained by DAPI. Shown is the quantification of yeast cells with prominent Sod1 nuclear localization. Error bars indicate ± SD of triplicates and at least 100 cells were counted per replicate.

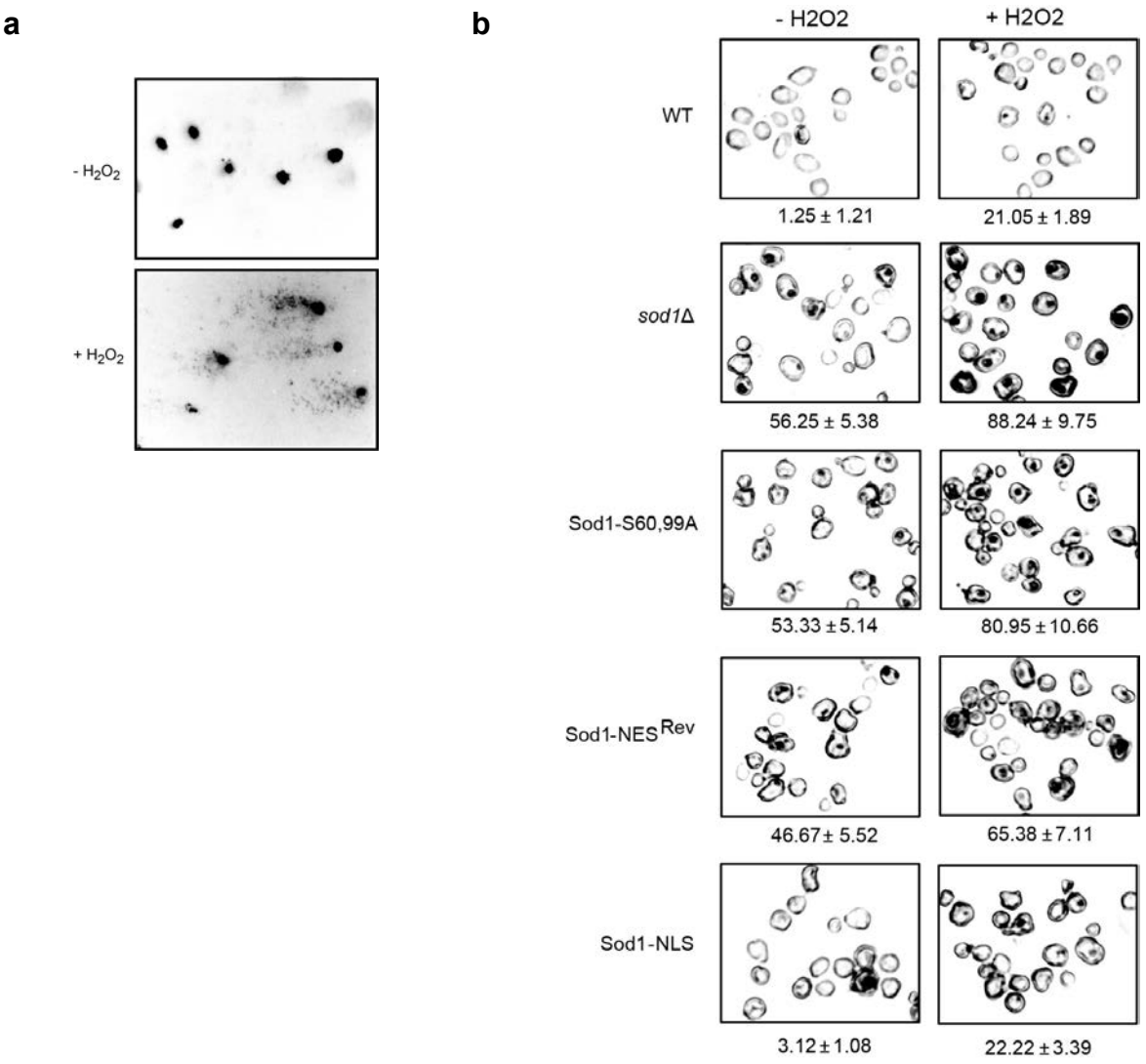


Supplementary Figure 2. Menadione but not Camptothecan (CPT) causes Sod1 nuclear localization

WT yeast cells (SZy1051) were treated with oxidative chemical menadione (0.5 mM) or DNA damaging drug camptothecin (CPT, 20 μM) for 1 hr. Sod1-Myc9 localization was analyzed by IF. Scale bar, 10μm (left panel). Error bars indicate ± SD of triplicates and at least 100 cells were counted per replicate (right panel).



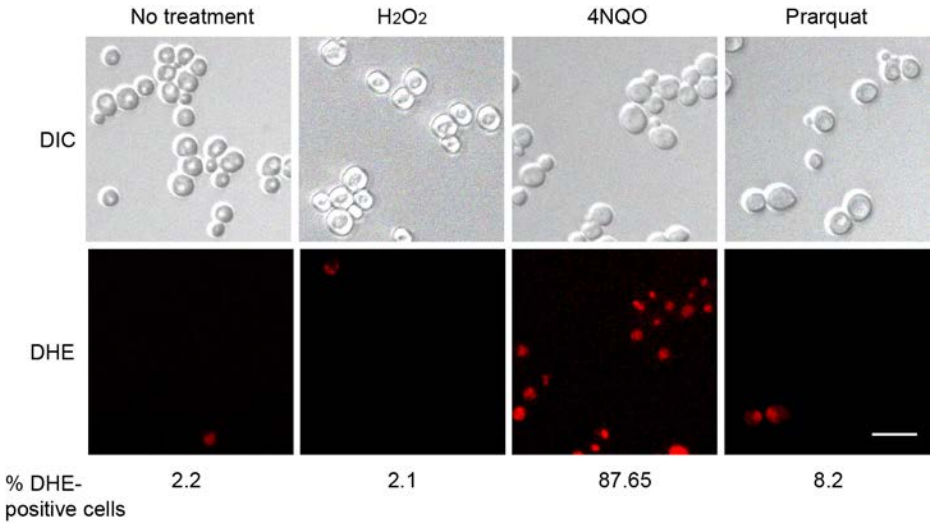
Supplementary Figure 3. 4NQO, H_2O_2 and paraquat treatment causes significant increase in cellular ROS level in yeast. WT yeast cells were treated without or with 5 μg/ml 4NQO, 0.4 mM H_2O_2, or 1 mM Paraquat for 20 min, and stained with dihydrorhodamine (DHR) and examined by fluorescence microscopy. Lower panel are enlarged images to show the details of DHR staining. Scale bar, 10μm.



Supplementary Figure 4. H_2O_2 treatment leads to genomic DNA damage as determined by Comet and TUNEL assays

(a) H_2O_2 burst causes genomic DNA damage as determined by Comet assay. WT yeast cells (SZy1051) were treated without or with H_2O_2 for 20 min and assayed for genomic DNA damage by Comet assay.

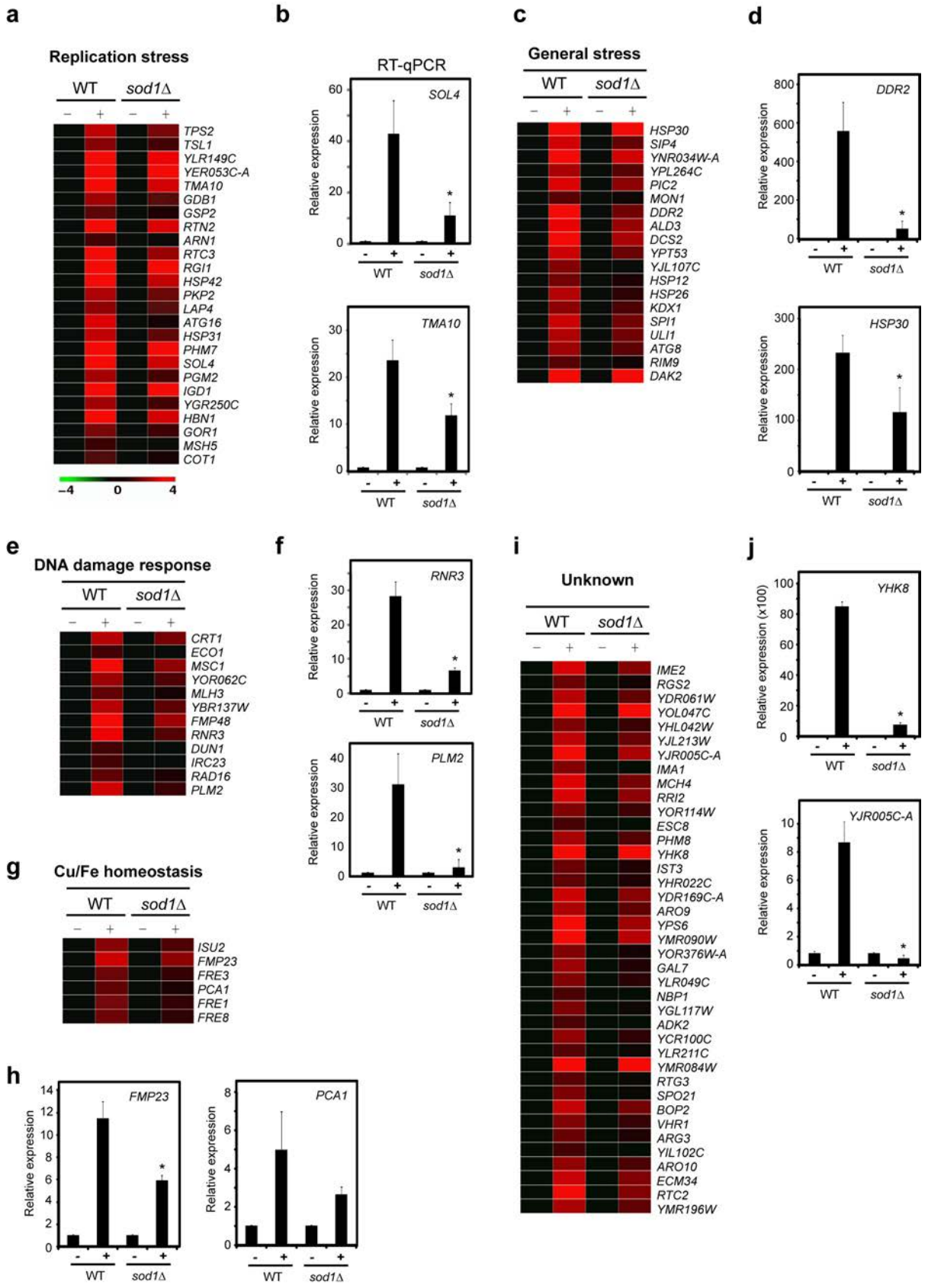
(b) Nuclear, but not cytoplasmic Sod1 plays a critical role against oxidative DNA damage. WT (SZy1051), *sod1Δ* (SZy1050), $Sod1^{S60,99A}$ (SZy2501), $Sod1^{NLS}$ (SZy2489) and $Sod1^{NES}$ (SZy2499) cells were treated without or with 0.4 mM H_2O_2 for 20 min and assayed for genomic DNA damage by TUNEL assay. The percentage of TUNEL-positive cells is used to qualitatively describe genomic DNA damage. Data represent mean ± SD from triplicates and at least 100 cells were counted.



Supplementary Figure 5. 4NQO and Paraquat, but not H_2O_2 increase cellular superoxide

WT yeast cells were treated with 0.4 mM H_2O_2, 5 µg/ml 4NQO or 1 mM Paraquat for 20 min. Cellular superoxide was stained with Dihydroethidium (DHE) and analyzed by fluorescence microscopy (n >100). Scale bar, 10µm.

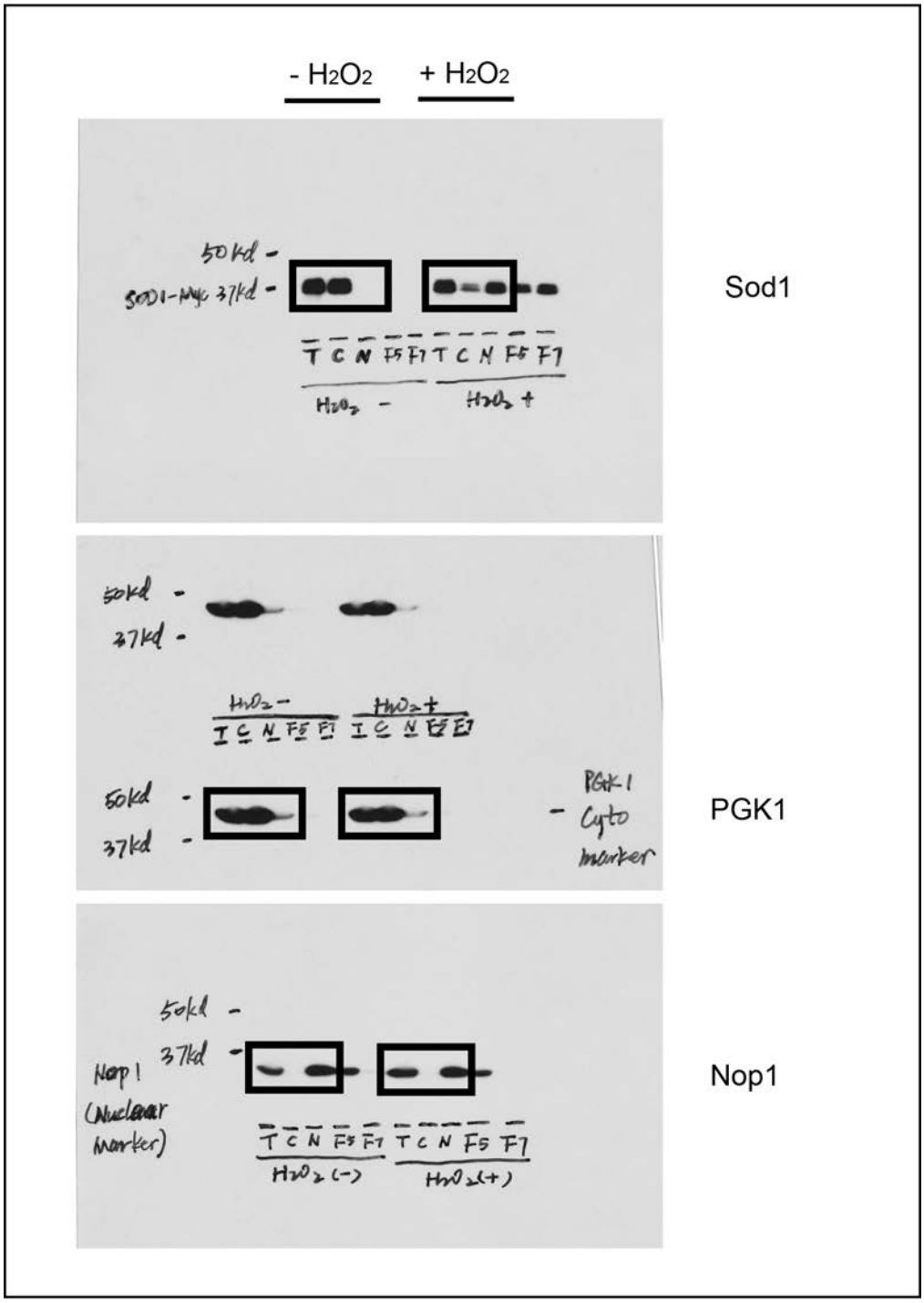
Note: oxidized product of DHE by superoxide subsequently binds to DNA and generates fluorescent signal in the presence of DNA (Free Radic Biol Med.34:1359). Thus the site of fluorescence signal is not the subcellular site where DHE oxidation occurs.



Supplementary Figure 6. Sod1 is required for the induction of oxidative response (OR) genes. WT or *sod1*Δ cells were treated without or with H_2O_2 for 20 min and analyzed for global gene

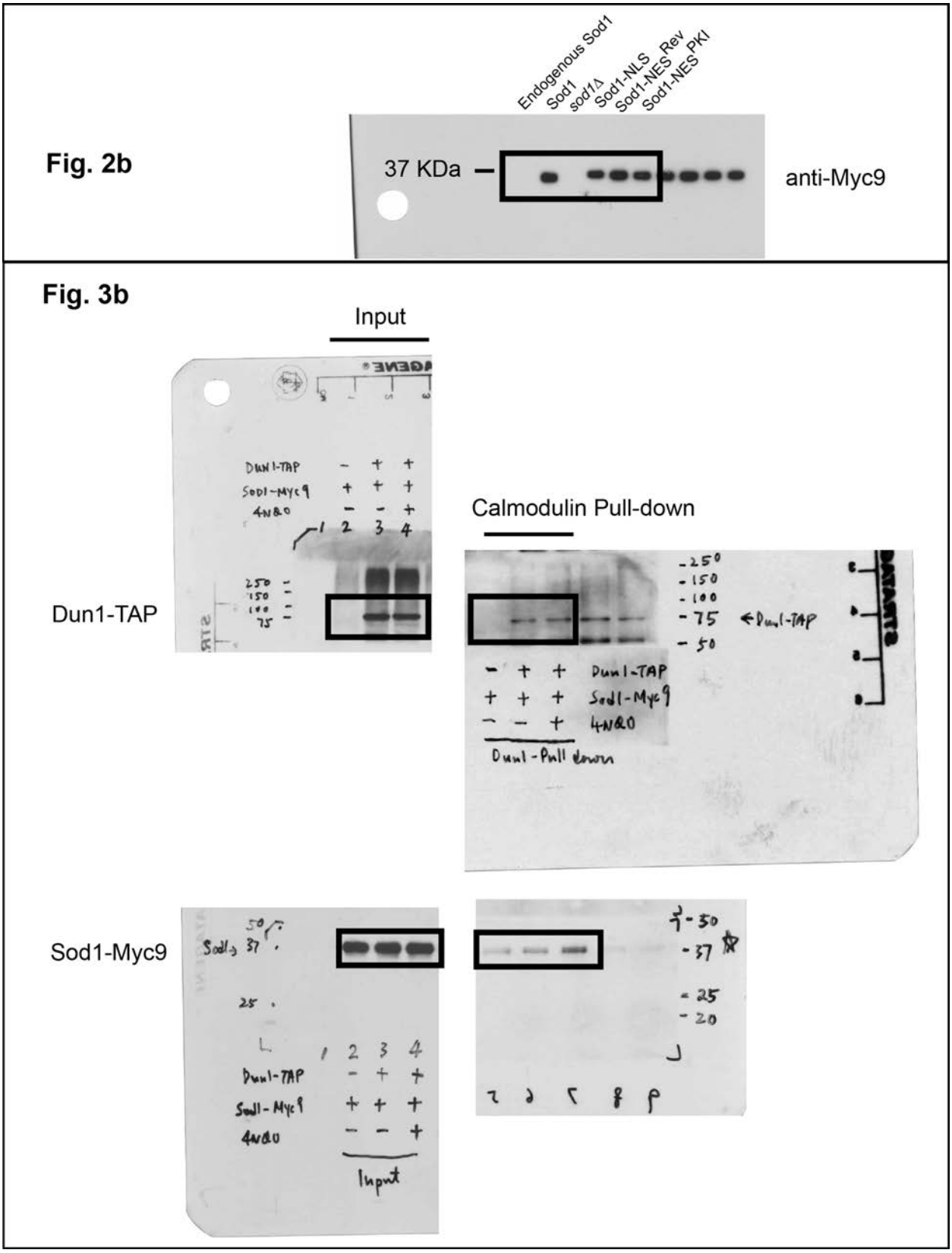
expression profile by microarray. 123 genes were identified whose induction by H_2O_2 was reduced by the *sod1*Δ mutation by more than 50%. They were classified into different categories. **(a), (c), (e), (g)** and **(i)** are the heat maps for genes in the category of replication stress, general stress, DNA damage response, Cu/Fe homeostasis and unknown/others. **(b), (d), (f), (h)** and **(j)** RT-qPCR verification of representative genes in different functional categories. *ACT1* expression was used as a reference gene to normalize that of target genes. Error bars indicate ± SD from triplicates of two independent experiments. * $p < 0.05$, Student's *t*-test.

Fig. 1f



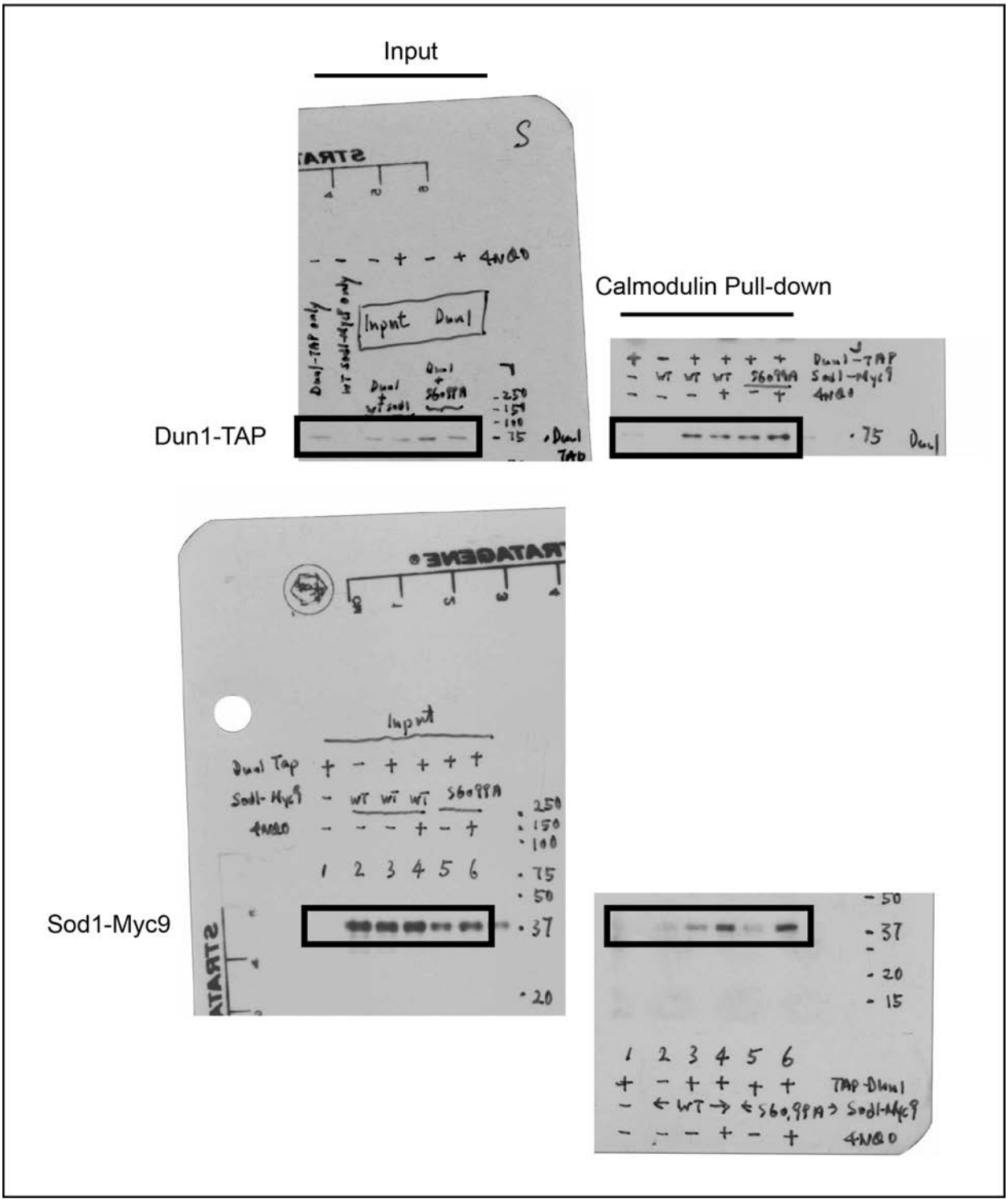
Supplementary Figure 7. Full scans of important original western blots used in this study

Panels corresponding to the figures in the paper are indicated.

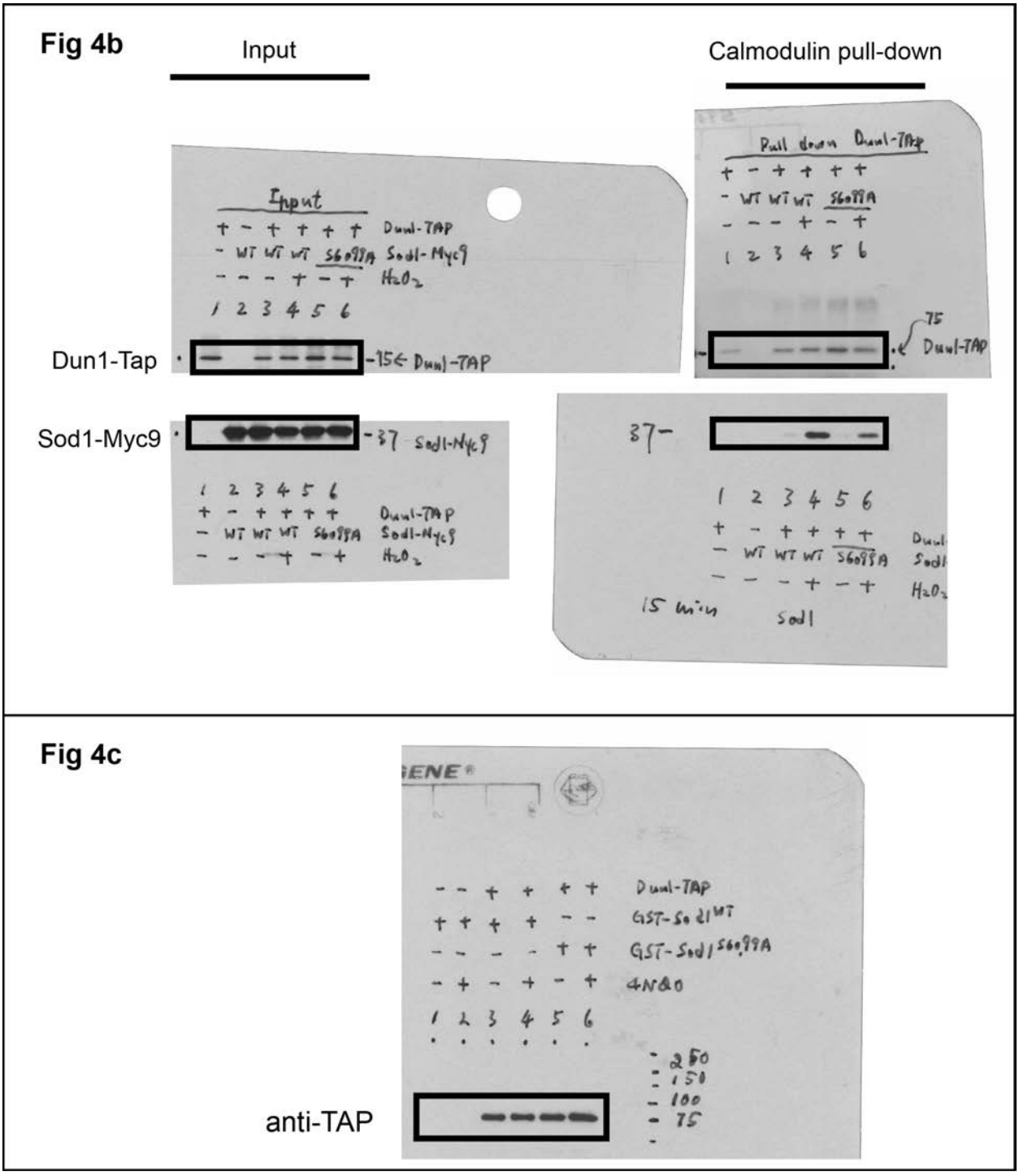


Supplementary Figure 7. Full scans of important original western blots used in this study continued. Panels corresponding to the figures in the paper are indicated.

Fig. 4a



Supplementary Figure 7. Full scans of important original western blots used in this study continued. Panels corresponding to the figures in the paper are indicated.



Supplementary Figure 7. Full scans of important original western blots used in this study continued. Panels corresponding to the figures in the paper are indicated.

Supplementary Table 1. Yeast Strains

Strains	Genotype
SZy1050	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415*
SZy1051	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415(SOD1-MYC9)*
SZy 2489	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415(SOD1-NLS-MYC9)*
SZy 2490	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415(SOD1-NES^{REV}-MYC9)*
SZy 2491	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415(SOD1-NES^{PKI}-MYC9)*
SZy 2492	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 pRS415(SOD1-MYC9)*
SZy 2493	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 dun1Δ::KanMX pRS415(SOD1-MYC9)*
SZy 2494	*MATa leu2 ura3 trp1 his3 mec1-1 pRS415(SOD1-MYC9)*
SZy 2495	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415(SOD1-MYC9) pRS423*
SZy 2496	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415 pRS423(DUN1-TAP)*
SZy 2497	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415(SOD1-MYC9) pRS423(DUN1-TAP)*
SZy 2498	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415(SOD1-S60,99A-MYC9) pRS423(DUN1-TAP)*
SZy 2499	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415(SOD1-S60A-MYC9)*
SZy 2500	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415(SOD1-S99A-MYC9)*
SZy 2501	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 sod1Δ::KanMX pRS415(SOD1-S60,99A-MYC9)*
SZy 2502	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 glr1Δ::KanMX pRS415(SOD1-MYC9)*
SZy 2503	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 ctt1Δ::KanMX pRS415(SOD1-MYC9)*
SZy 2504	*MATa hisΔ1 leu2Δ0 met15Δ0 ura3Δ0 yap1Δ::KanMX pRS415(SOD1-MYC9)*

Supplementary Table 2. Primers for Plasmid Construction and Mutagenesis

Name	Construct	Sequence
SZ2196	SOD1-NLS (forward)	TCATTGGTCTAACCAACCCTAAGAAGAAGAGGAAGGTTTCCGGTTCTGCTG CTAG
SZ2197	SOD1-NLS (reverse)	CTAGCAGCAGAACCGGAAACCTTCCTCTTCTTCTTAGGGTTGGTTAGACCA ATGA
SZ2274	SOD1-NES^{PKI} (forward)	CATTGGTCTAACCAACTTAGCCTTGAAATTAGCAGGTCTTGATATC AACTCCGGTTCTGCTGCTAG
SZ2275	SOD1-NES^{PKI} (reverse)	CTAGCAGCAGAACCGGAGTT GAT ATC AAG ACC TGC TAA TTT CAA GGC TAA GTTGGTTAGACCAATG
SZ2276	SOD1-NES^{REV} (forward)	CATTGGTCTAACCAACCTT CAG CTA CCA CCG CTT GAG AGA CTT ACT CTTTCCGGTTCTGCTGCTAG
Sz2277	SOD1-NES^{REV} (reverse)	CTAGCAGCAGAACCGGAAAG AGT AAG TCT CTC AAG CGG TGG TAG CTG AAG GTTGGTTAGACCAATG
SZ2317	GST-SOD1 (forward)	CCGGAATTCATGGTTCAAGCAGTCGCAGT
SZ2318	GST-SOD1 (reverse)	CCGCTCGAGGTTGGTTAGACCAATGACACCAC
SZ2155	SOD1 ^{S60A} (forward)	CACCAATGGTTGTGTCGCTGCTGGTCCTCACTT
SZ2156	SOD1 ^{S60A} (reverse)	AAGTGAGGACCAGCAGCGACACAACCATTGGTG
Sz2161	SOD1 ^{S99A} (forward)	GTGTGGCCAAGGGCGCCTTCAAGGACTCT
SZ2162	SOD1 ^{S99A} (reverse)	AGAGTCCTTGAAGGCGCCCTTGGCCACAC

Supplementary Table 3. Primers used for RT-qPCR and ChIP assay

Name	Target gene	Sequence
SZ2429	*ACT1 (forward)*	GTC TGG ATT GGT GGT TCT ATC
SZ2430	*ACT1 (reverse)*	GGA CCA CTT TCG TCG TAT TC
SZ2431	*DDR2 (forward)*	ATT TCT GCC ATC TCT GTC TTC
SZ2432	*DDR2 (reverse)*	ACT CCG GCG TTT AGT AGT
SZ2433	*FMP23 (forward)*	ATC CAT CGG AGA CAG GAT AG
SZ2434	*FMP23 (reverse)*	GAA GGA GTG TCC TCC ATT TAG
SZ2435	*GRE2 (forward)*	CCG GAA CTA TTT GGT GGA TAC
SZ2436	*GRE2 (reverse)*	CCT CCG ATA CGA TTA GTC TTT G
SZ2437	*HMX1 (forward)*	CCG CTA CTA CAG CAG TTT ATC
SZ2438	*HMX1 (reverse)*	AAG TAC AGA ACG TGA CAG TAA G
SZ2439	*HSP30 (forward)*	CTA GAG GGT TCA ATG CAC TTA T
SZ2440	*HSP30 (reverse)*	CTC ACC GTC TGG TTG AAT AC
SZ2441	*PCA1 (forward)*	ACC CAT GGA GAC AAA GAA AG
SZ2442	*PCA1 (reverse)*	CTC GAA GAG TGT CCA GAA ATA G
SZ2443	*PLM2 (forward)*	CGG AGG ATG AGT TGT GTT TAT
SZ2444	*PLM2 (reverse)*	CTG TTC TGT ACG AGG TGA ATG
SZ2445	*RNR3 (forward)*	GAA CAG AGT TAT CGA CCG TAA T
SZ2446	*RNR3 (reverse)*	CTG GAC ACC AAG AGC AAT AG
SZ2447	*SOL4 (forward)*	AGT GTG TGC TTT CTC GTT AG
SZ2448	*SOL4 (reverse)*	CAC ACT AGG TAG TTC GCT ATT T
SZ2449	*STF2 (forward)*	ACT ACG GTG AAT CTC CAA ATC
SZ2450	*STF2 (reverse)*	TGA GCC TCT TCT ATC TTT CTT G
SZ2451	*TMA10 (reverse)*	CCC TTC TGG TCT TGT TGA AG
SZ2452	*TMA10 (forward)*	AGA GGA GGC TAT GGG AAA G
SZ2453	*TSA2 (forward)*	CCA ACC TTC CCA GAA AAG AC
SZ2454	*TSA2 (reverse)*	CGC CAT AGT CTC TGG ATA AG
SZ2455	*YHK8 (forward)*	GAT ACT CTC GGC TCC TAC TT
SZ2456	*YHK8 (reverse)*	GGA GTC TTG ACG CCA TTA TT
SZ2457	*YJR005C-A (forward)*	CTA GAA GCT CAA GAA GCT CAG
SZ2458	*YJR005C-A (reverse)*	CGG CTA GTA ATT GGT CTC TTT
SZ2459	*YML131W (forward)*	GGT GAG AAT ACC GTG GAT TAC
SZ2460	*YML131W (reverse)*	TAG CAC CAC AGG CTA TCA
SZ2461	*RNR3 promoter (forward)*	ACG CCA CAT CCT CAA ATG
SZ2462	*RNR3 promoter (reverse)*	CTG TGG AAC GGA TGT TGT T
SZ2463	*GRE2 promoter (forward)*	AGT CTA TCT CTG TAG CGT TGA
SZ2464	*GRE2 promoter (reverse)*	CAA TGT GTT GGG CAA TGA AC
SZ631	*ACT1 promoter (forward)*	CGTGAT AAG TGA TAG TGA TAT TC
SZ302	*ACT1 promoter (reverse)*	CAT GAT ACC TTG GTG TCT TG