Supplemental Table S1: Genes differentially expressed more than two-fold between WT and *htbK123R* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YLR410W-B		-1.79	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes
YLR346C		-1.71	Putative protein of unknown function found in mitochondria; expression is regulated by transcription factors involved in pleiotropic drug resistance, Pdr1p and Yrr1p; YLR346C is not an essential gene
YER035W	*EDC2*	-1.65	RNA-binding protein, activates mRNA decapping directly by binding to the mRNA substrate and enhancing the activity of the decapping proteins Dcp1p and Dcp2p; has a role in translation during heat stress
YER053C-A		-1.63	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the endoplasmic reticulum
YDR406W	*PDR15*	-1.52	Plasma membrane ATP binding cassette (ABC) transporter, multidrug transporter and general stress response factor implicated in cellular detoxification; regulated by Pdr1p, Pdr3p and Pdr8p; promoter contains a PDR responsive element
YOR289W		-1.48	Putative protein of unknown function; transcription induced by the unfolded protein response; green fluorescent protein (GFP)-fusion protein localizes to both the cytoplasm and the nucleus
YNL160W	*YGP1*	-1.43	Cell wall-related secretory glycoprotein; induced by nutrient deprivation-associated growth arrest and upon entry into stationary phase; may be involved in adaptation prior to stationary phase entry; has similarity to Sps100p
YLR030W		-1.42	Putative protein of unknown function
YHR094C	*HXT1,HOR4*	-1.41	Low-affinity glucose transporter of the major facilitator superfamily, expression is induced by Hxk2p in the presence of glucose and repressed by Rgt1p when glucose is limiting
YAL061W	*BDH2*	-1.40	Putative medium-chain alcohol dehydrogenase with similarity to BDH1; transcription induced by constitutively active PDR1 and PDR3
YMR013W-A		-1.39	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; completely overlaps the characterized snoRNA gene snR73
YDR074W	*TPS2,PFK3,HOG2*	-1.38	Phosphatase subunit of the trehalose-6-phosphate synthase/phosphatase complex, which synthesizes the storage carbohydrate trehalose; expression is induced by stress conditions and repressed by the Ras-cAMP pathway
YIL045W	*PIG2*	-1.31	Putative type-1 protein phosphatase targeting subunit that tethers Glc7p type-1 protein phosphatase to Gsy2p glycogen synthase

Supplemental Table S1: Genes differentially expressed more than two-fold between WT and *htbK123R* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YDR058C	*TGL2*	-1.31	Triacylglycerol lipase that is localized to the mitochondria; has lipolytic activity towards triacylglycerols and diacylglycerols when expressed in E. coli
YML100W	*TSL1*	-1.28	Large subunit of trehalose 6-phosphate synthase (Tps1p)/ phosphatase (Tps2p) complex, which converts uridine-5'-diphosphoglucose and glucose 6-phosphate to trehalose, homologous to Tps3p and may share function
YJL164C	*TPK1,SRA3,PKA1*	-1.24	cAMP-dependent protein kinase catalytic subunit; promotes vegetative growth in response to nutrients via the Ras-cAMP signaling pathway; inhibited by regulatory subunit Bcy1p in the absence of cAMP; partially redundant with Tpk2p and Tpk3p
YER037W	*PHM8*	-1.23	Protein of unknown function, expression is induced by low phosphate levels and by inactivation of Pho85p
YOL151W	*GRE2*	-1.19	3-methylbutanal reductase and NADPH-dependent methylglyoxal reductase (D-lactaldehyde dehydrogenase); stress induced (osmotic, ionic, oxidative, heat shock and heavy metals); regulated by the HOG pathway
YMR291W		-1.18	Putative kinase of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus; YMR291W is not an essential gene
YPR107C	*YTH1*	-1.18	Essential RNA-binding component of cleavage and polyadenylation factor, contains five zinc fingers; required for pre-mRNA 3'-end processing and polyadenylation
YEL020W-A	*TIM9*	-1.17	Essential protein of the mitochondrial intermembrane space, forms a complex with Tim10p (TIM10 complex) that delivers hydrophobic proteins to the TIM22 complex for insertion into the inner membrane
YLR453C	*RIF2*	-1.16	Protein that binds to the Rap1p C-terminus and acts synergistically with Rif1p to help control telomere length and establish telomeric silencing; deletion results in telomere elongation
YGL104C	*VPS73*	-1.16	Mitochondrial protein; mutation affects vacuolar protein sorting; putative transporter; member of the sugar porter family
YBR177C	*EHT1*	-1.14	Acyl-coenzymeA:ethanol O-acyltransferase that plays a minor role in medium-chain fatty acid ethyl ester biosynthesis; possesses short-chain esterase activity; localizes to lipid particles and the mitochondrial outer membrane
YHR037W	*PUT2*	-1.13	Delta-1-pyrroline-5-carboxylate dehydrogenase, nuclear-encoded mitochondrial protein involved in utilization of proline as sole nitrogen source; deficiency of the human homolog causes HPII, an autosomal recessive inborn error of metabolism

Supplemental Table S1: Genes differentially expressed more than two-fold between WT and *htbK123R* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YIL077C		-1.11	Putative protein of unknown function; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies; deletion confers sensitivity to 4-(N-(S-glutathionylacetyl)amino) phenylarsenoxide (GSAO)
YPR036W-A		-1.10	Protein of unknown function; transcription is regulated by Pdr1p
YOR273C	*TPO4*	-1.09	Polyamine transport protein, recognizes spermine, putrescine, and spermidine; localizes to the plasma membrane; member of the major facilitator superfamily
YDL115C	*IWR1*	-1.08	Protein involved in transcription from polymerase II promoters; interacts with with most of the polymerase II subunits; nucleo-cytoplasmic shuttling protein; deletion causes hypersensitivity to the K1 killer toxin
YDR288W	*NSE3*	-1.08	Essential subunit of the Mms21-Smc5-Smc6 complex; protein of unknown function; required for DNA repair and growth
YOR173W	*DCS2*	-1.08	Non-essential, stress induced regulatory protein containing a HIT (histidine triad) motif; modulates m7G-oligoribonucleotide metabolism; inhibits Dcs1p; regulated by Msn2p, Msn4p, and the Ras-cAMP-cAPK signaling pathway, similar to Dcs1p.
YGR017W		-1.08	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to both the nucleus and the cytoplasm
YDR383C	*NKP1*	-1.08	Non-essential kinetochore protein, subunit of the Ctf19 central kinetochore complex (Ctf19p-Mcm21p-Okp1p-Mcm22p-Mcm16p-Ctf3p-Chl4p-Mcm19p-Nkp1p-Nkp2p-Ame1p-Mtw1p)
YDL022W	*GPD1,OSR5, OSG1,HOR1, DAR1*	-1.05	NAD-dependent glycerol-3-phosphate dehydrogenase, key enzyme of glycerol synthesis, essential for growth under osmotic stress; expression regulated by high-osmolarity glycerol response pathway; homolog of Gpd2p
YBR149W	*ARA1*	-1.05	NADP+ dependent arabinose dehydrogenase, involved in carbohydrate metabolism; purified as homodimer; naturally occurs with a N-terminus degradation product
YOR153W	*PDR5,STS1, YDR1,LEM1*	-1.05	Plasma membrane ATP-binding cassette (ABC) transporter, multidrug transporter actively regulated by Pdr1p; also involved in steroid transport, cation resistance, and cellular detoxification during exponential growth
YJR059W	*PTK2,STK2*	-1.04	Putative serine/threonine protein kinase involved in regulation of ion transport across plasma membrane; enhances spermine uptake
YGL037C	*PNC1*	-1.03	Nicotinamidase that converts nicotinamide to nicotinic acid as part of the NAD(+) salvage pathway, required for life span extension by calorie restriction; PNC1 expression responds to all known stimuli that extend replicative life span

Supplemental Table S1: Genes differentially expressed more than two-fold between WT and *htbK123R* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YGR194C	*XKS1*	-1.02	Xylulokinase, converts D-xylulose and ATP to xylulose 5-phosphate and ADP; rate limiting step in fermentation of xylulose; required for xylose fermentation by recombinant S. cerevisiae strains
YOR036W	*PEP12,VPT13, VPS6,VPL6*	-1.01	Target membrane receptor (t-SNARE) for vesicular intermediates traveling between the Golgi apparatus and the vacuole; controls entry of biosynthetic, endocytic, and retrograde traffic into the prevacuolar compartment; syntaxin
YNR032C-A	*HUB1*	-1.01	Ubiquitin-like protein modifier, may function in modification of Sph1p and Hbt1p, functionally complemented by the human or S. pombe ortholog; mechanism of Hub1p adduct formation not yet clear
YBR093C	*PHO5, phoE*	1.00	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
YML116W-A		1.01	Putative protein of unknown function
YLR349W		1.02	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; overlaps the verified ORF DIC1/YLR348C
YPR143W	*RRP15*	1.04	Nucleolar protein, constituent of pre-60S ribosomal particles; required for proper processing of the 27S pre-rRNA at the A3 and B1 sites to yield mature 5.8S and 25S rRNAs
YPL250C	*ICY2*	1.04	Protein of unknown function; mobilized into polysomes upon a shift from a fermentable to nonfermentable carbon source; potential Cdc28p substrate
YJL037W	*IRC18*	1.04	Putative protein of unknown function; expression induced in respiratory-deficient cells and in carbon-limited chemostat cultures; similar to adjacent ORF, YJL038C; null mutant displays increased levels of spontaneous Rad52p foci
YNR065C	*YSN1*	1.05	Protein of unknown function; protein-protein interactions suggest a possible role in actin patch formation; YNR065C is not an essential gene
YIL099W	*SGA1*	1.05	Intracellular sporulation-specific glucoamylase involved in glycogen degradation; induced during starvation of a/a diploids late in sporulation, but dispensable for sporulation
YLR176C	*RFX1,CRT1*	1.05	Major transcriptional repressor of DNA-damage-regulated genes, recruits repressors Tup1p and Cyc8p to their promoters; involved in DNA damage and replication checkpoint pathway; similar to a family of mammalian DNA binding RFX1-4 proteins
YCL027W	*FUS1*	1.06	Membrane protein localized to the shmoo tip, required for cell fusion; expression regulated by mating pheromone; proposed to coordinate signaling, fusion, and polarization events required for fusion; potential Cdc28p substrate

Supplemental Table S1: Genes differentially expressed more than two-fold between WT and *htbK123R* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YAR050W	*FLO1,FLO4,FLO2*	1.06	Lectin-like protein involved in flocculation, cell wall protein that binds to mannose chains on the surface of other cells, confers floc-forming ability that is chymotrypsin sensitive and heat resistant; similar to Flo5p
YLR237W	*THI7,THI10*	1.06	Plasma membrane transporter responsible for the uptake of thiamine, member of the major facilitator superfamily of transporters; mutation of human ortholog causes thiamine-responsive megaloblastic anemia
YER119C-A		1.06	Dubious open reading frame, not conserved in closely related Saccharomyces species; deletion mutation blocks replication of Brome mosaic virus in S. cerevisiae, but this is likely due to effects on the overlapping gene SCS2
YLR374C		1.06	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the uncharacterized ORF STP3/ YLR375W
YLR307W	*CDA1*	1.07	Chitin deacetylase, together with Cda2p involved in the biosynthesis ascospore wall component, chitosan; required for proper rigidity of the ascospore wall
YAL062W	*GDH3,FUN51*	1.07	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
YNR064C		1.09	Epoxide hydrolase, member of the alpha/beta hydrolase fold family; may have a role in detoxification of epoxides
YJL038C	*LOH1,OSW4*	1.09	Protein of unknown function with proposed roles in maintenance of genome integrity and also in spore wall assembly; induced during sporulation; repressed during vegetative growth by Sum1p and Hst1p; sequence similar to IRC1
YBR296C	*PHO89,ITN1*	1.11	Na+/Pi cotransporter, active in early growth phase; similar to phosphate transporters of Neurospora crassa; transcription regulated by inorganic phosphate concentrations and Pho4p
YGL126W	*SCS3,FIT2B*	1.13	Protein required for inositol prototrophy, identified as an ortholog of the FIT family of proteins involved in triglyceride droplet biosynthesis; disputed role in the synthesis of inositol phospholipids from inositol
YKL216W	*URA1*	1.13	Dihydroorotate dehydrogenase, catalyzes the fourth enzymatic step in the de novo biosynthesis of pyrimidines, converting dihydroorotic acid into orotic acid
YLR363W-A		1.13	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the nucleus
YPL171C	*OYE3,ZRG6*	1.14	Conserved NADPH oxidoreductase containing flavin mononucleotide (FMN), homologous to Oye2p with slight differences in ligand binding and catalytic properties; expression induced in cells treated with the mycotoxin patulin

Supplemental Table S1: Genes differentially expressed more than two-fold between WT and *htbK123R* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YDR524C-B		1.14	Putative protein of unknown function
YGR032W	*GSC2,FKS2*	1.14	Catalytic subunit of 1,3-beta-glucan synthase, involved in formation of the inner layer of the spore wall; activity positively regulated by Rho1p and negatively by Smk1p; has similarity to an alternate catalytic subunit, Fks1p (Gsc1p)
YLL005C	*SPO75*	1.15	Meiosis-specific protein of unknown function, required for spore wall formation during sporulation; dispensable for both nuclear divisions during meiosis
YNL113W	*RPC19*	1.15	RNA polymerase subunit AC19, common to RNA polymerases I and III
YDL218W		1.17	Putative protein of unknown function; YDL218W transcription is regulated by Azf1p and induced by starvation and aerobic conditions; expression also induced in cells treated with the mycotoxin patulin
YMR011W	*HXT2*	1.17	High-affinity glucose transporter of the major facilitator superfamily, expression is induced by low levels of glucose and repressed by high levels of glucose
YHR126C	*ANS1*	1.18	Putative protein of unknown function; transcription dependent upon Azf1p
YCL033C	*MXR2,MSRB*	1.19	Methionine-R-sulfoxide reductase, involved in the response to oxidative stress; protects iron-sulfur clusters from oxidative inactivation along with MXR1; involved in the regulation of lifespan
YAL067C	*SEO1*	1.23	Putative permease, member of the allantoate transporter subfamily of the major facilitator superfamily; mutation confers resistance to ethionine sulfoxide
YPR195C		1.23	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data
YJL088W	*ARG3,argF*	1.23	Ornithine carbamoyltransferase (carbamoylphosphate:L-ornithine carbamoyltransferase), catalyzes the sixth step in the biosynthesis of the arginine precursor ornithine
YML058W-A	*HUG1*	1.24	Protein involved in the Mec1p-mediated checkpoint pathway that responds to DNA damage or replication arrest, transcription is induced by DNA damage
YLR437C	*DIF1*	1.25	Protein that regulates the nuclear localization of ribonucleotide reductase Rnr2p and Rnr4p subunits; phosphorylated by Dun1p in response to DNA damage and degraded; N-terminal half has similarity to S. pombe Spd1 protein
YPR015C		1.25	Putative protein of unknown function; overexpression causes a cell cycle delay or arrest

Supplemental Table S1: Genes differentially expressed more than two-fold between WT and *htbK123R* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YPR005C	*HAL1*	1.26	Cytoplasmic protein involved in halotolerance; decreases intracellular Na+ (via Ena1p) and increases intracellular K+ by decreasing efflux; expression repressed by Ssn6p-Tup1p and Sko1p and induced by NaCl, KCl, and sorbitol through Gcn4p
YLR434C		1.26	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the verified ORF TSR2/YLR435W
YMR122C		1.28	Dubious open reading frame unlikely to encode a functional protein, based on available experimental and comparative sequence data
YPL056C		1.30	Putative protein of unknown function; deletion mutant is fluconazole resistant
YMR095C	*SNO1*	1.33	Protein of unconfirmed function, involved in pyridoxine metabolism; expression is induced during stationary phase; forms a putative glutamine amidotransferase complex with Snz1p, with Sno1p serving as the glutaminase
YOR382W	*FIT2*	1.36	Mannoprotein that is incorporated into the cell wall via a glycosylphosphatidylinositol (GPI) anchor, involved in the retention of siderophore-iron in the cell wall
YCL026C-A	*FRM2,YCLX08C*	1.38	Protein of unknown function, involved in the integration of lipid signaling pathways with cellular homeostasis; expression induced in cells treated with the mycotoxin patulin; has similarity to bacterial nitroreductases
YFL011W	*HXT10*	1.38	Putative hexose transporter, expressed at low levels and expression is repressed by glucose
YHR032W-A		1.39	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the dubious ORF YHR032C-A
YDL241W		1.40	Putative protein of unknown function; YDL241W is not an essential gene
YLR307C-A		1.41	Putative protein of unknown function
YML083C		1.42	Putative protein of unknown function; strong increase in transcript abundance during anaerobic growth compared to aerobic growth; cells deleted for YML083C do not exhibit growth defects in anerobic or anaerobic conditions
YMR244W		1.42	Putative protein of unknown function
YDR534C	*FIT1*	1.45	Mannoprotein that is incorporated into the cell wall via a glycosylphosphatidylinositol (GPI) anchor, involved in the retention of siderophore-iron in the cell wall
YCL030C	*HIS4*	1.54	Multifunctional enzyme containing phosphoribosyl-ATP pyrophosphatase, phosphoribosyl-AMP cyclohydrolase, and histidinol dehydrogenase activities; catalyzes the second, third, ninth and tenth steps in histidine biosynthesis

Supplemental Table S1: Genes differentially expressed more than two-fold between WT and *htbK123R* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YNL195C		1.68	Putative protein of unknown function; shares a promoter with YNL194C; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies
YJR150C	*DAN1,CCW13*	1.70	Cell wall mannoprotein with similarity to Tir1p, Tir2p, Tir3p, and Tir4p; expressed under anaerobic conditions, completely repressed during aerobic growth
YLL037W		1.74	Dubious open reading frame unlikely to encode a functional protein; overlaps 3' end of essential PRP19 gene encoding an RNA splicing factor
YOL058W	*ARG1,ARG10*	1.78	Arginosuccinate synthetase, catalyzes the formation of L-argininosuccinate from citrulline and L-aspartate in the arginine biosynthesis pathway; potential Cdc28p substrate
YDL062W		1.80	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps uncharacterized ORF YDL063C; YDL062W is not essential
YNL270C	*ALP1,APL1*	1.95	Arginine transporter; expression is normally very low and it is unclear what conditions would induce significant expression
YJR047C	*ANB1,eIF-5A, TIF51B,HYP1*	1.95	Translation elongation factor eIF-5A, previously thought to function in translation initiation; similar to and functionally redundant with Hyp2p; undergoes an essential hypusination modification; expressed under anaerobic conditions
YLL053C		1.98	Putative protein; in the Sigma 1278B strain background YLL053C is contiguous with AQY2 which encodes an aquaporin
YFR023W	*PES4*	2.08	Poly(A) binding protein, suppressor of DNA polymerase epsilon mutation, similar to Mip6p
YOR072W-A		2.10	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the uncharacterized ORF YOR072W; originally identified by fungal homology and RT-PCR
YEL008W		2.21	Hypothetical protein predicted to be involved in metabolism
YGL170C	*SPO74*	2.26	Component of the meiotic outer plaque of the spindle pole body, involved in modifying the meiotic outer plaque that is required prior to prospore membrane formation
YLL052C	*AQY2*	2.30	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
YCL074W		3.00	Pseudogene: encodes fragment of Ty Pol protein
YHR079C-A	*SAE3*	--*	Meiosis specific protein involved in DMC1-dependent meiotic recombination, forms heterodimer with Mei5p; proposed to be an assembly factor for Dmc1p

*Gene is not expressed in the wild-type cells, but is expressed in the *htbK123R* mutant.
** All GO Annotations were retrieved from *Saccaromyces Cerevisiae* Genome Database (www.yeastgenome.org).

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YGL032C	*AGA2*	-5.54	Adhesion subunit of a-agglutinin of a-cells, C-terminal sequence acts as a ligand for alpha-agglutinin (Sag1p) during agglutination, modified with O-linked oligomannosyl chains, linked to anchorage subunit Aga1p via two disulfide bonds
YGR044C	*RME1,CSP1*	-5.10	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-alpha2 regulator; mediates cell type control of sporulation
YBL016W	*FUS3,DAC2*	-4.71	Mitogen-activated serine/threonine protein kinase involved in mating; phosphoactivated by Ste7p; substrates include Ste12p, Far1p, Bni1p, Sst2p; inhibits invasive growth during mating by phosphorylating Tec1p, promoting its degradation
YDR461W	*MFA1*	-4.66	Mating pheromone a-factor, made by a cells; interacts with alpha cells to induce cell cycle arrest and other responses leading to mating; biogenesis involves C-terminal modification, N-terminal proteolysis, and export; also encoded by MFA2
YFL026W	*STE2*	-4.59	Receptor for alpha-factor pheromone; seven transmembrane-domain GPCR that interacts with both pheromone and a heterotrimeric G protein to initiate the signaling response that leads to mating between haploid a and alpha cells
YHR005C	*GPA1,SCG1, DAC1,CDC70*	-4.57	GTP-binding alpha subunit of the heterotrimeric G protein that couples to pheromone receptors; negatively regulates the mating pathway by sequestering G(beta) gamma and by triggering an adaptive response; activates Vps34p at the endosome
YOR212W	*STE4,HMD2*	-3.88	G protein beta subunit, forms a dimer with Ste18p to activate the mating signaling pathway, forms a heterotrimer with Gpa1p and Ste18p to dampen signaling; may recruit Rho1p to the polarized growth site during mating; contains WD40 repeats
YKL209C	*STE6*	-3.81	Plasma membrane ATP-binding cassette (ABC) transporter required for the export of a-factor, catalyzes ATP hydrolysis coupled to a-factor transport; contains 12 transmembrane domains and two ATP binding domains; expressed only in MATa cells
YIL015W	*BAR1,SST1*	-3.81	Aspartyl protease secreted into the periplasmic space of mating type a cells, helps cells find mating partners, cleaves and inactivates alpha factor allowing cells to recover from alpha-factor-induced cell cycle arrest
YDR261W-B		-3.35	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells			
Systematic name	**Standard Name**	**Log2 (Fold change)**	**Gene Ontology Annotation**
YDR410C	*STE14*	-3.29	Farnesyl cysteine-carboxyl methyltransferase, mediates the carboxyl methylation step during C-terminal CAAX motif processing of a-factor and RAS proteins in the endoplasmic reticulum, localizes to the ER membrane
YDL227C	*HO*	-3.24	Site-specific endonuclease required for gene conversion at the MAT locus (homothallic switching) through the generation of a ds DNA break; expression restricted to mother cells in late G1 as controlled by Swi4p-Swi6p, Swi5p and Ash1p
YOR214C		-3.15	Putative protein of unknown function; YOR214C is not an essential gene
YLR265C	*NEJ1,LIF2*	-2.79	Protein involved in regulation of nonhomologous end joining; interacts with DNA ligase IV components Dnl4p and Lif1p; repressed by MAT heterozygosity; regulates cellular distribution of Lif1p
YDL160C-A		-2.67	Putative protein of unknown function
YBR157C	*ICS2*	-2.60	Protein of unknown function; null mutation does not confer any obvious defects in growth, spore germination, viability, or carbohydrate utilization
YDR379C-A		-2.57	Putative protein of unknown function; identified by homology with other fungi; GFP-fusion protein localized to the mitochondrion
YDR103W	*STE5,NUL3,HMD3*	-2.49	Pheromone-response scaffold protein; binds Ste11p, Ste7p, and Fus3p kinases, forming a MAPK cascade complex that interacts with the plasma membrane and Ste4p-Ste18p; allosteric activator of Fus3p that facilitates Ste7p-mediated activation
YBR293W	*VBA2*	-2.48	Permease of basic amino acids in the vacuolar membrane
YLR410W-B		-2.44	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes
YJL170C	*ASG7*	-2.38	Protein that regulates signaling from a G protein beta subunit Ste4p and its relocalization within the cell; specific to a-cells and induced by alpha-factor
YOL104C	*NDJ1,TAM1*	-2.32	Meiosis-specific telomere protein, required for bouquet formation, effective homolog pairing, ordered cross-over distribution, sister chromatid cohesion at meiotic telomeres, chromosomal segregation and telomere-led rapid prophase movement
YGL146C	*RRT6*	-2.29	Putative protein of unknown function; non-essential gene identified in a screen for mutants with increased levels of rDNA transcription; contains two putative transmembrane spans, but no significant homology to other known proteins

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YOL052C-A	*DDR2*	-2.22	Multistress response protein, expression is activated by a variety of xenobiotic agents and environmental or physiological stresses
YNL333W	*SNZ2*	-2.22	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 SNO2; interacts with Thi11p
YJR086W	*STE18*	-2.16	G protein gamma subunit, forms a dimer with Ste4p to activate the mating signaling pathway, forms a heterotrimer with Gpa1p and Ste4p to dampen signaling; C-terminus is palmitoylated and farnesylated, which are required for normal signaling
YGL248W	*PDE1*	-2.09	Low-affinity cyclic AMP phosphodiesterase, controls glucose and intracellular acidification-induced cAMP signaling, target of the cAMP-protein kinase A (PKA) pathway; glucose induces transcription and inhibits translation
YPL038W	*MET31*	-1.97	Zinc-finger DNA-binding protein, involved in transcriptional regulation of the methionine biosynthetic genes, similar to Met32p
YAL018C		-1.95	Putative protein of unknown function
YJL157C	*FAR1*	-1.95	Cyclin-dependent kinase inhibitor that mediates cell cycle arrest in response to pheromone; also forms a complex with Cdc24p, Ste4p, and Ste18p that may specify the direction of polarized growth during mating; potential Cdc28p substrate
YAR071W	*PHO11*	-1.93	One of three repressible acid phosphatases, a glycoprotein that is transported to the cell surface by the secretory pathway; induced by phosphate starvation and coordinately regulated by PHO4 and PHO2
YBR113W		-1.93	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the verified gene CYC8
YJL133C-A		-1.92	Putative protein of unknown function; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies
YDR170W-A		-1.92	Retrotransposon TYA Gag gene; Gag is a nucleocapsid protein that is the structural constituent of virus-like particles (VLPs); similar to retroviral Gag; YDR170W-A is part of a mutant retrotransposon
YOR343W-B		-1.91	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and Δ*sir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YOR284W	*HUA2*	-1.90	Cytoplasmic protein of unknown function; computational analysis of large-scale protein-protein interaction data suggests a possible role in actin patch assembly
YJR027W		-1.89	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes
YHL044W		-1.86	Putative integral membrane protein, member of DUP240 gene family; green fluorescent protein (GFP)-fusion protein localizes to the plasma membrane in a punctate pattern
YPR027C		-1.85	Putative protein of unknown function
YBL100W-B		-1.83	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes
YHR154W	*RTT107,ESC4*	-1.62	Protein implicated in Mms22-dependent DNA repair during S phase, DNA damage induces phosphorylation by Mec1p at one or more SQ/TQ motifs; interacts with Mms22p and Slx4p; has four BRCT domains; has a role in regulation of Ty1 transposition
YPR122W	*AXL1,STE22,FUS5*	-1.61	Haploid specific endoprotease that performs one of two N-terminal cleavages during maturation of a-factor mating pheromone; required for axial budding pattern of haploid cells
YHR105W	*YPT35*	-1.61	Endosomal protein of unknown function that contains a phox (PX) homology domain and binds to both phosphatidylinositol-3-phosphate (PtdIns(3)P) and proteins involved in ER-Golgi or vesicular transport
YJL164C	*TPK1,SRA3,PKA1*	-1.60	cAMP-dependent protein kinase catalytic subunit; promotes vegetative growth in response to nutrients via the Ras-cAMP signaling pathway; inhibited by regulatory subunit Bcy1p in the absence of cAMP; partially redundant with Tpk2p and Tpk3p
YMR141W-A		-1.59	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; overlaps the verified gene RPL13B/YMR142C
YJL107C		-1.57	Putative protein of unknown function; expression is induced by activation of the HOG1 mitogen-activated signaling pathway and this induction is Hog1p/Pbs2p dependent; YJL107C and adjacent ORF, YJL108C are merged in related fungi

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YKR034W	*DAL80,UGA43*	-1.57	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
YMR013W-A		-1.55	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; completely overlaps the characterized snoRNA gene snR73
YLR030W		-1.54	Putative protein of unknown function
YBR158W	*AMN1,CST13,ICS4*	-1.51	Protein required for daughter cell separation, multiple mitotic checkpoints, and chromosome stability; contains 12 degenerate leucine-rich repeat motifs; expression is induced by the Mitotic Exit Network (MEN)
YCL021W-A		-1.50	Putative protein of unknown function
YBR083W	*TEC1,ROC1*	-1.48	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
YOR156C	*NFI1,SIZ2*	-1.48	SUMO ligase, catalyzes the covalent attachment of SUMO (Smt3p) to proteins; involved in maintenance of proper telomere length
YLR452C	*SST2*	-1.47	GTPase-activating protein for Gpa1p, regulates desensitization to alpha factor pheromone; also required to prevent receptor-independent signaling of the mating pathway; member of the RGS (regulator of G-protein signaling) family
YHR097C		-1.47	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and the nucleus
YLL026W	*HSP104*	-1.43	Heat shock protein that cooperates with Ydj1p (Hsp40) and Ssa1p (Hsp70) to refold and reactivate previously denatured, aggregated proteins; responsive to stresses including: heat, ethanol, and sodium arsenite; involved in [PSI+] propagation
YFL027C	*GYP8*	-1.43	GTPase-activating protein for yeast Rab family members; Ypt1p is the preferred in vitro substrate but also acts on Sec4p, Ypt31p and Ypt32p; involved in the regulation of ER to Golgi vesicle transport
YMR173W	*DDR48,FSP*	-1.39	DNA damage-responsive protein, expression is increased in response to heat-shock stress or treatments that produce DNA lesions; contains multiple repeats of the amino acid sequence NNNDSYGS
YMR170C	*ALD2*	-1.38	Cytoplasmic aldehyde dehydrogenase, involved in ethanol oxidation and beta-alanine biosynthesis; uses NAD+ as the preferred coenzyme; expression is stress induced and glucose repressed; very similar to Ald3p

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YPR170C		-1.35	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the dubious ORFs YPR169W-A and YPR170W-B
YDR016C	*DAD1*	-1.35	Essential subunit of the Dam1 complex (aka DASH complex), couples kinetochores to the force produced by MT depolymerization thereby aiding in chromosome segregation; is transferred to the kinetochore prior to mitosis
YPR121W	*THI22*	-1.31	Protein with similarity to hydroxymethylpyrimidine phosphate kinases; member of a gene family with THI20 and THI21; not required for thiamine biosynthesis
YGR240C-A		-1.30	Putative protein of unknown function; identified by fungal homology and RT-PCR
YER037W	*PHM8*	-1.30	Protein of unknown function, expression is induced by low phosphate levels and by inactivation of Pho85p
YOR386W	*PHR1*	-1.29	DNA photolyase involved in photoreactivation, repairs pyrimidine dimers in the presence of visible light; induced by DNA damage; regulated by transcriptional repressor Rph1p
YLR040C		-1.27	Putative protein of unknown function; localizes to the cell wall; predicted to be a GPI-attached protein; upregulated by Mcm1p-Alpha1p transcription factor; partially overlaps the dubious ORF YLR041W; YLR040C is not essential
YLR210W	*CLB4*	-1.26	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
YJL023C	*PET130*	-1.26	Protein required for respiratory growth; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies
YMR136W	*GAT2*	-1.25	Protein containing GATA family zinc finger motifs; similar to Gln3p and Dal80p; expression repressed by leucine
YDR380W	*ARO10*	-1.24	Phenylpyruvate decarboxylase, catalyzes decarboxylation of phenylpyruvate to phenylacetaldehyde, which is the first specific step in the Ehrlich pathway
YHR087W	*RTC3*	-1.24	Protein of unknown function involved in RNA metabolism; has structural similarity to SBDS, the human protein mutated in Shwachman-Diamond Syndrome (the yeast SBDS ortholog = SDO1); null mutation suppresses cdc13-1 temperature sensitivity
YBR053C		-1.23	Putative protein of unknown function; induced by cell wall perturbation

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YBR046C	*ZTA1*	-1.22	NADPH-dependent quinone reductase, GFP-tagged protein localizes to the cytoplasm and nucleus; has similarity to E. coli quinone oxidoreductase and to human zeta-crystallin
YCR018C	*SRD1*	-1.21	Protein involved in the processing of pre-rRNA to mature rRNA; contains a C2/C2 zinc finger motif; srd1 mutation suppresses defects caused by the rrp1-1 mutation
YDR003W	*RCR2,SSH5*	-1.20	Vacuolar protein that presumably functions within the endosomal-vacuolar trafficking pathway, affecting events that determine whether plasma membrane proteins are degraded or routed to the plasma membrane; similar to Rcr1p
YDR536W	*STL1*	-1.20	Glycerol proton symporter of the plasma membrane, subject to glucose-induced inactivation, strongly but transiently induced when cells are subjected to osmotic shock
YJL155C	*FBP26*	-1.20	Fructose-2,6-bisphosphatase, required for glucose metabolism
YDL156W		-1.19	Putative protein of unknown function; protein sequence contains three WD domains (WD-40 repeat); green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus
YGR169C-A		-1.18	Putative protein of unknown function
YLR151C	*PCD1*	-1.18	Peroxisomal nudix pyrophosphatase with specificity for coenzyme A and CoA derivatives, may function to remove potentially toxic oxidized CoA disulfide from peroxisomes to maintain the capacity for beta-oxidation of fatty acids
YJL203W	*PRP21,SPP91*	-1.17	Subunit of the SF3a splicing factor complex, required for spliceosome assembly
YDR139C	*RUB1*	-1.17	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)
YEL025C	*SRI1*	-1.16	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to both the cytoplasm and the nucleus
YBL005W-B		-1.15	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YPL256C	*CLN2*	-1.15	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)
YOR331C		-1.14	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; open reading frame overlaps the verified gene VMA4/YOR332W
YGR142W	*BTN2*	-1.14	v-SNARE binding protein that facilitates specific protein retrieval from a late endosome to the Golgi; modulates arginine uptake, possible role in mediating pH homeostasis between the vacuole and plasma membrane H(+)-ATPase
YDR533C	*HSP31*	-1.14	Possible chaperone and cysteine protease with similarity to E. coli Hsp31; member of the DJ-1/ThiJ/PfpI superfamily, which includes human DJ-1 involved in Parkinson's disease; exists as a dimer and contains a putative metal-binding site
YDR320C-A	*DAD4,HSK2*	-1.14	Essential subunit of the Dam1 complex (aka DASH complex), couples kinetochores to the force produced by MT depolymerization thereby aiding in chromosome segregation; is transferred to the kinetochore prior to mitosis
YNL325C	*FIG4*	-1.14	Phosphatidylinositol 3,5-bisphosphate (PtdIns[3,5]P) phosphatase; required for efficient mating and response to osmotic shock; physically associates with and regulated by Vac14p; contains a SAC1-like domain
YDL157C		-1.14	Putative protein of unknown function; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies
YIL140W	*AXL2,SRO4,BUD10*	-1.13	Integral plasma membrane protein required for axial budding in haploid cells, localizes to the incipient bud site and bud neck; glycosylated by Pmt4p; potential Cdc28p substrate
YAL017W	*PSK1,FUN31*	-1.12	One of two (see also PSK2) PAS domain containing S/T protein kinases; coordinately regulates protein synthesis and carbohydrate metabolism and storage in response to a unknown metabolite that reflects nutritional status
YLR142W	*PUT1*	-1.12	Proline oxidase, nuclear-encoded mitochondrial protein involved in utilization of proline as sole nitrogen source; PUT1 transcription is induced by Put3p in the presence of proline and the absence of a preferred nitrogen source
YHR067W	*HTD2,RMD12*	-1.10	Mitochondrial 3-hydroxyacyl-thioester dehydratase involved in fatty acid biosynthesis, required for respiratory growth and for normal mitochondrial morphology

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YGR149W		-1.10	Putative protein of unknown function; predicted to be an integal membrane protein
YMR045C		-1.10	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes
YNL192W	*CHS1,USA4*	-1.09	Chitin synthase I, requires activation from zymogenic form in order to catalyze the transfer of N-acetylglucosamine (GlcNAc) to chitin; required for repairing the chitin septum during cytokinesis; transcription activated by mating factor
YDR251W	*PAM1*	-1.08	Essential protein of unknown function; exhibits variable expression during colony morphogenesis; overexpression permits survival without protein phosphatase 2A, inhibits growth, and induces a filamentous phenotype
YIL111W	*COX5B*	-1.08	Subunit Vb of cytochrome c oxidase, which is the terminal member of the mitochondrial inner membrane electron transport chain; predominantly expressed during anaerobic growth while its isoform Va (Cox5Ap) is expressed during aerobic growth
YDR085C	*AFR1*	-1.07	Protein required for pheromone-induced projection (shmoo) formation; regulates septin architecture during mating; has an RVXF motif that mediates targeting of Glc7p to mating projections; interacts with Cdc12p
YPR158W	*CUR1*	-1.06	Protein of unknown function involved in destabilization of [URE3] prions; similar in sequence to Btn2p
YIR002C	*MPH1*	-1.05	Member of the DEAH family of helicases, functions in an error-free DNA damage bypass pathway that involves homologous recombination, binds to flap DNA and stimulates activity of Rad27p and Dna2p; mutations confer a mutator phenotype
YPL240C	*HSP82,HSP90*	-1.04	Hsp90 chaperone required for pheromone signaling and negative regulation of Hsf1p; docks with Tom70p for mitochondrial preprotein delivery; promotes telomerase DNA binding and nucleotide addition; interacts with Cns1p, Cpr6p, Cpr7p, Sti1p
YJL019W	*MPS3*	-1.03	Nuclear envelope protein required for SPB duplication and nuclear fusion; localizes to the SPB half bridge and at telomeres during meiosis; required with Ndj1p and Csm4p for meiotic bouquet formation and telomere-led rapid prophase movement
YDR074W	*TPS2,PFK3,HOG2*	-1.02	Phosphatase subunit of the trehalose-6-phosphate synthase/phosphatase complex, which synthesizes the storage carbohydrate trehalose; expression is induced by stress conditions and repressed by the Ras-cAMP pathway

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells			
Systematic name	**Standard Name**	**Log2 (Fold change)**	**Gene Ontology Annotation**
YER048W-A	*ISD11*	-1.02	Protein required for mitochondrial iron-sulfur cluster biosynthesis
YOR273C	*TPO4*	-1.02	Polyamine transport protein, recognizes spermine, putrescine, and spermidine; localizes to the plasma membrane; member of the major facilitator superfamily
YGR194C	*XKS1*	-1.02	Xylulokinase, converts D-xylulose and ATP to xylulose 5-phosphate and ADP; rate limiting step in fermentation of xylulose; required for xylose fermentation by recombinant S. cerevisiae strains
YEL073C		-1.01	Putative protein of unknown function; located adjacent to ARS503 and the telomere on the left arm of chromosome V; regulated by inositol/choline
YCR014C	*POL4,POLX*	-1.01	DNA polymerase IV, undergoes pair-wise interactions with Dnl4p-Lif1p and Rad27p to mediate repair of DNA double-strand breaks by non-homologous end joining (NHEJ); homologous to mammalian DNA polymerase beta
YIL101C	*XBP1*	-1.01	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
YJL093C	*TOK1,YPK1,YORK,YKC1,DUK1*	-1.01	Outward-rectifier potassium channel of the plasma membrane with two pore domains in tandem, each of which forms a functional channel permeable to potassium; carboxy tail functions to prevent inner gate closures; target of K1 toxin
YGL193C		--*	Haploid-specific gene repressed by a1-alpha2, turned off in sir3 null strains, absence enhances the sensitivity of rad52-327 cells to campothecin almost 100-fold
YNL145W	*MFA2*	--*	Mating pheromone a-factor, made by a cells; interacts with alpha cells to induce cell cycle arrest and other responses leading to mating; biogenesis involves C-terminal modification, N-terminal proteolysis, and export; also encoded by MFA1
YLR055C		1.00	Subunit of the SAGA transcriptional regulatory complex but not present in SAGA-like complex SLIK/SALSA, required for SAGA-mediated inhibition at some promoters
YDR025W	*VBA3*	1.01	Protein component of the small (40S) ribosomal subunit; identical to Rps11Bp and has similarity to E. coli S17 and rat S11 ribosomal proteins
YKL043W		1.02	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

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YMR122C		1.07	Dubious open reading frame unlikely to encode a functional protein, based on available experimental and comparative sequence data
YJR114W	*HMRA1*	1.09	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the verified ORF RSM7/YJR113C
YPR099C	*APC11*	1.09	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the verified gene MRPL51/YPR100W
YHR175W	*BSC1*	1.09	Putative low-affinity copper transporter of the vacuolar membrane; mutation confers resistance to toxic copper concentrations, while overexpression confers resistance to copper starvation
YGL209W	*PRM7*	1.09	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
YPR195C	*STP4*	1.10	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data
YFR036W	*RPS11A*	1.10	Subunit of the Anaphase-Promoting Complex/ Cyclosome (APC/C), which is a ubiquitin-protein ligase required for degradation of anaphase inhibitors, including mitotic cyclins, during the metaphase/ anaphase transition
YEL033W	*MTH1,HTR1, DGT1,BPC1*	1.12	Predicted metabolic role based on network analysis derived from ChIP experiments, a large-scale deletion study and localization of transcription factor binding sites; null mutant is sensitive to temperature oscillation in a cdc13-1 mutant
YNL113W		1.15	RNA polymerase subunit AC19, common to RNA polymerases I and III
YMR070W		1.16	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
YLR242C		1.16	Protein functioning in transport of glycosylphosphatidylinositol intermediates into the ER lumen; required for normal intracellular sterol distribution and for sphingolipid metabolism; similar to Nup120p and C. elegans R05H5.5 protein
YPR133W-A	*MTC7*	1.17	Component of the TOM (translocase of outer membrane) complex responsible for recognition and initial import of all mitochondrially directed proteins; involved in transfer of precursors from the Tom70p and Tom20p receptors to the Tom40p pore

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YDR277C		1.18	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
YPR062W		1.20	Cytosine deaminase, zinc metalloenzyme that catalyzes the hydrolytic deamination of cytosine to uracil; of biomedical interest because it also catalyzes the deamination of 5-fluorocytosine (5FC) to form anticancer drug 5-fluorouracil (5FU)
YOR049C	*CDC26,SCD26, HIT3*	1.22	Suppressor of sphingoid long chain base (LCB) sensitivity of an LCB-lyase mutation; putative integral membrane transporter or flippase that may transport LCBs from the cytoplasmic side toward the extracytoplasmic side of the membrane
YDL008W	*MIG2,MLZ1*	1.23	Catalytic core subunit of the Anaphase-Promoting Complex/Cyclosome (APC/C), which is a ubiquitin-protein ligase required for degradation of anaphase inhibitors, including mitotic cyclins, during the metaphase/anaphase transition
YPR123C	*CTR2*	1.24	Hypothetical protein
YDL048C	*ARG3,argF*	1.25	Protein containing a Kruppel-type zinc-finger domain; has similarity to Stp1p, Stp2p, and Stp3p
YJL088W	*NCA3*	1.26	Ornithine carbamoyltransferase (carbamoylphosphate:L-ornithine carbamoyltransferase), catalyzes the sixth step in the biosynthesis of the arginine precursor ornithine
YJR115W	*SRF2*	1.26	Putative protein of unknown function
YCR097W	*PHD1*	1.33	Silenced copy of a1 at HMR; homeobox corepressor that interacts with Alpha2p to repress haploid-specific gene transcription in diploid cells
YLR374C		1.35	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the uncharacterized ORF STP3/YLR375W
YDR327W	*SPT8*	1.40	Dubious open reading frame unlikely to encode a protein, based on experimental and comparative sequence data; partially overlaps the verified gene SKP1
YPL056C		1.41	Putative protein of unknown function; deletion mutant is fluconazole resistant
YKR075C	*ARV1*	1.43	Protein of unknown function; similar to YOR062Cp and Reg1p; expression regulated by glucose and Rgt1p; GFP-fusion protein is induced in response to the DNA-damaging agent MMS
YDR524C-B		1.45	Putative protein of unknown function

Supplemental Table S2: Genes differentially expressed more than two-fold between WT and *Δsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YFL067W		1.47	Protein of unknown function, down-regulated at low calcium levels
YOR203W		1.54	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; overlaps 5' end of essential DED1 gene required for translation initiation
YLR349W	*MOT3,ROX7*	1.56	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; overlaps the verified ORF DIC1/YLR348C
YFR017C		1.59	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and is induced in response to the DNA-damaging agent MMS; YFR017C is not an essential gene
YDL039C	*RPC19*	1.60	Pheromone-regulated protein, predicted to have one transmembrane segment; promoter contains Gcn4p binding elements
YJL116C	*RSB1*	1.61	Protein that functions with Nca2p to regulate mitochondrial expression of subunits 6 (Atp6p) and 8 (Atp8p) of the Fo-F1 ATP synthase; member of the SUN family; expression induced in cells treated with the mycotoxin patulin
YDL037C		1.66	Protein of unconfirmed function, similar to cell surface flocculin Muc1p; ORF exhibits genomic organization compatible with a translational readthrough-dependent mode of expression
YBL109W		2.56	Dubious open reading frame unlikely to encode a protein, based on experimental and comparative sequence data
YLR198C	*FCY1,yCD*	3.05	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; overlaps the verified gene SIK1/YLR197W
YCL074W		3.82	Pseudogene: encodes fragment of Ty Pol protein
YCL069W		--***	Permease of basic amino acids in the vacuolar membrane
YCL076W	*TOM5,MOM8A*	--***	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data
YDR544C		--***	Dubious open reading frame unlikely to encode a functional protein, based on available experimental and comparative sequence data

* These genes were expressed in the wildtype strain, but not expressed in the *sir4*Δ mutant.
*** These genes were not expressed in the wildtype strain, but are expressed in the *sir4*Δ mutant.

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YDR227W	UTH2,STE9,ASD1	-7.46	Silent information regulator that, together with SIR2 and SIR3, is involved in assembly of silent chromatin domains at telomeres and the silent mating-type loci; potentially phosphorylated by Cdc28p; some alleles of SIR4 prolong lifespan
YNL145W		-5.43	Mating pheromone a-factor, made by a cells; interacts with alpha cells to induce cell cycle arrest and other responses leading to mating; biogenesis involves C-terminal modification, N-terminal proteolysis, and export; also encoded by MFA1
YDR461W		-5.07	Mating pheromone a-factor, made by a cells; interacts with alpha cells to induce cell cycle arrest and other responses leading to mating; biogenesis involves C-terminal modification, N-terminal proteolysis, and export; also encoded by MFA2
YFL026W		-3.64	Receptor for alpha-factor pheromone; seven transmembrane-domain GPCR that interacts with both pheromone and a heterotrimeric G protein to initiate the signaling response that leads to mating between haploid a and alpha cells
YGL032C		-3.37	Adhesion subunit of a-agglutinin of a-cells, C-terminal sequence acts as a ligand for alpha-agglutinin (Sag1p) during agglutination, modified with O-linked oligomannosyl chains, linked to anchorage subunit Aga1p via two disulfide bonds
YIL015W	SST1	-3.26	Aspartyl protease secreted into the periplasmic space of mating type a cells, helps cells find mating partners, cleaves and inactivates alpha factor allowing cells to recover from alpha-factor-induced cell cycle arrest
YBL016W	DAC2	-3.18	Mitogen-activated serine/threonine protein kinase involved in mating; phosphoactivated by Ste7p; substrates include Ste12p, Far1p, Bni1p, Sst2p; inhibits invasive growth during mating by phosphorylating Tec1p, promoting its degradation
YDL227C		-3.16	Site-specific endonuclease required for gene conversion at the MAT locus (homothallic switching) through the generation of a ds DNA break; expression restricted to mother cells in late G1 as controlled by Swi4p-Swi6p, Swi5p and Ash1p
YKL209C		-3.11	Plasma membrane ATP-binding cassette (ABC) transporter required for the export of a-factor, catalyzes ATP hydrolysis coupled to a-factor transport; contains 12 transmembrane domains and two ATP binding domains; expressed only in MATa cells
YGL193C		-2.83	Haploid-specific gene repressed by a1-alpha2, turned off in sir3 null strains, absence enhances the sensitivity of rad52-327 cells to campothecin almost 100-fold

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells			
Systematic name	**Standard Name**	**Log2 (Fold change)**	**Gene Ontology Annotation**
YLR265C	LIF2	-2.62	Protein involved in regulation of nonhomologous end joining; interacts with DNA ligase IV components Dnl4p and Lif1p; repressed by MAT heterozygosity; regulates cellular distribution of Lif1p
YPL061W	ALD1	-2.61	Cytosolic aldehyde dehydrogenase, activated by Mg2+ and utilizes NADP+ as the preferred coenzyme; required for conversion of acetaldehyde to acetate; constitutively expressed; locates to the mitochondrial outer surface upon oxidative stress
YGR044C	CSP1	-2.60	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-alpha2 regulator; mediates cell type control of sporulation
YHR005C	SCG1,DAC1,CDC70	-2.46	GTP-binding alpha subunit of the heterotrimeric G protein that couples to pheromone receptors; negatively regulates the mating pathway by sequestering G(beta) gamma and by triggering an adaptive response; activates Vps34p at the endosome
YKR039W		-2.44	General amino acid permease; localization to the plasma membrane is regulated by nitrogen source
YOR343W-B		-2.40	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes
YER133W-A		-2.37	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps uncharacterized gene YER134C.
YDR410C		-2.19	Farnesyl cysteine-carboxyl methyltransferase, mediates the carboxyl methylation step during C-terminal CAAX motif processing of a-factor and RAS proteins in the endoplasmic reticulum, localizes to the ER membrane
YJR073C	PEM2	-2.19	Phospholipid methyltransferase (methylene-fatty-acyl-phospholipid synthase), catalyzes the last two steps in phosphatidylcholine biosynthesis
YDR261W-B		-2.17	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes
YOL052C-A		-2.05	Multistress response protein, expression is activated by a variety of xenobiotic agents and environmental or physiological stresses

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YLR410W-B		-2.00	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes
YBR293W		-1.99	Permease of basic amino acids in the vacuolar membrane
YAL061W		-1.91	Putative medium-chain alcohol dehydrogenase with similarity to BDH1; transcription induced by constitutively active PDR1 and PDR3
YDL160C-A		-1.86	Putative protein of unknown function
YPR009W		-1.80	Putative transcription factor; multicopy suppressor of mutations that cause low activity of the cAMP/protein kinase A pathway; highly similar to Sut1p
YFL027C		-1.74	GTPase-activating protein for yeast Rab family members; Ypt1p is the preferred in vitro substrate but also acts on Sec4p, Ypt31p and Ypt32p; involved in the regulation of ER to Golgi vesicle transport
YER037W		-1.73	Protein of unknown function, expression is induced by low phosphate levels and by inactivation of Pho85p
YMR013W-A		-1.72	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; completely overlaps the characterized snoRNA gene snR73
YLR346C		-1.70	Putative protein of unknown function found in mitochondria; expression is regulated by transcription factors involved in pleiotropic drug resistance, Pdr1p and Yrr1p; YLR346C is not an essential gene
YNL054W-B		-1.69	TyB Gag-Pol protein; proteolytically processed to make the Gag, RT, PR, and IN proteins that are required for retrotransposition
YJR086W		-1.68	G protein gamma subunit, forms a dimer with Ste4p to activate the mating signaling pathway, forms a heterotrimer with Gpa1p and Ste4p to dampen signaling; C-terminus is palmitoylated and farnesylated, which are required for normal signaling
YDR506C		-1.65	Possible membrane-localized protein
YGL248W		-1.59	Low-affinity cyclic AMP phosphodiesterase, controls glucose and intracellular acidification-induced cAMP signaling, target of the cAMP-protein kinase A (PKA) pathway; glucose induces transcription and inhibits translation
YOR077W	YOR29-28	-1.55	Basic zinc-finger protein, similar to human and mouse Kin17 proteins which are chromatin-associated proteins involved in UV response and DNA replication

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YDR502C	ETH2	-1.55	S-adenosylmethionine synthetase, catalyzes transfer of the adenosyl group of ATP to the sulfur atom of methionine; one of two differentially regulated isozymes (Sam1p and Sam2p)
YEL056W		-1.53	Subunit of the Hat1p-Hat2p histone acetyltransferase complex; required for high affinity binding of the complex to free histone H4, thereby enhancing Hat1p activity; similar to human RbAp46 and 48; has a role in telomeric silencing
YJL157C		-1.51	Cyclin-dependent kinase inhibitor that mediates cell cycle arrest in response to pheromone; also forms a complex with Cdc24p, Ste4p, and Ste18p that may specify the direction of polarized growth during mating; potential Cdc28p substrate
YMR045C		-1.51	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes
YBL100W-B		-1.50	Retrotransposon TYA Gag and TYB Pol genes; transcribed/translated as one unit; polyprotein is processed to make a nucleocapsid-like protein (Gag), reverse transcriptase (RT), protease (PR), and integrase (IN); similar to retroviral genes
YDR100W		-1.49	Integral membrane protein localized to late Golgi vesicles along with the v-SNARE Tlg2p
YBR113W		-1.49	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the verified gene CYC8
YGL149W		-1.47	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the verified ORF INO80/YGL150C.
YNL142W		-1.44	Ammonium permease involved in regulation of pseudohyphal growth; belongs to a ubiquitous family of cytoplasmic membrane proteins that transport only ammonium (NH4+); expression is under the nitrogen catabolite repression regulation
YDL156W		-1.44	Putative protein of unknown function; protein sequence contains three WD domains (WD-40 repeat); green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus
YBR157C		-1.43	Protein of unknown function; null mutation does not confer any obvious defects in growth, spore germination, viability, or carbohydrate utilization

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YER035W		-1.42	RNA-binding protein, activates mRNA decapping directly by binding to the mRNA substrate and enhancing the activity of the decapping proteins Dcp1p and Dcp2p; has a role in translation during heat stress
YLR126C		-1.41	Putative protein of unknown function with similarity to glutamine amidotransferase proteins; has Aft1p-binding motif in the promoter; may be involved in copper and iron homeostasis; YLR126C is not an essential protein
YDR406W		-1.40	Plasma membrane ATP binding cassette (ABC) transporter, multidrug transporter and general stress response factor implicated in cellular detoxification; regulated by Pdr1p, Pdr3p and Pdr8p; promoter contains a PDR responsive element
YJL107C		-1.39	Putative protein of unknown function; expression is induced by activation of the HOG1 mitogen-activated signaling pathway and this induction is Hog1p/Pbs2p dependent; YJL107C and adjacent ORF, YJL108C are merged in related fungi
YDR016C		-1.37	Essential subunit of the Dam1 complex (aka DASH complex), couples kinetochores to the force produced by MT depolymerization thereby aiding in chromosome segregation; is transferred to the kinetochore prior to mitosis
YOL111C	GET5,TMA24	-1.36	Protein required for efficient mating; involved in shmoo formation and nuclear migration in the pre-zygote; associates with ribosomes and interacts with Get4p; has a possible role in insertion of tail-anchored proteins into the ER membrane
YNL160W		-1.35	Cell wall-related secretory glycoprotein; induced by nutrient deprivation-associated growth arrest and upon entry into stationary phase; may be involved in adaptation prior to stationary phase entry; has similarity to Sps100p
YHR037W		-1.34	Delta-1-pyrroline-5-carboxylate dehydrogenase, nuclear-encoded mitochondrial protein involved in utilization of proline as sole nitrogen source; deficiency of the human homolog causes HPII, an autosomal recessive inborn error of metabolism
YOR212W	HMD2	-1.33	G protein beta subunit, forms a dimer with Ste18p to activate the mating signaling pathway, forms a heterotrimer with Gpa1p and Ste18p to dampen signaling; may recruit Rho1p to the polarized growth site during mating; contains WD40 repeats
YLR299W	CIS2	-1.31	Gamma-glutamyltranspeptidase, major glutathione-degrading enzyme; involved in detoxification of electrophilic xenobiotics; expression induced mainly by nitrogen starvation

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YBR083W	ROC1	-1.29	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
YDR251W		-1.29	Essential protein of unknown function; exhibits variable expression during colony morphogenesis; overexpression permits survival without protein phosphatase 2A, inhibits growth, and induces a filamentous phenotype
YGL157W		-1.29	NADPH-dependent aldehyde reductase, utilizes aromatic and alophatic aldehyde substrates; member of the short-chain dehydrogenase/reductase superfamily
YJL019W	NEP98	-1.28	Nuclear envelope protein required for SPB duplication and nuclear fusion; localizes to the SPB half bridge and at telomeres during meiosis; required with Ndj1p and Csm4p for meiotic bouquet formation and telomere-led rapid prophase movement
YPR122W	STE22,FUS5	-1.28	Haploid specific endoprotease that performs one of two N-terminal cleavages during maturation of a-factor mating pheromone; required for axial budding pattern of haploid cells
YHL044W		-1.27	Putative integral membrane protein, member of DUP240 gene family; green fluorescent protein (GFP)-fusion protein localizes to the plasma membrane in a punctate pattern
YLR082C		-1.26	Protein of unknown function; overexpression suppresses the lethality caused by a rad53 null mutation
YPR124W		-1.22	High-affinity copper transporter of the plasma membrane, mediates nearly all copper uptake under low copper conditions; transcriptionally induced at low copper levels and degraded at high copper levels
YFL010W-A		-1.21	Protein required for the negative regulation by ammonia of Gap1p, which is a general amino acid permease
YBR073W	TID1	-1.21	DNA-dependent ATPase, stimulates strand exchange by modifying the topology of double-stranded DNA; involved in recombinational repair of DNA double-strand breaks during mitosis and meiosis; proposed to be involved in crossover interference
YER134C		-1.21	Putative protein of unknown function; non-essential gene
YKL096W	YJU1	-1.18	Cell wall mannoprotein that localizes specifically to birth scars of daughter cells, linked to a beta-1,3- and beta-1,6-glucan heteropolymer through a phosphodiester bond; required for propionic acid resistance

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YGR281W	YRS1	-1.17	Plasma membrane ATP-binding cassette (ABC) transporter, multidrug transporter mediates export of many different organic anions including oligomycin; similar to human cystic fibrosis transmembrane receptor (CFTR)
YHL019C		-1.17	Protein of unknown function, homologous to the medium chain of mammalian clathrin-associated protein complex; involved in vesicular transport
YNL078W	JIP1	-1.17	Protein localized in the bud neck at G2/M phase; physically interacts with septins; possibly involved in a mitotic signaling network
YBR158W	CST13, ICS4	-1.14	Protein required for daughter cell separation, multiple mitotic checkpoints, and chromosome stability; contains 12 degenerate leucine-rich repeat motifs; expression is induced by the Mitotic Exit Network (MEN)
YNL258C	RNS1	-1.13	Peripheral membrane protein needed for Golgi-to-ER retrograde traffic; forms a complex with Sec39p and Tip20p that interacts with ER SNAREs Sec20p and Use1p; component of the ER target site that interacts with coatomer; interacts with Cin5p
YOR153W	STS1,YDR1,LEM1	-1.12	Plasma membrane ATP-binding cassette (ABC) transporter, multidrug transporter actively regulated by Pdr1p; also involved in steroid transport, cation resistance, and cellular detoxification during exponential growth
YPL231W		-1.10	Alpha subunit of fatty acid synthetase, which catalyzes the synthesis of long-chain saturated fatty acids; contains beta-ketoacyl reductase and beta-ketoacyl synthase activities; phosphorylated
YJL155C		-1.07	Fructose-2,6-bisphosphatase, required for glucose metabolism
YMR015C	CYP61	-1.07	C-22 sterol desaturase, a cytochrome P450 enzyme that catalyzes the formation of the C-22(23) double bond in the sterol side chain in ergosterol biosynthesis; may be a target of azole antifungal drugs
YMR291W		-1.07	Putative kinase of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus; YMR291W is not an essential gene
YDL232W		-1.06	Subunit of the oligosaccharyltransferase complex of the ER lumen, which catalyzes protein asparagine-linked glycosylation; type I membrane protein required for incorporation of Ost3p or Ost6p into the OST complex
YIL140W	SRO4,BUD10	-1.06	Integral plasma membrane protein required for axial budding in haploid cells, localizes to the incipient bud site and bud neck; glycosylated by Pmt4p; potential Cdc28p substrate

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YOL108C		-1.05	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
YLR153C		-1.05	Acetyl-coA synthetase isoform which, along with Acs1p, is the nuclear source of acetyl-coA for histone acetylation; mutants affect global transcription; required for growth on glucose; expressed under anaerobic conditions
YDL174C		-1.05	D-lactate dehydrogenase, oxidizes D-lactate to pyruvate, transcription is heme-dependent, repressed by glucose, and derepressed in ethanol or lactate; located in the mitochondrial inner membrane
YER088C-A		-1.04	Dubious open reading frame unlikely to encode a functional protein, based on available experimental and comparative sequence data
YLL038C		-1.03	Protein of unknown function, contains an N-terminal epsin-like domain; proposed to be involved in the trafficking of Arn1p in the absence of ferrichrome
YPL038W		-1.03	Zinc-finger DNA-binding protein, involved in transcriptional regulation of the methionine biosynthetic genes, similar to Met32p
YIL051C	IBM1	-1.02	Mitochondrial protein involved in maintenance of the mitochondrial genome
YDL128W	MNR1,HUM1	-1.01	Vacuolar H+/Ca2+ exchanger involved in control of cytosolic Ca2+ concentration; has similarity to sodium/calcium exchangers, including the bovine Na+/Ca2+,K+ antiporter
YLR228C		-1.01	Sterol regulatory element binding protein, regulates transcription of sterol biosynthetic genes; contains Zn[2]-Cys[6] binuclear cluster; homologous to Upc2p; relocates from intracellular membranes to perinuclear foci on sterol depletion
YLR452C		-1.01	GTPase-activating protein for Gpa1p, regulates desensitization to alpha factor pheromone; also required to prevent receptor-independent signaling of the mating pathway; member of the RGS (regulator of G-protein signaling) family
YMR170C		-1.01	Cytoplasmic aldehyde dehydrogenase, involved in ethanol oxidation and beta-alanine biosynthesis; uses NAD+ as the preferred coenzyme; expression is stress induced and glucose repressed; very similar to Ald3p
YHR066W	SSF1	1.00	Constituent of 66S pre-ribosomal particles, required for ribosomal large subunit maturation; functionally redundant with Ssf2p; member of the Brix family

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YNL191W	DUG3	1.01	Probable glutamine amidotransferase, forms a complex with Dug1p and Dug2p to degrade glutathione (GSH) and other peptides containing a gamma-glu-X bond in an alternative pathway to GSH degradation by gamma-glutamyl transpeptidase (Ecm38p)
YLR303W	MET17,MET25,MET15	1.01	Methionine and cysteine synthase (O-acetyl homoserine-O-acetyl serine sulfhydrylase), required for sulfur amino acid synthesis
YNL110C	NOP15	1.02	Constituent of 66S pre-ribosomal particles, involved in 60S ribosomal subunit biogenesis; localizes to both nucleolus and cytoplasm
YPL264C		1.02	Putative membrane protein of unknown function; physically interacts with Hsp82p; YPL264C is not an essential gene
YDR272W	GLO2	1.03	Cytoplasmic glyoxalase II, catalyzes the hydrolysis of S-D-lactoylglutathione into glutathione and D-lactate
YGR087C	PDC6	1.03	Minor isoform of pyruvate decarboxylase, decarboxylates pyruvate to acetaldehyde, involved in amino acid catabolism; transcription is glucose- and ethanol-dependent, and is strongly induced during sulfur limitation
YLR134W	PDC5	1.03	Minor isoform of pyruvate decarboxylase, key enzyme in alcoholic fermentation, decarboxylates pyruvate to acetaldehyde, regulation is glucose- and ethanol-dependent, repressed by thiamine, involved in amino acid catabolism
YER062C	HOR2,GPP2	1.03	One of two redundant DL-glycerol-3-phosphatases (RHR2/GPP1 encodes the other) involved in glycerol biosynthesis; induced in response to hyperosmotic stress and oxidative stress, and during the diauxic transition
YHR139C	SPS100	1.03	Protein required for spore wall maturation; expressed during sporulation; may be a component of the spore wall; expression also induced in cells treated with the mycotoxin patulin
YDL168W	SFA1,ADH5	1.04	Bifunctional enzyme containing both alcohol dehydrogenase and glutathione-dependent formaldehyde dehydrogenase activities, functions in formaldehyde detoxification and formation of long chain and complex alcohols, regulated by Hog1p-Sko1p
YDL063C		1.04	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus; predicted to be involved in ribosome biogenesis
YMR280C	CAT8,MSP8,DIL1	1.04	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

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YNL308C	KRI1	1.04	Essential nucleolar protein required for 40S ribosome biogenesis; physically and functionally interacts with Krr1p
YDR059C	UBC5	1.05	Ubiquitin-conjugating enzyme that mediates selective degradation of short-lived, abnormal, or excess proteins, including histone H3; central component of the cellular stress response; expression is heat inducible
YJL103C	GSM1	1.05	Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis
YPR099C		1.06	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the verified gene MRPL51/YPR100W
YLR054C	OSW2	1.06	Protein of unknown function proposed to be involved in the assembly of the spore wall
YFL023W	BUD27,URI1	1.06	Protein involved in bud-site selection, nutrient signaling, and gene expression controlled by TOR kinase; diploid mutants show a random budding pattern rather than the wild-type bipolar pattern; plays a role in regulating Ty1 transposition
YLR307W	CDA1	1.07	Chitin deacetylase, together with Cda2p involved in the biosynthesis ascospore wall component, chitosan; required for proper rigidity of the ascospore wall
YJL116C	NCA3	1.07	Protein that functions with Nca2p to regulate mitochondrial expression of subunits 6 (Atp6p) and 8 (Atp8p) of the Fo-F1 ATP synthase; member of the SUN family; expression induced in cells treated with the mycotoxin patulin
YLR434C		1.07	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the verified ORF TSR2/YLR435W
YPR017C	DSS4	1.07	Guanine nucleotide dissociation stimulator for Sec4p, functions in the post-Golgi secretory pathway; binds zinc, found both on membranes and in the cytosol
YKL078W	DHR2	1.08	Predominantly nucleolar DEAH-box ATP-dependent RNA helicase, required for 18S rRNA synthesis
YGL111W	NSA1	1.08	Constituent of 66S pre-ribosomal particles, involved in 60S ribosomal subunit biogenesis
YGR103W	NOP7,YPH1	1.08	Component of several different pre-ribosomal particles; forms a complex with Ytm1p and Erb1p that is required for maturation of the large ribosomal subunit; required for exit from G₀ and the initiation of cell proliferation
YGR248W	SOL4	1.08	6-phosphogluconolactonase with similarity to Sol3p

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YMR095C	SNO1	1.08	Protein of unconfirmed function, involved in pyridoxine metabolism; expression is induced during stationary phase; forms a putative glutamine amidotransferase complex with Snz1p, with Sno1p serving as the glutaminase
YKL217W	JEN1	1.08	Lactate transporter, required for uptake of lactate and pyruvate; phosphorylated; expression is derepressed by transcriptional activator Cat8p during respiratory growth, and repressed in the presence of glucose, fructose, and mannose
YHR032W-A		1.08	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the dubious ORF YHR032C-A
YLR068W	FYV7	1.08	Essential protein required for maturation of 18S rRNA; required for survival upon exposure to K1 killer toxin
YOR298W	MUM3	1.08	Protein of unknown function involved in the organization of the outer spore wall layers; has similarity to the tafazzins superfamily of acyltransferases
YGR129W	SYF2,NTC31	1.09	Member of the NineTeen Complex (NTC) that contains Prp19p and stabilizes U6 snRNA in catalytic forms of the spliceosome containing U2, U5, and U6 snRNAs; isy1 syf2 cells have defective spindles activiating cell cycle arrest
YFR036W	CDC26,SCD26,HIT3	1.09	Subunit of the Anaphase-Promoting Complex/ Cyclosome (APC/C), which is a ubiquitin-protein ligase required for degradation of anaphase inhibitors, including mitotic cyclins, during the metaphase/ anaphase transition
YPL277C		1.09	Putative protein of unknown function; localized to the membranes; gene expression regulated by copper levels
YDR040C	ENA1,PMR2,HOR6	1.09	P-type ATPase sodium pump, involved in Na+ and Li+ efflux to allow salt tolerance
YIL007C	NAS2	1.09	Proteasome-interacting protein involved in the assembly of the base subcomplex of the 19S proteasomal regulatory particle (RP); similar to mammalian proteasomal modulator subunit; non-essential gene; interacts with Rpn4p
YNL277W	MET2	1.09	L-homoserine-O-acetyltransferase, catalyzes the conversion of homoserine to O-acetyl homoserine which is the first step of the methionine biosynthetic pathway
YJL045W		1.09	Minor succinate dehydrogenase isozyme; homologous to Sdh1p, the major isozyme reponsible for the oxidation of succinate and transfer of electrons to ubiquinone; induced during the diauxic shift in a Cat8p-dependent manner

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YKR045C		1.09	Putative protein of unknown function; epitope-tagged protein localizes to the cytoplasm
YPL230W	USV1,NSF1	1.10	Putative transcription factor containing a C2H2 zinc finger; mutation affects transcriptional regulation of genes involved in growth on non-fermentable carbon sources, response to salt stress and cell wall biosynthesis
YLR176C	RFX1,CRT1	1.10	Major transcriptional repressor of DNA-damage-regulated genes, recruits repressors Tup1p and Cyc8p to their promoters; involved in DNA damage and replication checkpoint pathway; similar to a family of mammalian DNA binding RFX1-4 proteins
YGL179C	TOS3	1.11	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
YDR277C	MTH1,HTR1,DGT1,BPC1	1.11	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
YNL248C	RPA49	1.11	RNA polymerase I subunit A49
YOL080C	REX4	1.13	Putative RNA exonuclease possibly involved in pre-rRNA processing and ribosome assembly
YBL039C	URA7	1.13	Major CTP synthase isozyme (see also URA8), catalyzes the ATP-dependent transfer of the amide nitrogen from glutamine to UTP, forming CTP, the final step in de novo biosynthesis of pyrimidines; involved in phospholipid biosynthesis
YNL015W	PBI2	1.13	Cytosolic inhibitor of vacuolar proteinase B, required for efficient vacuole inheritance; with thioredoxin forms protein complex LMA1, which assists in priming SNARE molecules and promotes vacuole fusion
YKL221W	MCH2	1.13	Protein with similarity to mammalian monocarboxylate permeases, which are involved in transport of monocarboxylic acids across the plasma membrane; mutant is not deficient in monocarboxylate transport
YMR312W	ELP6,KTI4.TOT6,HAP3	1.13	Subunit of Elongator complex, which is required for modification of wobble nucleosides in tRNA; required for Elongator structural integrity
YML116W	ATR1,SNQ1	1.13	Multidrug efflux pump of the major facilitator superfamily, required for resistance to aminotriazole and 4-nitroquinoline-N-oxide
YLL062C	MHT1	1.14	S-methylmethionine-homocysteine methyltransferase, functions along with Sam4p in the conversion of S-adenosylmethionine (AdoMet) to methionine to control the methionine/AdoMet ratio

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells			
Systematic name	**Standard Name**	**Log2 (Fold change)**	**Gene Ontology Annotation**
YBR256C	RIB5	1.14	Riboflavin synthase; catalyzes the last step of the riboflavin biosynthesis pathway
YML042W	CAT2,YCAT	1.14	Carnitine acetyl-CoA transferase present in both mitochondria and peroxisomes, transfers activated acetyl groups to carnitine to form acetylcarnitine which can be shuttled across membranes
YOL041C	NOP12	1.14	Nucleolar protein involved in pre-25S rRNA processing and biogenesis of large 60S ribosomal subunit; contains an RNA recognition motif (RRM); binds to Ebp2; similar to Nop13p and Nsr1p
YER187W		1.14	Putative protein of unknown function; induced in respiratory-deficient cells
YBR296C	PHO89,ITN1	1.14	Na+/Pi cotransporter, active in early growth phase; similar to phosphate transporters of Neurospora crassa; transcription regulated by inorganic phosphate concentrations and Pho4p
YNL234W		1.15	Protein of unknown function with similarity to globins; has a functional heme-binding domain; transcription is induced by hypoxia and other stress conditions; proposed to be involved in glucose signaling or metabolism; regulated by Rgt1p
YJL009W		1.15	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps CCT8/ YJL008C, a verified gene encoding a subunit of the cytosolic chaperonin Cct ring complex
YPR071W		1.15	Putative membrane protein; YPR071W is not an essential gene
YJR063W	RPA12,RRN4	1.16	RNA polymerase I subunit A12.2; contains two zinc binding domains, and the N terminal domain is responsible for anchoring to the RNA pol I complex
YCL030C	HIS4	1.16	Multifunctional enzyme containing phosphoribosyl-ATP pyrophosphatase, phosphoribosyl-AMP cyclohydrolase, and histidinol dehydrogenase activities; catalyzes the second, third, ninth and tenth steps in histidine biosynthesis
YNL141W	AAH1	1.17	Adenine deaminase (adenine aminohydrolase), converts adenine to hypoxanthine; involved in purine salvage; transcriptionally regulated by nutrient levels and growth phase; Aah1p degraded upon entry into quiescence via SCF and the proteasome
YCR054C	CTR86	1.17	Essential protein of unknown function; upstream region contains a Gcn4p responsive site suggesting a possible role in amino acid biosynthesis
YLR312C	QNQ1	1.18	Putative protein of unknown function
YNL113W	RPC19	1.19	RNA polymerase subunit AC19, common to RNA polymerases I and III

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YLR327C	TMA10,RBF9	1.19	Protein of unknown function that associates with ribosomes
YDR126W	SWF1,PSL10	1.20	Palmitoyltransferase that acts on the SNAREs Snc1p, Syn8p, Tlg1p and likely on all SNAREs; member of a family of putative palmitoyltransferases containing an Asp-His-His-Cys-cysteine rich (DHHC-CRD) domain; may have a role in vacuole fusion
YNL270C	ALP1,APL1	1.20	Arginine transporter; expression is normally very low and it is unclear what conditions would induce significant expression
YIL099W	SGA1	1.20	Intracellular sporulation-specific glucoamylase involved in glycogen degradation; induced during starvation of a/a diploids late in sporulation, but dispensable for sporulation
YKL055C	OAR1	1.21	Mitochondrial 3-oxoacyl-[acyl-carrier-protein] reductase, may comprise a type II mitochondrial fatty acid synthase along with Mct1p
YBR297W	MAL33,MALR,MAL3R	1.22	MAL-activator protein, part of complex locus MAL3; nonfunctional in genomic reference strain S288C
YKL001C	MET14	1.22	Adenylylsulfate kinase, required for sulfate assimilation and involved in methionine metabolism
YOR237W	HES1,OSH5	1.22	Protein implicated in the regulation of ergosterol biosynthesis; one of a seven member gene family with a common essential function and non-essential unique functions; similar to human oxysterol binding protein (OSBP)
YHR033W		1.23	Putative protein of unknown function; epitope-tagged protein localizes to the cytoplasm
YGL158W	RCK1	1.24	Protein kinase involved in the response to oxidative stress; identified as suppressor of S. pombe cell cycle checkpoint mutations
YER011W	TIR1,SRP1	1.24	Cell wall mannoprotein of the Srp1p/Tip1p family of serine-alanine-rich proteins; expression is downregulated at acidic pH and induced by cold shock and anaerobiosis; abundance is increased in cells cultured without shaking
YDL048C	STP4	1.24	Protein containing a Kruppel-type zinc-finger domain; has similarity to Stp1p, Stp2p, and Stp3p
YDL037C	BSC1	1.24	Protein of unconfirmed function, similar to cell surface flocculin Muc1p; ORF exhibits genomic organization compatible with a translational readthrough-dependent mode of expression
YNL195C		1.24	Putative protein of unknown function; shares a promoter with YNL194C; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YHR136C	SPL2	1.25	Protein with similarity to cyclin-dependent kinase inhibitors; downregulates low-affinity phosphate transport during phosphate limitation; overproduction suppresses a plc1 null mutation; GFP-fusion protein localizes to the cytoplasm
YBR093C	PHO5,phoE	1.25	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
YLL005C	SPO75	1.25	Meiosis-specific protein of unknown function, required for spore wall formation during sporulation; dispensable for both nuclear divisions during meiosis
YHL024W	RIM4	1.25	Putative RNA-binding protein required for the expression of early and middle sporulation genes
YER042W	MXR1,MSRA	1.26	Methionine-S-sulfoxide reductase, involved in the response to oxidative stress; protects iron-sulfur clusters from oxidative inactivation along with MXR2; involved in the regulation of lifespan
YPL119C	DBP1,LPH8	1.26	Putative ATP-dependent RNA helicase of the DEAD-box protein family; mutants show reduced stability of the 40S ribosomal subunit scanning through 5' untranslated regions of mRNAs
YLL053C		1.28	Putative protein; in the Sigma 1278B strain background YLL053C is contiguous with AQY2 which encodes an aquaporin
YDR274C		1.28	Dubious open reading frame unlikely to encode a functional protein, based on available experimental and comparative sequence data
YDR223W	CRF1	1.29	Transcriptional corepressor involved in repression of ribosomal protein (RP) gene transcription via the TOR signaling pathway which promotes accumulation of Crf1p in the nucleus; role in repression of RP genes varies by strain
YMR096W	SNZ1	1.29	Protein involved in vitamin B6 biosynthesis; member of a stationary phase-induced gene family; coregulated with SNO1; interacts with Sno1p and with Yhr198p, perhaps as a multiprotein complex containing other Snz and Sno proteins
YLL042C	ATG10,APG10	1.30	Conserved E2-like conjugating enzyme that mediates formation of the Atg12p-Atg5p conjugate, which is a critical step in autophagy
YHR126C	ANS1	1.33	Putative protein of unknown function; transcription dependent upon Azf1p
YMR244W		1.35	Putative protein of unknown function

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YDL241W		1.35	Putative protein of unknown function; YDL241W is not an essential gene
YDR524W-C		1.36	Putative protein of unknown function; small ORF identified by SAGE; deletion strains are moderately sensitive to the radiomimetic drug bleomycin
YKR060W	UTP30	1.37	Subunit of U3-containing 90S preribosome complex involved in production of 18S rRNA and assembly of small ribosomal subunit
YPR143W	RRP15	1.37	Nucleolar protein, constituent of pre-60S ribosomal particles; required for proper processing of the 27S pre-rRNA at the A3 and B1 sites to yield mature 5.8S and 25S rRNAs
YLR237W	THI7,THI10	1.37	Plasma membrane transporter responsible for the uptake of thiamine, member of the major facilitator superfamily of transporters; mutation of human ortholog causes thiamine-responsive megaloblastic anemia
YPL250C	ICY2	1.38	Protein of unknown function; mobilized into polysomes upon a shift from a fermentable to nonfermentable carbon source; potential Cdc28p substrate
YOR351C	MEK1,MRE4	1.38	Meiosis-specific serine/threonine protein kinase, functions in meiotic checkpoint, promotes recombination between homologous chromosomes by suppressing double strand break repair between sister chromatids
YNR050C	LYS9,LYS13	1.39	Saccharopine dehydrogenase (NADP+, L-glutamate-forming); catalyzes the formation of saccharopine from alpha-aminoadipate 6-semialdehyde, the seventh step in lysine biosynthesis pathway; exhibits genetic and physical interactions with TRM112
YNL179C	SRF6	1.41	Dubious open reading frame, unlikely to encode a protein; not conserved in closely related Saccharomyces species; deletion in cyr1 mutant results in loss of stress resistance
YHR092C	HXT4,RAG1,LGT1	1.43	High-affinity glucose transporter of the major facilitator superfamily, expression is induced by low levels of glucose and repressed by high levels of glucose
YNR063W		1.44	Putative zinc-cluster protein of unknown function
YEL035C	UTR5	1.45	Protein of unknown function; transcription may be regulated by Gcr1p; essential for growth under standard (aerobic) conditions but not under anaerobic conditions
YER179W	DMC1,ISC2	1.45	Meiosis-specific protein required for repair of double-strand breaks and pairing between homologous chromosomes; homolog of Rad51p and the bacterial RecA protein

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YMR120C	ADE17	1.46	Enzyme of 'de novo' purine biosynthesis containing both 5-aminoimidazole-4-carboxamide ribonucleotide transformylase and inosine monophosphate cyclohydrolase activities, isozyme of Ade16p; ade16 ade17 mutants require adenine and histidine
YFR017C		1.46	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and is induced in response to the DNA-damaging agent MMS; YFR017C is not an essential gene
YLR037C	PAU23,DAN2	1.46	Cell wall mannoprotein with similarity to Tir1p, Tir2p, Tir3p, and Tir4p; member of the seripauperin multigene family encoded mainly in subtelomeric regions; expressed under anaerobic conditions, completely repressed during aerobic growth
YDL039C	PRM7,YDL038C	1.47	Pheromone-regulated protein, predicted to have one transmembrane segment; promoter contains Gcn4p binding elements
YPL056C		1.48	Putative protein of unknown function; deletion mutant is fluconazole resistant
YDR079W	PET100	1.48	Chaperone that specifically facilitates the assembly of cytochrome c oxidase, integral to the mitochondrial inner membrane; interacts with a subcomplex of subunits VII, VIIa, and VIII (Cox7p, Cox9p, and Cox8p) but not with the holoenzyme
YER095W	RAD51,MUT5	1.49	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
YDR215C		1.50	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; null mutant displays elevated sensitivity to expression of a mutant huntingtin fragment or of alpha-synuclein
YLL052C	AQY2	1.51	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
YCR098C	GIT1	1.52	Plasma membrane permease, mediates uptake of glycerophosphoinositol and glycerophosphocholine as sources of the nutrients inositol and phosphate; expression and transport rate are regulated by phosphate and inositol availability
YMR107W	SPG4	1.52	Protein required for survival at high temperature during stationary phase; not required for growth on nonfermentable carbon sources

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells			
Systematic name	**Standard Name**	**Log2 (Fold change)**	**Gene Ontology Annotation**
YDR344C		1.54	Dubious open reading frame unlikely to encode a functional protein, based on available experimental and comparative sequence data
YDL182W	LYS20	1.55	Homocitrate synthase isozyme, catalyzes the condensation of acetyl-CoA and alpha-ketoglutarate to form homocitrate, which is the first step in the lysine biosynthesis pathway; highly similar to the other isozyme, Lys21p
YCR097W	HMRA1	1.55	Silenced copy of a1 at HMR; homeobox corepressor that interacts with Alpha2p to repress haploid-specific gene transcription in diploid cells
YER128W		1.57	Putative protein of unknown function
YJL043W		1.58	Putative protein of unknown function; YJL043W is a non-essential gene
YNR034W-A		1.58	Putative protein of unknown function; expression is regulated by Msn2p/Msn4p
YOR203W		1.58	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; overlaps 5' end of essential DED1 gene required for translation initiation
YLR349W		1.59	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; overlaps the verified ORF DIC1/YLR348C
YKR073C		1.59	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data
YIL011W	TIR3,YIB1	1.60	Cell wall mannoprotein of the Srp1p/Tip1p family of serine-alanine-rich proteins; expressed under anaerobic conditions and required for anaerobic growth
YPL104W	MSD1,LPG5	1.60	Mitochondrial aspartyl-tRNA synthetase, required for acylation of aspartyl-tRNA; yeast and bacterial aspartyl-, asparaginyl-, and lysyl-tRNA synthetases contain regions with high sequence similarity, suggesting a common ancestral gene
YEL070W	DSF1	1.61	Deletion suppressor of mpt5 mutation
YLL037W		1.61	Dubious open reading frame unlikely to encode a functional protein; overlaps 3' end of essential PRP19 gene encoding an RNA splicing factor
YBL098W	BNA4	1.61	Kynurenine 3-mono oxygenase, required for the de novo biosynthesis of NAD from tryptophan via kynurenine; expression regulated by Hst1p; putative therapeutic target for Huntington disease

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YLR400W		1.62	Dubious open reading frame unlikely to encode a functional protein, based on available experimental and comparative sequence data
YPR133W-A	TOM5,MOM8A	1.63	Component of the TOM (translocase of outer membrane) complex responsible for recognition and initial import of all mitochondrially directed proteins; involved in transfer of precursors from the Tom70p and Tom20p receptors to the Tom40p pore
YIL160C	POT1,POX3,FOX3	1.63	3-ketoacyl-CoA thiolase with broad chain length specificity, cleaves 3-ketoacyl-CoA into acyl-CoA and acetyl-CoA during beta-oxidation of fatty acids
YOL058W	ARG1,ARG10	1.64	Arginosuccinate synthetase, catalyzes the formation of L-argininosuccinate from citrulline and L-aspartate in the arginine biosynthesis pathway; potential Cdc28p substrate
YOL014W		1.65	Putative protein of unknown function
YLR363W-A		1.66	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the nucleus
YDL181W	INH1	1.68	Protein that inhibits ATP hydrolysis by the F1F0-ATP synthase; inhibitory function is enhanced by stabilizing proteins Stf1p and Stf2p; has similarity to Stf1p; has a calmodulin-binding motif and binds calmodulin in vitro
YNL332W	THI12	1.70	Protein involved in synthesis of the thiamine precursor hydroxymethylpyrimidine (HMP); member of a subtelomeric gene family including THI5, THI11, THI12, and THI13
YJL088W	ARG3,argF	1.70	Ornithine carbamoyltransferase (carbamoylphosphate:L-ornithine carbamoyltransferase), catalyzes the sixth step in the biosynthesis of the arginine precursor ornithine
YFR026C	ULI1	1.71	Putative protein of unknown function involved in and induced by the endoplasmic reticulum unfolded protein response
YPR157W		1.73	Putative protein of unknown function; induced by treatment with 8-methoxypsoralen and UVA irradiation
YHR048W	YHK8	1.74	Presumed antiporter of the DHA1 family of multidrug resistance transporters; contains 12 predicted transmembrane spans; expression of gene is up-regulated in cells exhibiting reduced susceptibility to azoles
YJL037W	IRC18	1.75	Putative protein of unknown function; expression induced in respiratory-deficient cells and in carbon-limited chemostat cultures; similar to adjacent ORF, YJL038C; null mutant displays increased levels of spontaneous Rad52p foci

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YML083C		1.76	Putative protein of unknown function; strong increase in transcript abundance during anaerobic growth compared to aerobic growth; cells deleted for YML083C do not exhibit growth defects in anerobic or anaerobic conditions
YNR064C		1.76	Epoxide hydrolase, member of the alpha/beta hydrolase fold family; may have a role in detoxification of epoxides
YER067W		1.78	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus; YER067W is not an essential gene; protein abundance is increased upon intracellular iron depletion
YJR150C	DAN1,CCW13	1.80	Cell wall mannoprotein with similarity to Tir1p, Tir2p, Tir3p, and Tir4p; expressed under anaerobic conditions, completely repressed during aerobic growth
YCL026C-A	FRM2,YCLX08C	1.83	Protein of unknown function, involved in the integration of lipid signaling pathways with cellular homeostasis; expression induced in cells treated with the mycotoxin patulin; has similarity to bacterial nitroreductases
YDL152W		1.83	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the verified ORF SAS10/YDL153C, a component of the small ribosomal subunit processosome
YPL171C	OYE3,ZRG6	1.85	Conserved NADPH oxidoreductase containing flavin mononucleotide (FMN), homologous to Oye2p with slight differences in ligand binding and catalytic properties; expression induced in cells treated with the mycotoxin patulin
YGR260W	TNA1	1.86	High affinity nicotinic acid plasma membrane permease, responsible for uptake of low levels of nicotinic acid; expression of the gene increases in the absence of extracellular nicotinic acid or para-aminobenzoate (PABA)
YFL051C		1.86	Putative protein of unknown function; YFL051C is not an essential gene
YER150W	SPI1	1.87	GPI-anchored cell wall protein involved in weak acid resistance; basal expression requires Msn2p/Msn4p; expression is induced under conditions of stress and during the diauxic shift; similar to Sed1p
YLL017W	SDC25	1.88	Non-essential Ras guanine nucleotide exchange factor (GEF) localized to the membrane; expressed in poor nutrients and on non-fermentable carbon sources; homologous to CDC25; contains a stop codon in S288C; full-length gene includes YLL016W
YGR243W	FMP43	1.93	Putative protein of unknown function; expression regulated by osmotic and alkaline stresses; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YFL020C	PAU5	1.95	Member of the seripauperin multigene family encoded mainly in subtelomeric regions; induced during alcoholic fermentation; induced by low temperature and also by anaerobic conditions; negatively regulated by oxygen and repressed by heme
YLR307C-A		1.97	Putative protein of unknown function
YDR029W		2.00	Dubious ORF unlikely to encode a protein, based on available experimental and comparative sequence data
YOR313C	SPS4	2.00	Protein whose expression is induced during sporulation; not required for sporulation; heterologous expression in E. coli induces the SOS response that senses DNA damage
YML131W		2.06	Putative protein of unknown function with similarity to medium chain dehydrogenase/reductases; expression induced by stresses including osmotic shock, DNA damaging agents, and other chemicals; GFP-fusion protein localizes to the cytoplasm
YJR095W	SFC1,ACR1	2.09	Mitochondrial succinate-fumarate transporter, transports succinate into and fumarate out of the mitochondrion; required for ethanol and acetate utilization
YGL170C	SPO74	2.10	Component of the meiotic outer plaque of the spindle pole body, involved in modifying the meiotic outer plaque that is required prior to prospore membrane formation
YJR047C	ANB1,eIF-5A	2.10	Translation elongation factor eIF-5A, previously thought to function in translation initiation; similar to and functionally redundant with Hyp2p; undergoes an essential hypusination modification; expressed under anaerobic conditions
YEL039C	CYC7	2.12	Cytochrome c isoform 2, expressed under hypoxic conditions; electron carrier of the mitochondrial intermembrane space that transfers electrons from ubiquinone-cytochrome c oxidoreductase to cytochrome c oxidase during cellular respiration
YCL048W-A		2.15	Putative protein of unknown function
YER137C		2.18	Putative protein of unknown function
YIR034C	LYS1	2.26	Saccharopine dehydrogenase (NAD+, L-lysine-forming), catalyzes the conversion of saccharopine to L-lysine, which is the final step in the lysine biosynthesis pathway
YGR138C	TPO2	2.28	Polyamine transport protein specific for spermine; localizes to the plasma membrane; transcription of TPO2 is regulated by Haa1p; member of the major facilitator superfamily
YIL014C-A		2.37	Putative protein of unknown function

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells

Systematic name	Standard Name	Log2 (Fold change)	Gene Ontology Annotation
YEL008W		2.41	Hypothetical protein predicted to be involved in metabolism
YOR072W-A		2.41	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the uncharacterized ORF YOR072W; originally identified by fungal homology and RT-PCR
YDL021W	GPM2	2.49	Homolog of Gpm1p phosphoglycerate mutase, which converts 3-phosphoglycerate to 2-phosphoglycerate in glycolysis; may be non-functional derivative of a gene duplication event
YGL033W	HOP2	2.49	Meiosis-specific protein that localizes to chromosomes, preventing synapsis between nonhomologous chromosomes and ensuring synapsis between homologs; complexes with Mnd1p to promote homolog pairing and meiotic double-strand break repair
YFR023W	PES4	2.52	Poly(A) binding protein, suppressor of DNA polymerase epsilon mutation, similar to Mip6p
YER096W	SHC1	2.56	Sporulation-specific activator of Chs3p (chitin synthase III), required for the synthesis of the chitosan layer of ascospores; has similarity to Skt5p, which activates Chs3p during vegetative growth; transcriptionally induced at alkaline pH
YLR198C		2.70	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; overlaps the verified gene SIK1/YLR197W
YBR040W	FIG1	2.70	Integral membrane protein required for efficient mating; may participate in or regulate the low affinity Ca2+ influx system, which affects intracellular signaling and cell-cell fusion during mating
YBL109W		2.75	Dubious open reading frame unlikely to encode a protein, based on experimental and comparative sequence data
YOL024W		2.77	Putative protein of unknown function; predicted to have thiol-disulfide oxidoreductase active site
YCR021C	HSP30,YRO1	2.94	Hydrophobic plasma membrane localized, stress-responsive protein that negatively regulates the H(+)-ATPase Pma1p; induced by heat shock, ethanol treatment, weak organic acid, glucose limitation, and entry into stationary phase
YML058W-A	HUG1	2.97	Protein involved in the Mec1p-mediated checkpoint pathway that responds to DNA damage or replication arrest, transcription is induced by DNA damage
YLR308W	CDA2	3.32	Chitin deacetylase, together with Cda1p involved in the biosynthesis ascospore wall component, chitosan; required for proper rigidity of the ascospore wall

Supplemental Table S3: Genes differentially expressed more than two-fold between WT and *htbK123RΔsir4* cells			
Systematic name	**Standard Name**	**Log2 (Fold change)**	**Gene Ontology Annotation**
YCL075W		3.33	Pseudogene: encodes fragment of Ty Pol protein
YLL046C	RNP1	3.64	Ribonucleoprotein that contains two RNA recognition motifs (RRM)
YFL015C		3.64	Dubious open reading frame unlikely to encode a protein; partially overlaps dubious ORF YFL015W-A; YFL015C is not an essential gene
YPL073C		3.83	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; completely overlaps with verified gene UBP16/YPL072W; may interact with ribosome based on co-purification experiments
YOR255W	OSW1	3.92	Protein involved in sporulation; required for the construction of the outer spore wall layers; required for proper localization of Spo14p
YCL074W		4.08	Pseudogene: encodes fragment of Ty Pol protein
YCL069W	VBA3	--*	Permease of basic amino acids in the vacuolar membrane
YCL073C		--*	Protein of unconfirmed function; displays a topology characteristic of the Major Facilitators Superfamily of membrane proteins; coding sequence 98% identical to that of YKR106W
YCL076W		--*	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data
YDR544C		--*	Dubious open reading frame unlikely to encode a functional protein, based on available experimental and comparative sequence data
YFR057W		--*	Putative protein of unknown function
YGR273C		--*	Putative protein of unknown function; expression downregulated by treatment with 8-methoxypsoralen plus UVA irradiation; YGR273C is not an essential gene
YOR186W		--*	Putative protein of unknown function; proper regulation of expression during heat stress is sphingolipid-dependent

* These genes were not expressed in the wild-type strain, but are expressed in the *htbK123RΔsir4* mutant.

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YCL074W		2.99	1.08	Pseudogene: encodes fragment of Ty Pol protein
YML058W-A	HUG1	1.23	1.73	Protein involved in the Mec1p-mediated checkpoint pathway that responds to DNA damage or replication arrest, transcription is induced by DNA damage
YPL171C	OYE3	1.14	0.71	Conserved NADPH oxidoreductase containing flavin mononucleotide (FMN), homologous to Oye2p with different ligand binding and catalytic properties; has potential roles in oxidative stress response and programmed cell death
YNR064C		1.09	0.67	Epoxide hydrolase, member of the alpha/beta hydrolase fold family; may have a role in detoxification of epoxides
YJL037W	IRC18	1.04	0.70	Putative protein of unknown function; expression induced in respiratory-deficient cells and in carbon-limited chemostat cultures; similar to adjacent ORF, YJL038C; null mutant displays increased levels of spontaneous Rad52p foci
YLR349W		1.02	0.57	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; overlaps the verified ORF DIC1/YLR348C
YBR093C	PHO5	1.01	0.25	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
YFR026C	ULI1	0.97	0.73	Putative protein of unknown function involved in and induced by the endoplasmic reticulum unfolded protein response
YMR120C	ADE17	0.96	0.50	Enzyme of 'de novo' purine biosynthesis containing both 5-aminoimidazole-4-carboxamide ribonucleotide transformylase and inosine monophosphate cyclohydrolase activities, isozyme of Ade16p; ade16 ade17 mutants require adenine and histidine
YDR524W-C		0.90	0.46	Putative protein of unknown function; small ORF identified by SAGE; deletion strains are moderately sensitive to the radiomimetic drug bleomycin

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YOR203W		0.89	0.69	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; overlaps 5' end of essential DED1 gene required for translation initiation
YHR033W		0.88	0.35	Putative protein of unknown function; epitope-tagged protein localizes to the cytoplasm
YFR017C		0.86	0.60	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and is induced in response to the DNA-damaging agent MMS; YFR017C is not an essential gene
YBL039C	URA7	0.82	0.30	Major CTP synthase isozyme (see also URA8), catalyzes the ATP-dependent transfer of the amide nitrogen from glutamine to UTP, forming CTP, the final step in de novo biosynthesis of pyrimidines; involved in phospholipid biosynthesis
YHR136C	SPL2	0.81	0.43	Protein with similarity to cyclin-dependent kinase inhibitors; downregulates low-affinity phosphate transport during phosphate limitation; overproduction suppresses a plc1 null mutation; GFP-fusion protein localizes to the cytoplasm
YGL111W	NSA1	0.78	0.29	Constituent of 66S pre-ribosomal particles, involved in 60S ribosomal subunit biogenesis
YHR092C	HXT4	0.78	0.67	High-affinity glucose transporter of the major facilitator superfamily, expression is induced by low levels of glucose and repressed by high levels of glucose
YGR138C	TPO2	0.74	1.53	Polyamine transport protein specific for spermine; localizes to the plasma membrane; transcription of TPO2 is regulated by Haa1p; member of the major facilitator superfamily
YBL098W	BNA4	0.73	0.88	Kynurenine 3-mono oxygenase, required for the de novo biosynthesis of NAD from tryptophan via kynurenine; expression regulated by Hst1p; putative therapeutic target for Huntington disease
YGR260W	TNA1	0.73	1.13	High affinity nicotinic acid plasma membrane permease, responsible for uptake of low levels of nicotinic acid; expression of the gene increases in the absence of extracellular nicotinic acid or para-aminobenzoate (PABA)

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YNL141W	AAH1	0.71	0.46	Adenine deaminase (adenine aminohydrolase), converts adenine to hypoxanthine; involved in purine salvage; transcriptionally regulated by nutrient levels and growth phase; Aah1p degraded upon entry into quiescence via SCF and the proteasome
YLR303W	MET17	0.71	0.30	Methionine and cysteine synthase (O-acetyl homoserine-O-acetyl serine sulfhydrylase), required for sulfur amino acid synthesis
YPL093W	NOG1	0.70	0.20	Putative GTPase that associates with free 60S ribosomal subunits in the nucleolus and is required for 60S ribosomal subunit biogenesis; constituent of 66S pre-ribosomal particles; member of the ODN family of nucleolar G-proteins
YER150W	SPI1	0.70	1.17	GPI-anchored cell wall protein involved in weak acid resistance; basal expression requires Msn2p/Msn4p; expression is induced under conditions of stress and during the diauxic shift; similar to Sed1p
YDL008W	APC11	0.70	0.26	Catalytic core subunit of the Anaphase-Promoting Complex/Cyclosome (APC/C), which is a ubiquitin-protein ligase required for degradation of anaphase inhibitors, including mitotic cyclins, during the metaphase/anaphase transition
YGR103W	NOP7	0.69	0.38	Component of several different pre-ribosomal particles; forms a complex with Ytm1p and Erb1p that is required for maturation of the large ribosomal subunit; required for exit from G0 and the initiation of cell proliferation
YPR016C	TIF6	0.69	0.20	Constituent of 66S pre-ribosomal particles, has similarity to human translation initiation factor 6 (eIF6); may be involved in the biogenesis and or stability of 60S ribosomal subunits
YML093W	UTP14	0.68	0.22	Subunit of U3-containing Small Subunit (SSU) processome complex involved in production of 18S rRNA and assembly of small ribosomal subunit
YCR098C	GIT1	0.67	0.84	Plasma membrane permease, mediates uptake of glycerophosphoinositol and glycerophosphocholine as sources of the nutrients inositol and phosphate; expression and transport rate are regulated by phosphate and inositol availability

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YMR229C	RRP5	0.65	0.23	RNA binding protein with preference for single stranded tracts of U's involved in synthesis of both 18S and 5.8S rRNAs; component of both the ribosomal small subunit (SSU) processosome and the 90S preribosome
YLR276C	DBP9	0.64	0.23	ATP-dependent RNA helicase of the DEAD-box family involved in biogenesis of the 60S ribosomal subunit
YMR096W	SNZ1	0.63	0.66	Protein involved in vitamin B6 biosynthesis; member of a stationary phase-induced gene family; coregulated with SNO1; interacts with Sno1p and with Yhr198p, perhaps as a multiprotein complex containing other Snz and Sno proteins
YNL248C	RPA49	0.63	0.47	RNA polymerase I subunit A49
YIR034C	LYS1	0.62	1.64	Saccharopine dehydrogenase (NAD+, L-lysine-forming), catalyzes the conversion of saccharopine to L-lysine, which is the final step in the lysine biosynthesis pathway
YNL308C	KRI1	0.62	0.42	Essential nucleolar protein required for 40S ribosome biogenesis; physically and functionally interacts with Krr1p
YHR170W	NMD3	0.61	0.24	Protein involved in nuclear export of the large ribosomal subunit; acts as a Crm1p-dependent adapter protein for export of nascent ribosomal subunits through the nuclear pore complex
YHR197W	RIX1	0.60	0.36	Essential component of the Rix1 complex (Rix1p, Ipi1p, Ipi3p) that is required for processing of ITS2 sequences from 35S pre-rRNA; Rix1 complex associates with Mdn1p in pre-60S ribosomal particles
YOR341W	RPA190	0.60	0.18	RNA polymerase I largest subunit A190
YOR202W	HIS3	0.58	0.39	Imidazoleglycerol-phosphate dehydratase, catalyzes the sixth step in histidine biosynthesis; mutations cause histidine auxotrophy and sensitivity to Cu, Co, and Ni salts; transcription is regulated by general amino acid control via Gcn4p
YBR256C	RIB5	0.58	0.56	Riboflavin synthase; catalyzes the last step of the riboflavin biosynthesis pathway

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YNL277W	MET2	0.57	0.52	L-homoserine-O-acetyltransferase, catalyzes the conversion of homoserine to O-acetyl homoserine which is the first step of the methionine biosynthetic pathway
YDL167C	NRP1	0.57	0.33	Putative RNA binding protein of unknown function; localizes to stress granules induced by glucose deprivation; predicted to be involved in ribosome biogenesis
YDR500C	RPL37B	0.56	0.26	Protein component of the large (60S) ribosomal subunit, has similarity to Rpl37Ap and to rat L37 ribosomal protein
YJL136C	RPS21B	0.56	0.17	Protein component of the small (40S) ribosomal subunit; nearly identical to Rps21Ap and has similarity to rat S21 ribosomal protein
YDL048C	STP4	0.56	0.68	Protein containing a Kruppel-type zinc-finger domain; has similarity to Stp1p, Stp2p, and Stp3p
YAL036C	RBG1	0.56	0.26	Member of the DRG family of GTP-binding proteins; associates with translating ribosomes; interacts with Tma46p, Ygr250cp, Gir2p and Yap1p via two-hybrid
YKL009W	MRT4	0.55	0.30	Protein involved in mRNA turnover and ribosome assembly, localizes to the nucleolus
YLR409C	UTP21	0.55	0.36	Subunit of U3-containing 90S preribosome and Small Subunit (SSU) processome complexes involved in production of 18S rRNA and assembly of small ribosomal subunit; synthetic defect with STI1 Hsp90 cochaperone; human homolog linked to glaucoma
YJR137C	MET5	0.54	0.44	Sulfite reductase beta subunit, involved in amino acid biosynthesis, transcription repressed by methionine
YPR144C	NOC4	0.54	0.42	Nucleolar protein, forms a complex with Nop14p that mediates maturation and nuclear export of 40S ribosomal subunits
YEL033W	MTC7	0.54	0.44	Predicted metabolic role based on network analysis derived from ChIP experiments, a large-scale deletion study and localization of transcription factor binding sites; null mutant is sensitive to temperature oscillation in a cdc13-1 mutant

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YKL099C	UTP11	0.54	0.40	Subunit of U3-containing Small Subunit (SSU) processome complex involved in production of 18S rRNA and assembly of small ribosomal subunit
YEL054C	RPL12A	0.54	0.37	Protein component of the large (60S) ribosomal subunit, nearly identical to Rpl12Bp; rpl12a rpl12b double mutant exhibits slow growth and slow translation; has similarity to E. coli L11 and rat L12 ribosomal proteins
YDR496C	PUF6	0.53	0.39	Pumilio-homology domain protein that binds the 3' UTR of ASH1 mRNA and represses its translation, resulting in proper asymmetric localization of ASH1 mRNA; also co-sediments with the 60S ribosomal subunit and is required for its biogenesis
YPL086C	ELP3	0.52	0.36	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
YDL031W	DBP10	0.52	0.32	Putative ATP-dependent RNA helicase of the DEAD-box protein family, constituent of 66S pre-ribosomal particles; essential protein involved in ribosome biogenesis
YGL055W	OLE1	0.51	0.45	Delta(9) fatty acid desaturase, required for monounsaturated fatty acid synthesis and for normal distribution of mitochondria
YNL112W	DBP2	0.49	0.20	Essential ATP-dependent RNA helicase of the DEAD-box protein family, involved in nonsense-mediated mRNA decay and rRNA processing
YCL054W	SPB1	0.48	0.28	AdoMet-dependent methyltransferase involved in rRNA processing and 60S ribosomal subunit maturation; methylates G2922 in the tRNA docking site of the large subunit rRNA and in the absence of snR52, U2921; suppressor of PAB1 mutants
YDR465C	RMT2	0.48	0.43	Arginine N5 methyltransferase; methylates ribosomal protein Rpl12 (L12) on Arg67
YCL059C	KRR1	0.48	0.38	Essential nucleolar protein required for the synthesis of 18S rRNA and for the assembly of 40S ribosomal subunit

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YJL151C	SNA3	0.47	0.30	Integral membrane protein localized to vacuolar intralumenal vesicles, computational analysis of large-scale protein-protein interaction data suggests a possible role in either cell wall synthesis or protein-vacuolar targeting
YDL153C	SAS10	0.46	0.27	Essential subunit of U3-containing Small Subunit (SSU) processome complex involved in production of 18S rRNA and assembly of small ribosomal subunit; disrupts silencing when overproduced
YDL166C	FAP7	0.46	0.34	Essential NTPase required for small ribosome subunit synthesis, mediates processing of the 20S pre-rRNA at site D in the cytoplasm but associates only transiently with 43S preribosomes via Rps14p, may be the endonuclease for site D
YOR303W	CPA1	0.45	0.30	Small subunit of carbamoyl phosphate synthetase, which catalyzes a step in the synthesis of citrulline, an arginine precursor; translationally regulated by an attenuator peptide encoded by YOR302W within the CPA1 mRNA 5'-leader
YLR194C		0.45	0.39	Structural constituent of the cell wall attached to the plasma membrane by a GPI-anchor; expression is upregulated in response to cell wall stress
YOL077C	BRX1	0.44	0.40	Nucleolar protein, constituent of 66S pre-ribosomal particles; depletion leads to defects in rRNA processing and a block in the assembly of large ribosomal subunits; possesses a sigma (70)-like RNA-binding motif
YDR120C	TRM1	0.43	0.31	tRNA methyltransferase; two forms of the protein are made by alternative translation starts; localizes to both the nucleus and mitochondrion to produce the modified base N2,N2-dimethylguanosine in tRNAs in both compartments
YLR197W	NOP56	0.42	0.33	Essential evolutionarily-conserved nucleolar protein component of the box C/D snoRNP complexes that direct 2'-O-methylation of pre-rRNA during its maturation; overexpression causes spindle orientation defects

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion				
Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YLL034C	RIX7	0.42	0.31	Putative ATPase of the AAA family, required for export of pre-ribosomal large subunits from the nucleus; distributed between the nucleolus, nucleoplasm, and nuclear periphery depending on growth conditions
YCL036W	GFD2	0.41	0.25	Protein of unknown function, identified as a high-copy suppressor of a dbp5 mutation
YLL045C	RPL8B	0.40	0.28	Ribosomal protein L4 of the large (60S) ribosomal subunit, nearly identical to Rpl8Ap and has similarity to rat L7a ribosomal protein; mutation results in decreased amounts of free 60S subunits
YGR175C	ERG1	0.40	0.16	Squalene epoxidase, catalyzes the epoxidation of squalene to 2,3-oxidosqualene; plays an essential role in the ergosterol-biosynthesis pathway and is the specific target of the antifungal drug terbinafine
YKL014C	URB1	0.39	0.31	Nucleolar protein required for the normal accumulation of 25S and 5.8S rRNAs, associated with the 27SA2 pre-ribosomal particle; proposed to be involved in the biogenesis of the 60S ribosomal subunit
YNL182C	IPI3	0.39	0.29	Essential component of the Rix1 complex (Rix1p, Ipi1p, Ipi3p) that is required for processing of ITS2 sequences from 35S pre-rRNA; highly conserved and contains WD40 motifs; Rix1 complex associates with Mdn1p in pre-60S ribosomal particles
YLR447C	VMA6	0.37	0.19	Subunit d of the five-subunit V0 integral membrane domain of vacuolar H+-ATPase (V-ATPase), an electrogenic proton pump found in the endomembrane system; stabilizes VO subunits; required for V1 domain assembly on the vacuolar membrane
YHR146W	CRP1	0.37	0.47	Protein that binds to cruciform DNA structures
YMR217W	GUA1	0.36	0.44	GMP synthase, an enzyme that catalyzes the second step in the biosynthesis of GMP from inosine 5'-phosphate (IMP); transcription is not subject to regulation by guanine but is negatively regulated by nutrient starvation

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YPL019C	VTC3	0.36	0.36	Subunit of the vacuolar transporter chaperone (VTC) complex involved in membrane trafficking, vacuolar polyphosphate accumulation, microautophagy and non-autophagic vacuolar fusion
YLR106C	MDN1	0.34	0.18	Huge dynein-related AAA-type ATPase (midasin), forms extended pre-60S particle with the Rix1 complex (Rix1p-Ipi1p-Ipi3p); acts in removal of ribosomal biogenesis factors at successive steps of pre-60S assembly and export from nucleus
YPL090C	RPS6A	0.34	0.16	Protein component of the small (40S) ribosomal subunit; identical to Rps6Bp and has similarity to rat S6 ribosomal protein
YLR344W	RPL26A	0.33	0.47	Protein component of the large (60S) ribosomal subunit, nearly identical to Rpl26Bp and has similarity to E. coli L24 and rat L26 ribosomal proteins; binds to 5.8S rRNA
YLR222C	UTP13	0.32	0.40	Nucleolar protein, component of the small subunit (SSU) processome containing the U3 snoRNA that is involved in processing of pre-18S rRNA
YBL004W	UTP20	0.31	0.43	Component of the small-subunit (SSU) processome, which is involved in the biogenesis of the 18S rRNA
YCR031C	RPS14A	0.31	0.25	Ribosomal protein 59 of the small subunit, required for ribosome assembly and 20S pre-rRNA processing; mutations confer cryptopleurine resistance; nearly identical to Rps14Bp and similar to E. coli S11 and rat S14 ribosomal proteins
YPR163C	TIF3	0.31	0.20	Translation initiation factor eIF-4B, has RNA annealing activity; contains an RNA recognition motif and binds to single-stranded RNA
YJL200C	ACO2	0.31	0.48	Putative mitochondrial aconitase isozyme; similarity to Aco1p, an aconitase required for the TCA cycle; expression induced during growth on glucose, by amino acid starvation via Gcn4p, and repressed on ethanol
YMR242C	RPL20A	0.30	0.25	Protein component of the large (60S) ribosomal subunit, nearly identical to Rpl20Bp and has similarity to rat L18a ribosomal protein

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YBR011C	IPP1	0.29	0.33	Cytoplasmic inorganic pyrophosphatase (PPase), homodimer that catalyzes the rapid exchange of oxygens from Pi with water, highly expressed and essential for viability, active-site residues show identity to those from E. coli PPase
YJL050W	MTR4	0.28	0.22	ATP-dependent 3'-5' RNA helicase of the Dead-box family, involved in nuclear RNA processing and degradation both as a component of the TRAMP complex and in TRAMP independent processes; has a KOW domain that shows RNA binding activity
YOR310C	NOP58	0.27	0.17	Protein involved in pre-rRNA processing, 18S rRNA synthesis, and snoRNA synthesis; component of the small subunit processome complex, which is required for processing of pre-18S rRNA
YKL172W	EBP2	0.27	0.26	Essential protein required for the maturation of 25S rRNA and 60S ribosomal subunit assembly, localizes to the nucleolus; constituent of 66S pre-ribosomal particles
YGR286C	BIO2	0.26	0.54	Biotin synthase, catalyzes the conversion of dethiobiotin to biotin, which is the last step of the biotin biosynthesis pathway; complements E. coli bioB mutant
YJL174W	KRE9	0.25	0.27	Glycoprotein involved in cell wall beta-glucan assembly; null mutation leads to severe growth defects, aberrant multibudded morphology, and mating defects
YIL075C	RPN2	0.25	0.31	Subunit of the 26S proteasome, substrate of the N-acetyltransferase Nat1p
YDL082W	RPL13A	0.24	0.29	Protein component of the large (60S) ribosomal subunit, nearly identical to Rpl13Bp; not essential for viability; has similarity to rat L13 ribosomal protein
YNL247W		0.24	0.25	Cysteinyl-tRNA synthetase; may interact with ribosomes, based on co-purification experiments
YBR189W	RPS9B	0.23	0.15	Protein component of the small (40S) ribosomal subunit; nearly identical to Rps9Ap and has similarity to E. coli S4 and rat S9 ribosomal proteins

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YFL038C	YPT1	0.22	0.21	Rab family GTPase, involved in the ER-to-Golgi step of the secretory pathway; complex formation with the Rab escort protein Mrs6p is required for prenylation of Ypt1p by protein geranylgeranyltransferase type II (Bet2p-Bet4p)
YIL052C	RPL34B	0.22	0.20	Protein component of the large (60S) ribosomal subunit, nearly identical to Rpl34Ap and has similarity to rat L34 ribosomal protein
YMR308C	PSE1	0.21	0.31	Karyopherin/importin that interacts with the nuclear pore complex; acts as the nuclear import receptor for specific proteins, including Pdr1p, Yap1p, Ste12p, and Aft1p
YGL189C	RPS26A	0.21	0.30	Protein component of the small (40S) ribosomal subunit; nearly identical to Rps26Bp and has similarity to rat S26 ribosomal protein
YHR021C	RPS27B	0.21	0.27	Protein component of the small (40S) ribosomal subunit; nearly identical to Rps27Ap and has similarity to rat S27 ribosomal protein
YJL008C	CCT8	0.20	0.25	Subunit of the cytosolic chaperonin Cct ring complex, related to Tcp1p, required for the assembly of actin and tubulins in vivo
YEL027W	CUP5	0.19	0.23	Proteolipid subunit of the vacuolar H(+)-ATPase V0 sector (subunit c; dicyclohexylcarbodiimide binding subunit); required for vacuolar acidification and important for copper and iron metal ion homeostasis
YHR190W	ERG9	0.19	0.23	Farnesyl-diphosphate farnesyl transferase (squalene synthase), joins two farnesyl pyrophosphate moieties to form squalene in the sterol biosynthesis pathway
YOL059W	GPD2	0.19	0.19	NAD-dependent glycerol 3-phosphate dehydrogenase, homolog of Gpd1p, expression is controlled by an oxygen-independent signaling pathway required to regulate metabolism under anoxic conditions; located in cytosol and mitochondria
YML028W	TSA1	0.18	0.24	Thioredoxin peroxidase, acts as both a ribosome-associated and free cytoplasmic antioxidant; self-associates to form a high-molecular weight chaperone complex under oxidative stress; deletion results in mutator phenotype

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YBL092W	RPL32	0.18	0.19	Protein component of the large (60S) ribosomal subunit, has similarity to rat L32 ribosomal protein; overexpression disrupts telomeric silencing
YER131W	RPS26B	0.18	0.18	Protein component of the small (40S) ribosomal subunit; nearly identical to Rps26Ap and has similarity to rat S26 ribosomal protein
YML056C	IMD4	0.16	0.37	Inosine monophosphate dehydrogenase, catalyzes the first step of GMP biosynthesis, member of a four-gene family in S. cerevisiae, constitutively expressed
YML063W	RPS1B	0.12	0.29	Ribosomal protein 10 (rp10) of the small (40S) subunit; nearly identical to Rps1Ap and has similarity to rat S3a ribosomal protein
YLL053C		1.97	-0.70	Putative protein; in the Sigma 1278B strain background YLL053C is contiguous with AQY2 which encodes an aquaporin
YCL030C	HIS4	1.53	-0.37	Multifunctional enzyme containing phosphoribosyl-ATP pyrophosphatase, phosphoribosyl-AMP cyclohydrolase, and histidinol dehydrogenase activities; catalyzes the second, third, ninth and tenth steps in histidine biosynthesis
YDR534C	FIT1	1.47	-1.00	Mannoprotein that is incorporated into the cell wall via a glycosylphosphatidylinositol (GPI) anchor, involved in the retention of siderophore-iron in the cell wall
YFL011W	HXT10	1.38	-1.21	Putative hexose transporter, expressed at low levels and expression is repressed by glucose
YLR437C	DIF1	1.24	-0.39	Protein that regulates the nuclear localization of ribonucleotide reductase Rnr2p and Rnr4p subunits; phosphorylated by Dun1p in response to DNA damage and degraded; N-terminal half has similarity to S. pombe Spd1 protein
YPR195C		1.22	-0.89	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data
YCL033C	MXR2	1.19	-0.29	Methionine-R-sulfoxide reductase, involved in the response to oxidative stress; protects iron-sulfur clusters from oxidative inactivation along with MXR1; involved in the regulation of lifespan

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YMR011W	HXT2	1.17	-0.74	High-affinity glucose transporter of the major facilitator superfamily, expression is induced by low levels of glucose and repressed by high levels of glucose
YDL218W		1.17	-0.57	Putative protein of unknown function; YDL218W transcription is regulated by Azf1p and induced by starvation and aerobic conditions; expression also induced in cells treated with the mycotoxin patulin
YGR032W	GSC2	1.14	-0.95	Catalytic subunit of 1,3-beta-glucan synthase, involved in formation of the inner layer of the spore wall; activity positively regulated by Rho1p and negatively by Smk1p; has similarity to an alternate catalytic subunit, Fks1p (Gsc1p)
YDR524C-B		1.14	-0.67	Putative protein of unknown function
YKL216W	URA1	1.12	-0.50	Dihydroorotate dehydrogenase, catalyzes the fourth enzymatic step in the de novo biosynthesis of pyrimidines, converting dihydroorotic acid into orotic acid
YGL126W	SCS3	1.12	-0.43	Protein required for inositol prototrophy, identified as an ortholog of the FIT family of proteins involved in triglyceride droplet biosynthesis; disputed role in the synthesis of inositol phospholipids from inositol
YPL223C	GRE1	1.09	-0.80	Hydrophilin of unknown function; stress induced (osmotic, ionic, oxidative, heat shock and heavy metals); regulated by the HOG pathway
YAR050W	FLO1	1.07	-0.57	Lectin-like protein involved in flocculation, cell wall protein that binds to mannose chains on the surface of other cells, confers floc-forming ability that is chymotrypsin sensitive and heat resistant; similar to Flo5p
YLR374C		1.06	-0.75	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the uncharacterized ORF STP3/YLR375W
YCL027W	FUS1	1.06	-1.29	Membrane protein localized to the shmoo tip, required for cell fusion; expression regulated by mating pheromone; proposed to coordinate signaling, fusion, and polarization events required for fusion; potential Cdc28p substrate

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YNR065C		1.05	-0.53	Protein of unknown function; protein-protein interactions suggest a possible role in actin patch formation; YNR065C is not an essential gene
YCR047C	BUD23	0.95	-0.27	Methyltransferase, methylates residue G1575 of 18S rRNA; required for rRNA processing and nuclear export of 40S ribosomal subunits independently of methylation activity; diploid mutant displays random budding pattern
YNR066C		0.93	-1.24	Putative membrane-localized protein of unknown function
YBL081W		0.90	-0.44	Non-essential protein of unknown function; null mutation results in a decrease in plasma membrane electron transport
YER153C	PET122	0.90	-0.84	Mitochondrial translational activator specific for the COX3 mRNA, acts together with Pet54p and Pet494p; located in the mitochondrial inner membrane
YJR114W		0.90	-0.62	Dubious open reading frame unlikely to encode a protein, based on available experimental and comparative sequence data; partially overlaps the verified ORF RSM7/YJR113C
YER018C	SPC25	0.89	-0.94	Component of the evolutionarily conserved kinetochore-associated Ndc80 complex (Ndc80p-Nuf2p-Spc24p-Spc25p); involved in chromosome segregation, spindle checkpoint activity and kinetochore clustering
YLR420W	URA4	0.77	-0.40	Dihydroorotase, catalyzes the third enzymatic step in the de novo biosynthesis of pyrimidines, converting carbamoyl-L-aspartate into dihydroorotate
YML113W	DAT1	0.77	-0.50	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
YIR019C	MUC1	0.76	-0.55	GPI-anchored cell surface glycoprotein (flocculin) required for pseudohyphal formation, invasive growth, flocculation, and biofilms; transcriptionally regulated by the MAPK pathway (via Ste12p and Tec1p) and the cAMP pathway (via Flo8p)

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YNR046W	TRM112	0.75	-0.35	Subunit of tRNA methyltransferase (MTase) complexes in combination with Trm9p and Trm11p; subunit of complex with Mtq2p that methylates Sup45p (eRF1) in the ternary complex eRF1-eRF3-GTP; deletion confers resistance to zymocin
YGL255W	ZRT1	0.75	-0.52	High-affinity zinc transporter of the plasma membrane, responsible for the majority of zinc uptake; transcription is induced under low-zinc conditions by the Zap1p transcription factor
YER040W	GLN3	0.74	-0.73	Transcriptional activator of genes regulated by nitrogen catabolite repression (NCR), localization and activity regulated by quality of nitrogen source
YAL020C	ATS1	0.74	-0.46	Protein required, with Elongator complex, Kti11p, and Kti12p, for modification of wobble nucleosides in tRNA; has a potential role in regulatory interactions between microtubules and the cell cycle
YDL160C	DHH1	0.74	-0.33	Cytoplasmic DExD/H-box helicase, stimulates mRNA decapping, coordinates distinct steps in mRNA function and decay, interacts with both the decapping and deadenylase complexes, may have a role in mRNA export and translation
YCR051W		0.74	-0.76	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus; contains ankyrin (Ank) repeats; YCR051W is not an essential gene
YGL026C	TRP5	0.73	-0.28	Tryptophan synthase, catalyzes the last step of tryptophan biosynthesis; regulated by the general control system of amino acid biosynthesis
YCR048W	ARE1	0.72	-0.28	Acyl-CoA:sterol acyltransferase, isozyme of Are2p; endoplasmic reticulum enzyme that contributes the major sterol esterification activity in the absence of oxygen
YFR034C	PHO4	0.72	-0.55	Basic helix-loop-helix (bHLH) transcription factor of the myc-family; binds cooperatively with Pho2p to the PHO5 promoter; function is regulated by phosphorylation at multiple sites and by phosphate availability

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion				
Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YBR067C	TIP1	0.72	-0.75	Major cell wall mannoprotein with possible lipase activity; transcription is induced by heat- and cold-shock; member of the Srp1p/Tip1p family of serine-alanine-rich proteins
YMR245W		0.71	-0.61	Dubious open reading frame unlikely to encode a functional protein, based on available experimental and comparative sequence data
YBR048W	RPS11B	0.71	-0.25	Protein component of the small (40S) ribosomal subunit; identical to Rps11Ap and has similarity to E. coli S17 and rat S11 ribosomal proteins
YBR289W	SNF5	0.71	-0.75	Subunit of the SWI/SNF chromatin remodeling complex involved in transcriptional regulation; functions interdependently in transcriptional activation with Snf2p and Snf6p
YLR449W	FPR4	0.70	-0.59	Peptidyl-prolyl cis-trans isomerase (PPIase) (proline isomerase) localized to the nucleus; catalyzes isomerization of proline residues in histones H3 and H4, which affects lysine methylation of those histones
YML102W	CAC2	0.70	-0.51	Component of the chromatin assembly complex (with Rlf2p and Msi1p) that assembles newly synthesized histones onto recently replicated DNA, required for building functional kinetochores, conserved from yeast to humans
YHR211W	FLO5	0.69	-0.45	Lectin-like cell wall protein (flocculin) involved in flocculation, binds to mannose chains on the surface of other cells, confers floc-forming ability that is chymotrypsin resistant but heat labile; similar to Flo1p
YBR016W		0.69	-0.39	Plasma membrane protein of unknown function, predicted to be palmitoylated; has similarity to hydrophilins, which are hydrophilic, glycine-rich proteins involved in the adaptive response to hyperosmotic conditions
YDR297W	SUR2	0.68	-0.64	Sphinganine C4-hydroxylase, catalyses the conversion of sphinganine to phytosphingosine in sphingolipid biosyntheis
YFL010C	WWM1	0.66	-1.11	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

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion				
Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YGL198W	YIP4	0.65	-0.69	Protein that interacts with Rab GTPases, localized to late Golgi vesicles; computational analysis of large-scale protein-protein interaction data suggests a possible role in vesicle-mediated transport
YOR188W	MSB1	0.65	-0.87	Protein involved in positive regulation of both 1,3-beta-glucan synthesis and the Pkc1p-MAPK pathway, potential Cdc28p substrate; multicopy suppressor of temperature-sensitive mutations in CDC24 and CDC42, and of mutations in BEM4
YNL322C	KRE1	0.65	-0.26	Cell wall glycoprotein involved in beta-glucan assembly; serves as a K1 killer toxin membrane receptor
YLR114C	AVL9	0.64	-0.53	Conserved protein involved in exocytic transport from the Golgi; mutation is synthetically lethal with apl2 vps1 double mutation; member of a protein superfamily with orthologs in diverse organisms
YKL056C	TMA19	0.64	-0.27	Protein that associates with ribosomes; homolog of translationally controlled tumor protein; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and relocates to the mitochondrial outer surface upon oxidative stress
YCR059C	YIH1	0.63	-0.28	Protein that inhibits activation of Gcn2p, an eIF2 alpha subunit protein kinase, by competing for Gcn1p binding, thus impacting gene expression in response to starvation; has sequence and functional similarity to the mouse IMPACT gene
YDR388W	RVS167	0.63	-0.84	Actin-associated protein, interacts with Rvs161p to regulate actin cytoskeleton, endocytosis, and viability following starvation or osmotic stress; homolog of mammalian amphiphysin
YIL153W	RRD1	0.63	-0.38	Peptidyl-prolyl cis/trans-isomerase, activator of the phosphotyrosyl phosphatase activity of PP2A; involved in G1 phase progression, microtubule dynamics, bud morphogenesis and DNA repair; subunit of the Tap42p-Sit4p-Rrd1p complex
YMR108W	ILV2	0.63	-0.24	Acetolactate synthase, catalyses the first common step in isoleucine and valine biosynthesis and is the target of several classes of inhibitors, localizes to the mitochondria; expression of the gene is under general amino acid control

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YMR236W	TAF9	0.61	-0.41	Subunit (17 kDa) of TFIID and SAGA complexes, involved in RNA polymerase II transcription initiation and in chromatin modification, similar to histone H3
YMR182C	RGM1	0.61	-0.57	Putative transcriptional repressor with proline-rich zinc fingers; overproduction impairs cell growth
YJR064W	CCT5	0.61	-0.25	Subunit of the cytosolic chaperonin Cct ring complex, related to Tcp1p, required for the assembly of actin and tubulins in vivo
YOR197W	MCA1	0.60	-0.31	Putative cysteine protease similar to mammalian caspases; involved in regulation of apoptosis upon hydrogen peroxide treatment; proposed to be involved in cell cycle progression
YMR070W	MOT3	0.60	-0.48	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
YOL067C	RTG1	0.60	-0.68	Transcription factor (bHLH) involved in interorganelle communication between mitochondria, peroxisomes, and nucleus
YDR025W	RPS11A	0.60	-0.19	Protein component of the small (40S) ribosomal subunit; identical to Rps11Bp and has similarity to E. coli S17 and rat S11 ribosomal proteins
YBL082C	ALG3	0.59	-0.93	Dolichol-P-Man dependent alpha(1-3) mannosyltransferase, involved in the synthesis of dolichol-linked oligosaccharide donor for N-linked glycosylation of proteins
YPL079W	RPL21B	0.58	-0.25	Protein component of the large (60S) ribosomal subunit, nearly identical to Rpl21Ap and has similarity to rat L21 ribosomal protein
YEL021W	URA3	0.58	-0.46	Orotidine-5'-phosphate (OMP) decarboxylase, catalyzes the sixth enzymatic step in the de novo biosynthesis of pyrimidines, converting OMP into uridine monophosphate (UMP); converts 5-FOA into 5-fluorouracil, a toxic compound
YER023W	PRO3	0.58	-0.71	Delta 1-pyrroline-5-carboxylate reductase, catalyzes the last step in proline biosynthesis

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YML010W	SPT5	0.58	-0.74	Protein involved in regulating Pol I and Pol II transcription and pre-mRNA processing; forms a complex with Spt4p; contains a C-terminal repeat domain that is a target for phosphorylation by Sgv1p
YPR093C	ASR1	0.57	-0.43	Ubiquitin ligase that modifies and regulates RNA Pol II; involved in a putative alcohol-responsive signaling pathway; accumulates in the nucleus under alcohol stress; contains a Ring/PHD finger domain similar to the mammalian rA9 protein
YMR246W	FAA4	0.56	-0.51	Long chain fatty acyl-CoA synthetase, activates imported fatty acids with a preference for C12:0-C16:0 chain lengths; functions in long chain fatty acid import; important for survival during stationary phase; localized to lipid particles
YIL018W	RPL2B	0.55	-0.17	Protein component of the large (60S) ribosomal subunit, identical to Rpl2Ap and has similarity to E. coli L2 and rat L8 ribosomal proteins; expression is upregulated at low temperatures
YPL234C	TFP3	0.55	-0.49	Vacuolar ATPase V0 domain subunit c', involved in proton transport activity; hydrophobic integral membrane protein (proteolipid) containing four transmembrane segments; N and C termini are in the vacuolar lumen
YER086W	ILV1	0.54	-0.26	Threonine deaminase, catalyzes the first step in isoleucine biosynthesis; expression is under general amino acid control; ILV1 locus exhibits highly positioned nucleosomes whose organization is independent of known ILV1 regulation
YNL300W	TOS6	0.54	-0.75	Glycosylphosphatidylinositol-dependent cell wall protein, expression is periodic and decreases in respone to ergosterol perturbation or upon entry into stationary phase; depletion increases resistance to lactic acid
YNL176C		0.54	-0.65	Cell cycle-regulated gene of unknown function, promoter bound by Fkh2p
YMR043W	MCM1	0.53	-0.41	Transcription factor involved in cell-type-specific transcription and pheromone response; plays a central role in the formation of both repressor and activator complexes

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YPL131W	RPL5	0.53	-0.12	Protein component of the large (60S) ribosomal subunit with similarity to E. coli L18 and rat L5 ribosomal proteins; binds 5S rRNA and is required for 60S subunit assembly
YNR044W	AGA1	0.52	-0.81	Anchorage subunit of a-agglutinin of a-cells, highly O-glycosylated protein with N-terminal secretion signal and C-terminal signal for addition of GPI anchor to cell wall, linked to adhesion subunit Aga2p via two disulfide bonds
YPR037C	ERV2	0.52	-0.72	Flavin-linked sulfhydryl oxidase localized to the endoplasmic reticulum lumen, involved in disulfide bond formation within the ER
YGL120C	PRP43	0.52	-0.52	RNA helicase in the DEAH-box family, functions in both RNA polymerase I and polymerase II transcript metabolism, involved in release of the lariat-intron from the spliceosome
YPL163C	SVS1	0.52	-1.14	Cell wall and vacuolar protein, required for wild-type resistance to vanadate
YPR145W	ASN1	0.51	-0.31	Asparagine synthetase, isozyme of Asn2p; catalyzes the synthesis of L-asparagine from L-aspartate in the asparagine biosynthetic pathway
YDR482C	CWC21	0.51	-0.48	Protein involved in RNA splicing by the spliceosome; component of a complex containing Cef1p; interacts genetically with ISY1 and BUD13; may bind RNA; has similarity to S. pombe Cwf21p
YKL191W	DPH2	0.51	-0.27	Protein required, along with Dph1p, Kti11p, Jjj3p, and Dph5p, for synthesis of diphthamide, which is a modified histidine residue of translation elongation factor 2 (Eft1p or Eft2p); may act in a complex with Dph1p and Kti11p
YKR042W	UTH1	0.51	-1.22	Mitochondrial outer membrane and cell wall localized SUN family member involved in cell wall biogenesis and required for mitochondrial autophagy; involved in the oxidative stress response, life span during starvation, and cell death
YGR063C	SPT4	0.50	-0.75	Protein involved in the regulating Pol I and Pol II transcription, pre-mRNA processing, kinetochore function, and gene silencing; forms a complex with Spt5p

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YDR172W	SUP35	0.50	-0.16	Translation termination factor eRF3; altered protein conformation creates the [PSI(+)] prion, a dominant cytoplasmically inherited protein aggregate that alters translational fidelity and creates a nonsense suppressor phenotype
YCL009C	ILV6	0.50	-0.35	Regulatory subunit of acetolactate synthase, which catalyzes the first step of branched-chain amino acid biosynthesis; enhances activity of the Ilv2p catalytic subunit, localizes to mitochondria
YNL289W	PCL1	0.50	-0.98	Cyclin, interacts with cyclin-dependent kinase Pho85p; member of the Pcl1,2-like subfamily, involved in the regulation of polarized growth and morphogenesis and progression through the cell cycle; localizes to sites of polarized cell growth
YPL055C	LGE1	0.49	-0.72	Protein of unknown function; null mutant forms abnormally large cells, and homozygous diploid null mutant displays delayed premeiotic DNA synthesis and reduced efficiency of meiotic nuclear division
YNL208W		0.49	-0.64	Protein of unknown function; may interact with ribosomes, based on co-purification experiments; authentic, non-tagged protein is detected in purified mitochondria in high-throughput studies; potential orthologs found in other fungi
YDR476C		0.49	-0.69	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the endoplasmic reticulum; YDR476C is not an essential gene
YLR314C	CDC3	0.49	-0.20	Component of the septin ring of the mother-bud neck that is required for cytokinesis; septins recruit proteins to the neck and can act as a barrier to diffusion at the membrane, and they comprise the 10nm filaments seen with EM
YGR159C	NSR1	0.48	-0.38	Nucleolar protein that binds nuclear localization sequences, required for pre-rRNA processing and ribosome biogenesis
YOL007C	CSI2	0.47	-0.50	Protein of unknown function; green fluorescent protein (GFP)- fusion protein localizes to the mother side of the bud neck and the vacuole; YOL007C is not an essential gene

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YER055C	HIS1	0.47	-0.22	ATP phosphoribosyltransferase, a hexameric enzyme, catalyzes the first step in histidine biosynthesis; mutations cause histidine auxotrophy and sensitivity to Cu, Co, and Ni salts; transcription is regulated by general amino acid control
YDL140C	RPO21	0.47	-0.18	RNA polymerase II largest subunit B220, part of central core; phosphorylation of C-terminal heptapeptide repeat domain regulates association with transcription and splicing factors; similar to bacterial beta-prime
YAL019W	FUN30	0.47	-0.28	Protein whose overexpression affects chromosome stability, potential Cdc28p substrate; homolog of Snf2p; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies
YHR058C	MED6	0.47	-0.47	Subunit of the RNA polymerase II mediator complex; associates with core polymerase subunits to form the RNA polymerase II holoenzyme; essential for transcriptional regulation
YCR084C	TUP1	0.46	-0.57	General repressor of transcription, forms complex with Cyc8p, involved in the establishment of repressive chromatin structure through interactions with histones H3 and H4, appears to enhance expression of some genes
YPR035W	GLN1	0.46	-0.19	Glutamine synthetase (GS), synthesizes glutamine from glutamate and ammonia; with Glt1p, forms the secondary pathway for glutamate biosynthesis from ammonia; expression regulated by nitrogen source and by amino acid limitation
YKR013W	PRY2	0.46	-0.81	Protein of unknown function
YLR167W	RPS31	0.45	-0.28	Fusion protein that is cleaved to yield a ribosomal protein of the small (40S) subunit and ubiquitin; ubiquitin may facilitate assembly of the ribosomal protein into ribosomes; interacts genetically with translation factor eIF2B
YAL014C	SYN8	0.45	-0.64	Endosomal SNARE related to mammalian syntaxin 8

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YCL008C	STP22	0.45	-0.51	Component of the ESCRT-I complex, which is involved in ubiquitin-dependent sorting of proteins into the endosome; homologous to the mouse and human Tsg101 tumor susceptibility gene; mutants exhibit a Class E Vps phenotype
YOL110W	SHR5	0.44	-1.24	Subunit of a palmitoyltransferase, composed of Shr5p and Erf2p, that adds a palmitoyl lipid moiety to heterolipidated substrates such as Ras1p and Ras2p through a thioester linkage; palmitoylation is required for Ras2p membrane localization
YMR303C	ADH2	0.43	-0.36	Glucose-repressible alcohol dehydrogenase II, catalyzes the conversion of ethanol to acetaldehyde; involved in the production of certain carboxylate esters; regulated by ADR1
YDR481C	PHO8	0.43	-0.25	Repressible alkaline phosphatase, a glycoprotein localized to the vacuole; regulated by levels of inorganic phosphate and by a system consisting of Pho4p, Pho9p, Pho80p, Pho81p and Pho85p; dephosphorylates phosphotyrosyl peptides
YLR390W-A	CCW14	0.43	-0.48	Covalently linked cell wall glycoprotein, present in the inner layer of the cell wall
YOL109W	ZEO1	0.42	-0.66	Peripheral membrane protein of the plasma membrane that interacts with Mid2p; regulates the cell integrity pathway mediated by Pkc1p and Slt2p; the authentic protein is detected in a phosphorylated state in highly purified mitochondria
YOR348C	PUT4	0.42	-1.27	Proline permease, required for high-affinity transport of proline; also transports the toxic proline analog azetidine-2-carboxylate (AzC); PUT4 transcription is repressed in ammonia-grown cells
YLR179C		0.41	-0.50	Protein of unknown function with similarity to Tfs1p; transcription is activated by paralogous proteins Yrm1p and Yrr1p along with proteins involved in multidrug resistance; GFP-tagged protein localizes to the cytoplasm and nucleus
YGR285C	ZUO1	0.41	-0.16	Ribosome-associated chaperone, functions in ribosome biogenesis and, in partnership with Ssz1p and SSb1/2, as a chaperone for nascent polypeptide chains; contains a DnaJ domain and functions as a J-protein partner for Ssb1p and Ssb2p

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YNL283C	WSC2	0.41	-0.44	Partially redundant sensor-transducer of the stress-activated PKC1-MPK1 signaling pathway involved in maintenance of cell wall integrity and recovery from heat shock; secretory pathway Wsc2p is required for the arrest of secretion response
YBR249C	ARO4	0.40	-0.25	3-deoxy-D-arabino-heptulosonate-7-phosphate (DAHP) synthase, catalyzes the first step in aromatic amino acid biosynthesis and is feedback-inhibited by tyrosine or high concentrations of phenylalanine or tryptophan
YPL037C	EGD1	0.40	-0.25	Subunit beta1 of the nascent polypeptide-associated complex (NAC) involved in protein targeting, associated with cytoplasmic ribosomes; enhances DNA binding of the Gal4p activator; homolog of human BTF3b
YDL014W	NOP1	0.40	-0.61	Nucleolar protein, component of the small subunit processome complex, which is required for processing of pre-18S rRNA; has similarity to mammalian fibrillarin
YDR261C	EXG2	0.38	-0.41	Exo-1,3-beta-glucanase, involved in cell wall beta-glucan assembly; may be anchored to the plasma membrane via a glycosylphosphatidylinositol (GPI) anchor
YML123C	PHO84	0.37	-0.10	High-affinity inorganic phosphate (Pi) transporter and low-affinity manganese transporter; regulated by Pho4p and Spt7p; mutation confers resistance to arsenate; exit from the ER during maturation requires Pho86p
YER016W	BIM1	0.37	-0.85	Microtubule-binding protein that together with Kar9p makes up the cortical microtubule capture site and delays the exit from mitosis when the spindle is oriented abnormally
YER019W	ISC1	0.36	-0.62	Mitochondrial membrane localized inositol phosphosphingolipid phospholipase C, hydrolyzes complex sphingolipids to produce ceramide; activated by phosphatidylserine, cardiolipin, and phosphatidylglycerol; mediates Na+ and Li+ halotolerance
YDR232W	HEM1	0.36	-0.23	5-aminolevulinate synthase, catalyzes the first step in the heme biosynthetic pathway; an N-terminal signal sequence is required for localization to the mitochondrial matrix; expression is regulated by Hap2p-Hap3p

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YGL103W	RPL28	0.35	-0.76	Ribosomal protein of the large (60S) ribosomal subunit, has similarity to E. coli L15 and rat L27a ribosomal proteins; may have peptidyl transferase activity; can mutate to cycloheximide resistance
YBL046W	PSY4	0.35	-0.57	Putative regulatory subunit of an evolutionarily conserved protein phosphatase; localization is cell-cycle dependent and regulated by Cdc28p phosphorylation; required for cisplatin resistance; homolog of mammalian R2
YKR057W	RPS21A	0.35	-0.31	Protein component of the small (40S) ribosomal subunit; nearly identical to Rps21Bp and has similarity to rat S21 ribosomal protein
YIL154C	IMP2'	0.35	-0.57	Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat
YIL046W	MET30	0.35	-0.32	F-box protein containing five copies of the WD40 motif, controls cell cycle function, sulfur metabolism, and methionine biosynthesis as part of the ubiquitin ligase complex; interacts with and regulates Met4p, localizes within the nucleus
YOL051W	GAL11	0.34	-0.59	Subunit of the RNA polymerase II mediator complex; associates with core polymerase subunits to form the RNA polymerase II holoenzyme; affects transcription by acting as target of activators and repressors
YEL047C		0.34	-0.45	Soluble fumarate reductase, required with isoenzyme Osm1p for anaerobic growth; may interact with ribosomes, based on co-purification experiments; authentic, non-tagged protein is detected in purified mitochondria in high-throughput studies
YLR019W	PSR2	0.33	-0.90	Functionally redundant Psr1p homolog, a plasma membrane phosphatase involved in the general stress response; required with Psr1p and Whi2p for full activation of STRE-mediated gene expression, possibly through dephosphorylation of Msn2p

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YKL032C	IXR1	0.33	-0.73	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
YJR145C	RPS4A	0.33	-0.15	Protein component of the small (40S) ribosomal subunit; mutation affects 20S pre-rRNA processing; identical to Rps4Bp and has similarity to rat S4 ribosomal protein
YGR121C	MEP1	0.33	-0.42	Ammonium permease; belongs to a ubiquitous family of cytoplasmic membrane proteins that transport only ammonium (NH4+); expression is under the nitrogen catabolite repression regulation
YMR276W	DSK2	0.32	-0.55	Nuclear-enriched ubiquitin-like polyubiquitin-binding protein, required for spindle pole body (SPB) duplication and for transit through the G2/M phase of the cell cycle, involved in proteolysis, interacts with the proteasome
YOR369C	RPS12	0.32	-0.22	Protein component of the small (40S) ribosomal subunit; has similarity to rat ribosomal protein S12
YKL054C	DEF1	0.32	-0.58	RNAPII degradation factor, forms a complex with Rad26p in chromatin, enables ubiquitination and proteolysis of RNAPII present in an elongation complex; mutant is deficient in Zip1p loading onto chromosomes during meiosis
YJR072C	NPA3	0.32	-0.23	Essential, conserved, cytoplasmic ATPase; phosphorylated by the Pcl1p-Pho85p kinase complex
YKL104C	GFA1	0.31	-0.64	Glutamine-fructose-6-phosphate amidotransferase, catalyzes the formation of glucosamine-6-P and glutamate from fructose-6-P and glutamine in the first step of chitin biosynthesis
YLR340W	RPP0	0.30	-0.18	Conserved ribosomal protein P0 of the ribosomal stalk, which is involved in interaction between translational elongation factors and the ribosome; similar to rat P0, human P0, and E. coli L10e; phosphorylated on serine 302

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YNL067W	RPL9B	0.30	-0.17	Protein component of the large (60S) ribosomal subunit, nearly identical to Rpl9Ap and has similarity to E. coli L6 and rat L9 ribosomal proteins
YDR432W	NPL3	0.29	-0.39	RNA-binding protein that promotes elongation, regulates termination, and carries poly(A) mRNA from nucleus to cytoplasm; required for pre-mRNA splicing; dissociation from mRNAs promoted by Mtr10p; phosphorylated by Sky1p in the cytoplasm
YOL038W	PRE6	0.29	-0.46	Alpha 4 subunit of the 20S proteasome; may replace alpha 3 subunit (Pre9p) under stress conditions to create a more active proteasomal isoform; GFP-fusion protein relocates from cytosol to the mitochondrial surface upon oxidative stress
YIR006C	PAN1	0.29	-0.69	Part of actin cytoskeleton-regulatory complex Pan1p-Sla1p-End3p, associates with actin patches on the cell cortex; promotes protein-protein interactions essential for endocytosis; previously thought to be a subunit of poly(A) ribonuclease
YCR052W	RSC6	0.29	-0.50	Component of the RSC chromatin remodeling complex; essential for mitotic growth; homolog of SWI/SNF subunit Swp73p
YGR054W		0.28	-0.25	Eukaryotic initiation factor (eIF) 2A; associates specifically with both 40S subunits and 80 S ribosomes, and interacts genetically with both eIF5b and eIF4E; homologous to mammalian eIF2A
YGL106W	MLC1	0.28	-0.29	Essential light chain for Myo1p, light chain for Myo2p; stabilizes Myo2p by binding to the neck region; interacts with Myo1p, Iqg1p, and Myo2p to coordinate formation and contraction of the actomyosin ring with targeted membrane deposition
YKL096W-A	CWP2	0.28	-0.10	Covalently linked cell wall mannoprotein, major constituent of the cell wall; plays a role in stabilizing the cell wall; involved in low pH resistance; precursor is GPI-anchored
YER165W	PAB1	0.28	-0.15	Poly(A) binding protein, part of the 3'-end RNA-processing complex, mediates interactions between the 5' cap structure and the 3' mRNA poly(A) tail, involved in control of poly(A) tail length, interacts with translation factor eIF-4G

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YHL025W	SNF6	0.27	-0.30	Subunit of the SWI/SNF chromatin remodeling complex involved in transcriptional regulation; functions interdependently in transcriptional activation with Snf2p and Snf5p
YBR118W	TEF2	0.26	-0.30	Translational elongation factor EF-1 alpha; also encoded by TEF1; functions in the binding reaction of aminoacyl-tRNA (AA-tRNA) to ribosomes; may also have a role in tRNA re-export from the nucleus
YML026C	RPS18B	0.26	-0.17	Protein component of the small (40S) ribosomal subunit; nearly identical to Rps18Ap and has similarity to E. coli S13 and rat S18 ribosomal proteins
YJL130C	URA2	0.26	-0.60	Bifunctional carbamoylphosphate synthetase (CPSase)-aspartate transcarbamylase (ATCase), catalyzes the first two enzymatic steps in the de novo biosynthesis of pyrimidines; both activities are subject to feedback inhibition by UTP
YOR204W	DED1	0.25	-0.22	ATP-dependent DEAD (Asp-Glu-Ala-Asp)-box RNA helicase, required for translation initiation of all yeast mRNAs; mutations in human DEAD-box DBY are a frequent cause of male infertility
YGR061C	ADE6	0.25	-0.34	Formylglycinamidine-ribonucleotide (FGAM)-synthetase, catalyzes a step in the 'de novo' purine nucleotide biosynthetic pathway
YDL229W	SSB1	0.25	-0.21	Cytoplasmic ATPase that is a ribosome-associated molecular chaperone, functions with J-protein partner Zuo1p; may be involved in folding of newly-made polypeptide chains; member of the HSP70 family; interacts with phosphatase subunit Reg1p
YBR127C	VMA2	0.24	-0.22	Subunit B of the eight-subunit V1 peripheral membrane domain of the vacuolar H+-ATPase (V-ATPase), an electrogenic proton pump found throughout the endomembrane system; contains nucleotide binding sites; also detected in the cytoplasm
YER043C	SAH1	0.24	-0.72	S-adenosyl-L-homocysteine hydrolase, catabolizes S-adenosyl-L-homocysteine which is formed after donation of the activated methyl group of S-adenosyl-L-methionine (AdoMet) to an acceptor
YOL030W	GAS5	0.24	-0.31	1,3-beta-glucanosyltransferase, has similarity to Gas1p; localizes to the cell wall

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YAL039C	CYC3	0.24	-0.61	Cytochrome c heme lyase (holocytochrome c synthase), attaches heme to apo-cytochrome c (Cyc1p or Cyc7p) in the mitochondrial intermembrane space; human ortholog may have a role in microphthalmia with linear skin defects (MLS)
YLR110C	CCW12	0.24	-0.48	Cell wall mannoprotein, mutants are defective in mating and agglutination, expression is downregulated by alpha-factor
YHL020C	OPI1	0.23	-0.57	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
YMR008C	PLB1	0.23	-0.29	Phospholipase B (lysophospholipase) involved in lipid metabolism, required for deacylation of phosphatidylcholine and phosphatidylethanolamine but not phosphatidylinositol
YGL147C	RPL9A	0.23	-0.24	Protein component of the large (60S) ribosomal subunit, nearly identical to Rpl9Bp and has similarity to E. coli L6 and rat L9 ribosomal proteins
YBR286W	APE3	0.23	-0.35	Vacuolar aminopeptidase Y, processed to mature form by Prb1p
YGR189C	CRH1	0.22	-0.23	Chitin transglycosylase that functions in the transfer of chitin to beta(1-6) and beta(1-3) glucans in the cell wall; similar and functionally redundant to Utr2; localizes to sites of polarized growth; expression induced by cell wall stress
YJR073C	OPI3	0.22	-2.41	Phospholipid methyltransferase (methylene-fatty-acyl-phospholipid synthase), catalyzes the last two steps in phosphatidylcholine biosynthesis
YPR036W	VMA13	0.22	-0.35	Subunit H of the eight-subunit V1 peripheral membrane domain of the vacuolar H+-ATPase (V-ATPase), an electrogenic proton pump found throughout the endomembrane system; serves as an activator or a structural stabilizer of the V-ATPase
YFR031C-A	RPL2A	0.21	-0.17	Protein component of the large (60S) ribosomal subunit, identical to Rpl2Bp and has similarity to E. coli L2 and rat L8 ribosomal proteins

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YGR162W	TIF4631	0.20	-0.40	Translation initiation factor eIF4G, subunit of the mRNA cap-binding protein complex (eIF4F) that also contains eIF4E (Cdc33p); interacts with Pab1p and with eIF4A (Tif1p); also has a role in biogenesis of the large ribosomal subunit
YDL145C	COP1	0.20	-0.35	Alpha subunit of COPI vesicle coatomer complex, which surrounds transport vesicles in the early secretory pathway
YNL055C	POR1	0.20	-0.22	Mitochondrial porin (voltage-dependent anion channel), outer membrane protein required for the maintenance of mitochondrial osmotic stability and mitochondrial membrane permeability; phosphorylated
YHR203C	RPS4B	0.18	-0.19	Protein component of the small (40S) ribosomal subunit; identical to Rps4Ap and has similarity to rat S4 ribosomal protein
YMR202W	ERG2	0.18	-0.46	C-8 sterol isomerase, catalyzes the isomerization of the delta-8 double bond to the delta-7 position at an intermediate step in ergosterol biosynthesis
YAL042W	ERV46	0.18	-0.49	Protein localized to COPII-coated vesicles, forms a complex with Erv41p; involved in the membrane fusion stage of transport
YPR181C	SEC23	0.17	-0.35	GTPase-activating protein, stimulates the GTPase activity of Sar1p; component of the Sec23p-Sec24p heterodimer of the COPII vesicle coat, involved in ER to Golgi transport
YGL030W	RPL30	0.17	-0.11	Protein component of the large (60S) ribosomal subunit, has similarity to rat L30 ribosomal protein; involved in pre-rRNA processing in the nucleolus; autoregulates splicing of its transcript
YIL123W	SIM1	0.16	-0.79	Protein of the SUN family (Sim1p, Uth1p, Nca3p, Sun4p) that may participate in DNA replication, promoter contains SCB regulation box at -300 bp indicating that expression may be cell cycle-regulated
YJR016C	ILV3	0.16	-0.13	Dihydroxyacid dehydratase, catalyzes third step in the common pathway leading to biosynthesis of branched-chain amino acids
YOR375C	GDH1	0.15	-0.70	NADP(+)-dependent glutamate dehydrogenase, synthesizes glutamate from ammonia and alpha-ketoglutarate; rate of alpha-ketoglutarate utilization differs from Gdh3p; expression regulated by nitrogen and carbon sources

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YLR044C	PDC1	0.14	-0.31	Major of three pyruvate decarboxylase isozymes, key enzyme in alcoholic fermentation, decarboxylates pyruvate to acetaldehyde; subject to glucose-, ethanol-, and autoregulation; involved in amino acid catabolism
YLR249W	YEF3	0.12	-0.12	Gamma subunit of translational elongation factor eEF1B, stimulates the binding of aminoacyl-tRNA (AA-tRNA) to ribosomes by releasing eEF1A (Tef1p/Tef2p) from the ribosomal complex; contains two ABC cassettes; binds and hydrolyzes ATP
YJL159W	HSP150	0.11	-0.39	O-mannosylated heat shock protein that is secreted and covalently attached to the cell wall via beta-1,3-glucan and disulfide bridges; required for cell wall stability; induced by heat shock, oxidative stress, and nitrogen limitation
YOL086C	ADH1	0.11	-0.72	Alcohol dehydrogenase, fermentative isozyme active as homo- or heterotetramers; required for the reduction of acetaldehyde to ethanol, the last step in the glycolytic pathway
YDR077W	SED1	0.11	-0.74	Major stress-induced structural GPI-cell wall glycoprotein in stationary-phase cells, associates with translating ribosomes, possible role in mitochondrial genome maintenance; ORF contains two distinct variable minisatellites
YOR289W		-1.48	1.24	Putative protein of unknown function; transcription induced by the unfolded protein response; green fluorescent protein (GFP)-fusion protein localizes to both the cytoplasm and the nucleus
YHR094C	HXT1	-1.40	0.61	Low-affinity glucose transporter of the major facilitator superfamily, expression is induced by Hxk2p in the presence of glucose and repressed by Rgt1p when glucose is limiting
YDR074W	TPS2	-1.39	0.44	Phosphatase subunit of the trehalose-6-phosphate synthase/phosphatase complex, which synthesizes the storage carbohydrate trehalose; expression is induced by stress conditions and repressed by the Ras-cAMP pathway
YIL045W	PIG2	-1.32	1.21	Putative type-1 protein phosphatase targeting subunit that tethers Glc7p type-1 protein phosphatase to Gsy2p glycogen synthase

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YDR058C	TGL2	-1.31	1.59	Triacylglycerol lipase that is localized to the mitochondria; has lipolytic activity towards triacylglycerols and diacylglycerols when expressed in E. coli
YML100W	TSL1	-1.29	0.79	Large subunit of trehalose 6-phosphate synthase (Tps1p)/phosphatase (Tps2p) complex, which converts uridine-5'-diphosphoglucose and glucose 6-phosphate to trehalose, homologous to Tps3p and may share function
YOL151W	GRE2	-1.20	0.98	3-methylbutanal reductase and NADPH-dependent methylglyoxal reductase (D-lactaldehyde dehydrogenase); stress induced (osmotic, ionic, oxidative, heat shock and heavy metals); regulated by the HOG pathway
YEL020W-A	TIM9	-1.17	0.65	Essential protein of the mitochondrial intermembrane space, forms a complex with Tim10p (TIM10 complex) that delivers hydrophobic proteins to the TIM22 complex for insertion into the inner membrane
YGL104C	VPS73	-1.16	0.96	Mitochondrial protein; mutation affects vacuolar protein sorting; putative transporter; member of the sugar porter family
YPR036W-A		-1.10	0.87	Protein of unknown function; transcription is regulated by Pdr1p
YDR319C		-1.10	0.73	Putative protein of unknown function, identified as an ortholog of the highly conserved FIT family of proteins involved in triglyceride droplet biosynthesis; interacts with Sst2p and Hsp82p in high-throughput two-hybrid screens
YOR273C	TPO4	-1.09	0.70	Polyamine transport protein, recognizes spermine, putrescine, and spermidine; localizes to the plasma membrane; member of the major facilitator superfamily
YOR173W	DCS2	-1.08	1.34	Non-essential, stress induced regulatory protein containing a HIT (histidine triad) motif; modulates m7G-oligoribonucleotide metabolism; inhibits Dcs1p; regulated by Msn2p, Msn4p, and the Ras-cAMP-cAPK signaling pathway, similar to Dcs1p.
YDL022W	GPD1	-1.05	0.60	NAD-dependent glycerol-3-phosphate dehydrogenase, key enzyme of glycerol synthesis, essential for growth under osmotic stress; expression regulated by high-osmolarity glycerol response pathway; homolog of Gpd2p

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YBR149W	ARA1	-1.05	0.57	NADP+ dependent arabinose dehydrogenase, involved in carbohydrate metabolism; purified as homodimer; naturally occurs with a N-terminus degradation product
YGL037C	PNC1	-1.03	1.26	Nicotinamidase that converts nicotinamide to nicotinic acid as part of the NAD(+) salvage pathway, required for life span extension by calorie restriction; PNC1 expression responds to all known stimuli that extend replicative life span
YOR036W	PEP12	-1.02	0.87	Target membrane receptor (t-SNARE) for vesicular intermediates traveling between the Golgi apparatus and the vacuole; controls entry of biosynthetic, endocytic, and retrograde traffic into the prevacuolar compartment; syntaxin
YML128C	MSC1	-0.99	0.99	Protein of unknown function; mutant is defective in directing meiotic recombination events to homologous chromatids; the authentic, non-tagged protein is detected in highly purified mitochondria and is phosphorylated
YDL090C	RAM1	-0.97	1.05	Beta subunit of the CAAX farnesyltransferase (FTase) that prenylates the a-factor mating pheromone and Ras proteins; required for the membrane localization of Ras proteins and a-factor; homolog of the mammalian FTase beta subunit
YDR332W	IRC3	-0.97	1.40	Putative RNA helicase of the DEAH/D-box family; null mutant displays increased levels of spontaneous Rad52p foci; green fluorescent protein (GFP)-fusion protein localizes to the mitochondrion
YMR220W	ERG8	-0.97	0.56	Phosphomevalonate kinase, an essential cytosolic enzyme that acts in the biosynthesis of isoprenoids and sterols, including ergosterol, from mevalonate
YCL040W	GLK1	-0.97	0.95	Glucokinase, catalyzes the phosphorylation of glucose at C6 in the first irreversible step of glucose metabolism; one of three glucose phosphorylating enzymes; expression regulated by non-fermentable carbon sources
YMR251W-A	HOR7	-0.96	0.78	Protein of unknown function; overexpression suppresses Ca2+ sensitivity of mutants lacking inositol phosphorylceramide mannosyltransferases Csg1p and Csh1p; transcription is induced under hyperosmotic stress and repressed by alpha factor

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YNR049C	MSO1	-0.95	0.97	Probable component of the secretory vesicle docking complex, acts at a late step in secretion; shows genetic and physical interactions with Sec1p; required for prospore membrane formation during sporulation
YLR399C	BDF1	-0.91	0.48	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
YFL047W	RGD2	-0.91	0.97	GTPase-activating protein (RhoGAP) for Cdc42p and Rho5p
YGL005C	COG7	-0.91	0.66	Component of the conserved oligomeric Golgi complex (Cog1p through Cog8p), a cytosolic tethering complex that functions in protein trafficking to mediate fusion of transport vesicles to Golgi compartments
YPL004C	LSP1	-0.88	0.61	Primary component of eisosomes, which are large immobile patch structures at the cell cortex associated with endocytosis, along with Pil1p and Sur7p; null mutants show activation of Pkc1p/Ypk1p stress resistance pathways
YOR349W	CIN1	-0.88	0.73	Tubulin folding factor D involved in beta-tubulin (Tub2p) folding; isolated as mutant with increased chromosome loss and sensitivity to benomyl
YAL060W	BDH1	-0.88	0.96	NAD-dependent (R,R)-butanediol dehydrogenase, catalyzes oxidation of (R,R)-2,3-butanediol to (3R)-acetoin, oxidation of meso-butanediol to (3S)-acetoin, and reduction of acetoin; enhances use of 2,3-butanediol as an aerobic carbon source
YLL026W	HSP104	-0.88	0.79	Heat shock protein that cooperates with Ydj1p (Hsp40) and Ssa1p (Hsp70) to refold and reactivate previously denatured, aggregated proteins; responsive to stresses including: heat, ethanol, and sodium arsenite; involved in [PSI+] propagation
YKL003C	MRP17	-0.88	0.71	Mitochondrial ribosomal protein of the small subunit; MRP17 exhibits genetic interactions with PET122, encoding a COX3-specific translational activator

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YMR102C		-0.86	0.30	Protein of unknown function; transcription is activated by paralogous transcription factors Yrm1p and Yrr1p along with genes involved in multidrug resistance; mutant shows increased resistance to azoles; YMR102C is not an essential gene
YPR109W		-0.86	0.81	Predicted membrane protein; dipoid deletion strain has high budding index
YLR168C	UPS2	-0.85	0.72	Mitochondrial intermembrane space protein involved in regulation of mitochondrial cardiolipin and phosphatidylethanolamine levels; null has defects in mitochondrial morphology; similar to Ups1p, Ups3p and to human PRELI
YAL005C	SSA1	-0.85	0.28	ATPase involved in protein folding and nuclear localization signal (NLS)-directed nuclear transport; member of heat shock protein 70 (HSP70) family; forms a chaperone complex with Ydj1p; localized to the nucleus, cytoplasm, and cell wall
YMR105C	PGM2	-0.84	1.16	Phosphoglucomutase, catalyzes the conversion from glucose-1-phosphate to glucose-6-phosphate, which is a key step in hexose metabolism; functions as the acceptor for a Glc-phosphotransferase
YBR183W	YPC1	-0.83	1.06	Alkaline ceramidase that also has reverse (CoA-independent) ceramide synthase activity, catalyzes both breakdown and synthesis of phytoceramide; overexpression confers fumonisin B1 resistance
YGR010W	NMA2	-0.83	0.86	Nicotinic acid mononucleotide adenylyltransferase, involved in de novo and salvage synthesis of NAD(+)
YGR088W	CTT1	-0.83	1.03	Cytosolic catalase T, has a role in protection from oxidative damage by hydrogen peroxide
YDR438W	THI74	-0.83	0.93	Mitochondrial transporter repressible by thiamine
YPL007C	TFC8	-0.82	0.84	One of six subunits of RNA polymerase III transcription initiation factor complex (TFIIIC); part of TFIIIC TauB domain that binds BoxB promoter sites of tRNA and other genes; linker between TauB and TauA domains; human homolog is TFIIIC-90
YMR130W		-0.80	0.68	Putative protein of unknown function; YMR130W is not an essential gene

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YKR017C		-0.79	0.77	Putative protein of unknown function; contains a RING finger motif
YPL087W	YDC1	-0.79	0.86	Alkaline dihydroceramidase, involved in sphingolipid metabolism; preferentially hydrolyzes dihydroceramide to a free fatty acid and dihydrosphingosine; has a minor reverse activity
YLR345W		-0.77	0.72	Similar to 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase enzymes responsible for the metabolism of fructoso-2,6-bisphosphate; mRNA expression is repressed by the Rfx1p-Tup1p-Ssn6p repressor complex; YLR345W is not an essential gene
YBR037C	SCO1	-0.77	0.53	Copper-binding protein of the mitochondrial inner membrane, required for cytochrome c oxidase activity and respiration; may function to deliver copper to cytochrome c oxidase; has similarity to thioredoxins
YPL097W	MSY1	-0.75	0.41	Mitochondrial tyrosyl-tRNA synthetase
YJR101W	RSM26	-0.75	0.46	Mitochondrial ribosomal protein of the small subunit
YPL026C	SKS1	-0.75	0.80	Putative serine/threonine protein kinase; involved in the adaptation to low concentrations of glucose independent of the SNF3 regulated pathway
YPR176C	BET2	-0.74	1.12	Beta subunit of Type II geranylgeranyltransferase required for vesicular transport between the endoplasmic reticulum and the Golgi; provides a membrane attachment moiety to Rab-like proteins Ypt1p and Sec4p
YDR171W	HSP42	-0.74	1.56	Small heat shock protein (sHSP) with chaperone activity; forms barrel-shaped oligomers that suppress unfolded protein aggregation; involved in cytoskeleton reorganization after heat shock
YOR347C	PYK2	-0.73	0.57	Pyruvate kinase that appears to be modulated by phosphorylation; PYK2 transcription is repressed by glucose, and Pyk2p may be active under low glycolytic flux
YPR149W	NCE102	-0.73	0.89	Protein of unknown function; contains transmembrane domains; involved in secretion of proteins that lack classical secretory signal sequences; component of the detergent-insoluble glycolipid-enriched complexes (DIGs)

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YOR049C	RSB1	-0.73	0.76	Suppressor of sphingoid long chain base (LCB) sensitivity of an LCB-lyase mutation; putative integral membrane transporter or flippase that may transport LCBs from the cytoplasmic side toward the extracytoplasmic side of the membrane
YDL110C	TMA17	-0.72	0.77	Protein of unknown function that associates with ribosomes; heterozygous deletion demonstrated increases in chromosome instability in a rad9 deletion background; protein abundance is decreased upon intracellular iron depletion
YDR110W	FOB1	-0.71	0.67	Nucleolar protein that binds the rDNA replication fork barrier (RFB) site; required for replication fork blocking, recombinational hotspot activity, condensin recruitment to RFB and rDNA repeat segregation; related to retroviral integrases
YPL132W	COX11	-0.71	0.66	Mitochondrial inner membrane protein required for delivery of copper to the Cox1p subunit of cytochrome c oxidase; association with mitochondrial ribosomes suggests that copper delivery may occur during translation of Cox1p
YBR056W		-0.70	0.47	Putative cytoplasmic protein of unknown function
YBR009C	HHF1	-0.70	0.50	Histone H4, core histone protein required for chromatin assembly and chromosome function; one of two identical histone proteins (see also HHF2); contributes to telomeric silencing; N-terminal domain involved in maintaining genomic integrity
YCR023C		-0.70	0.66	Vacuolar membrane protein of unknown function; member of the multidrug resistance family; YCR023C is not an essential gene
YNL274C	GOR1	-0.70	0.94	Glyoxylate reductase; null mutation results in increased biomass after diauxic shift; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies
YHR168W	MTG2	-0.70	0.56	Putative GTPase, member of the Obg family; peripheral protein of the mitochondrial inner membrane that associates with the large ribosomal subunit; required for mitochondrial translation, possibly via a role in ribosome assembly

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YDL124W		-0.69	0.68	NADPH-dependent alpha-keto amide reductase; reduces aromatic alpha-keto amides, aliphatic alpha-keto esters, and aromatic alpha-keto esters; member of the aldo-keto reductase (AKR) family
YKL150W	MCR1	-0.69	0.79	Mitochondrial NADH-cytochrome b5 reductase, involved in ergosterol biosynthesis
YGR008C	STF2	-0.68	0.90	Protein involved in regulation of the mitochondrial F1F0-ATP synthase; Stf1p and Stf2p may act as stabilizing factors that enhance inhibitory action of the Inh1p protein
YOR230W	WTM1	-0.68	0.71	Transcriptional modulator involved in regulation of meiosis, silencing, and expression of RNR genes; required for nuclear localization of the ribonucleotide reductase small subunit Rnr2p and Rnr4p; contains WD repeats
YEL024W	RIP1	-0.68	0.48	Ubiquinol-cytochrome-c reductase, a Rieske iron-sulfur protein of the mitochondrial cytochrome bc1 complex; transfers electrons from ubiquinol to cytochrome c1 during respiration
YER053C	PIC2	-0.68	0.54	Mitochondrial phosphate carrier, imports inorganic phosphate into mitochondria; functionally redundant with Mir1p but less abundant than Mir1p under normal conditions; expression is induced at high temperature
YHR001W	OSH7	-0.67	0.66	Member of an oxysterol-binding protein family with seven members in S. cerevisiae; family members have overlapping, redundant functions in sterol metabolism and collectively perform a function essential for viability
YMR090W		-0.66	0.83	Putative protein of unknown function with similarity to DTDP-glucose 4,6-dehydratases; GFP-fusion protein localizes to the cytoplasm; up-regulated in response to the fungicide mancozeb; not essential for viability
YIL093C	RSM25	-0.66	0.37	Mitochondrial ribosomal protein of the small subunit
YFL028C	CAF16	-0.65	0.57	Part of evolutionarily-conserved CCR4-NOT regulatory complex; contains single ABC-type ATPase domain but no transmembrane domain; interacts with several subunits of Mediator

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YMR250W	GAD1	-0.65	0.81	Glutamate decarboxylase, converts glutamate into gamma-aminobutyric acid (GABA) during glutamate catabolism; involved in response to oxidative stress
YBR151W	APD1	-0.65	0.37	Protein of unknown function, required for normal localization of actin patches and for normal tolerance of sodium ions and hydrogen peroxide; localizes to both cytoplasm and nucleus
YLL039C	UBI4	-0.65	0.98	Ubiquitin, becomes conjugated to proteins, marking them for selective degradation via the ubiquitin-26S proteasome system; essential for the cellular stress response; encoded as a polyubiquitin precursor comprised of 5 head-to-tail repeats
YOR334W	MRS2	-0.64	0.94	Mitochondrial inner membrane Mg(2+) channel, required for maintenance of intramitochondrial Mg(2+) concentrations at the correct level to support splicing of group II introns
YHR216W	IMD2	-0.64	0.89	Inosine monophosphate dehydrogenase, catalyzes the rate-limiting step in GTP biosynthesis, expression is induced by mycophenolic acid resulting in resistance to the drug, expression is repressed by nutrient limitatio
YDR162C	NBP2	-0.63	0.56	Protein involved in the HOG (high osmolarity glycerol) pathway, negatively regulates Hog1p by recruitment of phosphatase Ptc1p the Pbs2p-Hog1p complex, found in the nucleus and cytoplasm, contains an SH3 domain that binds Pbs2p
YHR133C	NSG1	-0.63	0.46	Protein involved in regulation of sterol biosynthesis; specifically stabilizes Hmg2p, one of two HMG-CoA isoenzymes that catalyze the rate-limiting step in sterol biosynthesis; homolog of mammalian INSIG proteins
YDR358W	GGA1	-0.63	0.82	Golgi-localized protein with homology to gamma-adaptin, interacts with and regulates Arf1p and Arf2p in a GTP-dependent manner in order to facilitate traffic through the late Golgi
YER124C	DSE1	-0.63	0.71	Daughter cell-specific protein, may regulate cross-talk between the mating and filamentation pathways; deletion affects cell separation after division and sensitivity to alpha-factor and drugs affecting the cell wall

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YEL039C	CYC7	-0.62	2.77	Cytochrome c isoform 2, expressed under hypoxic conditions; electron carrier of the mitochondrial intermembrane space that transfers electrons from ubiquinone-cytochrome c oxidoreductase to cytochrome c oxidase during cellular respiration
YMR058W	FET3	-0.62	0.25	Ferro-O2-oxidoreductase required for high-affinity iron uptake and involved in mediating resistance to copper ion toxicity, belongs to class of integral membrane multicopper oxidases
YGL232W	TAN1	-0.62	0.72	Putative tRNA acetyltransferase, RNA-binding protein required for the formation of the modified nucleoside N(4)-acetylcytidine in serine and leucine tRNAs but not required for the same modification in 18S rRNA
YGR165W	MRPS35	-0.62	0.52	Mitochondrial ribosomal protein of the small subunit
YPR065W	ROX1	-0.62	0.47	Heme-dependent repressor of hypoxic genes; contains an HMG domain that is responsible for DNA bending activity
YOR298C-A	MBF1	-0.61	0.35	Transcriptional coactivator that bridges the DNA-binding region of Gcn4p and TATA-binding protein Spt15p; suppressor of frameshift mutations
YPL240C	HSP82	-0.61	0.77	Hsp90 chaperone required for pheromone signaling and negative regulation of Hsf1p; docks with Tom70p for mitochondrial preprotein delivery; promotes telomerase DNA binding and nucleotide addition; interacts with Cns1p, Cpr6p, Cpr7p, Sti1p
YGR247W	CPD1	-0.61	0.63	Cyclic nucleotide phosphodiesterase, hydrolyzes ADP-ribose 1'', 2''-cyclic phosphate to ADP-ribose 1''-phosphate; may have a role in tRNA splicing; no detectable phenotype is conferred by null mutation or by overexpression
YGL107C	RMD9	-0.61	0.35	Mitochondrial protein required for respiratory growth; mutant phenotype and genetic interactions suggest a role in delivering mt mRNAs to ribosomes; located on matrix face of the inner membrane and loosely associated with mitoribosomes
YBR062C		-0.61	0.54	Protein of unknown function that interacts with Msb2p; may play a role in activation of the filamentous growth pathway.

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YCL018W	LEU2	-0.61	0.58	Beta-isopropylmalate dehydrogenase (IMDH), catalyzes the third step in the leucine biosynthesis pathway
YER062C	HOR2	-0.60	1.63	One of two redundant DL-glycerol-3-phosphatases (RHR2/GPP1 encodes the other) involved in glycerol biosynthesis; induced in response to hyperosmotic stress and oxidative stress, and during the diauxic transition
YJL048C	UBX6	-0.60	0.56	UBX (ubiquitin regulatory X) domain-containing protein that interacts with Cdc48p, transcription is repressed when cells are grown in media containing inositol and choline
YKL196C	YKT6	-0.60	0.46	Vesicle membrane protein (v-SNARE) with acyltransferase activity; involved in trafficking to and within the Golgi, endocytic trafficking to the vacuole, and vacuolar fusion; membrane localization due to prenylation at the carboxy-terminus
YOL116W	MSN1	-0.60	0.98	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
YNL306W	MRPS18	-0.60	0.84	Mitochondrial ribosomal protein of the small subunit; essential for viability, unlike most other mitoribosomal proteins
YGL143C	MRF1	-0.59	0.61	Mitochondrial translation release factor, involved in stop codon recognition and hydrolysis of the peptidyl-tRNA bond during mitochondrial translation; lack of MRF1 causes mitochondrial genome instability
YML120C	NDI1	-0.59	0.51	NADH:ubiquinone oxidoreductase, transfers electrons from NADH to ubiquinone in the respiratory chain but does not pump protons, in contrast to the higher eukaryotic multisubunit respiratory complex I; phosphorylated; homolog of human AMID
YDL204W	RTN2	-0.59	1.08	Protein of unknown function; has similarity to mammalian reticulon proteins; member of the RTNLA (reticulon-like A) subfamily
YJL196C	ELO1	-0.58	0.88	Elongase I, medium-chain acyl elongase, catalyzes carboxy-terminal elongation of unsaturated C12-C16 fatty acyl-CoAs to C16-C18 fatty acids

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YDR050C	TPI1	-0.58	0.14	Triose phosphate isomerase, abundant glycolytic enzyme; mRNA half-life is regulated by iron availability; transcription is controlled by activators Reb1p, Gcr1p, and Rap1p through binding sites in the 5' non-coding region
YFR024C-A	LSB3	-0.58	0.38	Protein containing a C-terminal SH3 domain; binds Las17p, which is a homolog of human Wiskott-Aldrich Syndrome protein involved in actin patch assembly and actin polymerization
YOR256C	TRE2	-0.57	0.42	Protein that functions with Tre1p to regulate ubiquitylation and vacuolar degradation of the metal transporter Smf1p; has similarity to transferrin receptors; inviability of null mutant in systematic studies is due to proximity to CDC31
YDL125C	HNT1	-0.56	0.60	Adenosine 5'-monophosphoramidase; interacts physically and genetically with Kin28p, a CDK and TFIIK subunit, and genetically with CAK1; member of the histidine triad (HIT) superfamily of nucleotide-binding proteins and similar to Hint
YLR109W	AHP1	-0.56	0.47	Thiol-specific peroxiredoxin, reduces hydroperoxides to protect against oxidative damage; function in vivo requires covalent conjugation to Urm1p
YNL030W	HHF2	-0.56	0.52	Histone H4, core histone protein required for chromatin assembly and chromosome function; one of two identical histone proteins (see also HHF1); contributes to telomeric silencing; N-terminal domain involved in maintaining genomic integrity
YIL157C	COA1	-0.55	0.45	Mitochondrial inner membrane protein required for assembly of the cytochrome c oxidase complex (complex IV); interacts with complex IV assembly factor Shy1p during the early stages of assembly
YML078W	CPR3	-0.55	0.49	Mitochondrial peptidyl-prolyl cis-trans isomerase (cyclophilin), catalyzes the cis-trans isomerization of peptide bonds N-terminal to proline residues; involved in protein refolding after import into mitochondria
YLR225C		-0.55	0.45	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm; YLR225C is not an essential gene

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YCR005C	CIT2	-0.54	1.43	Citrate synthase, catalyzes the condensation of acetyl coenzyme A and oxaloacetate to form citrate, peroxisomal isozyme involved in glyoxylate cycle; expression is controlled by Rtg1p and Rtg2p transcription factors
YNL111C	CYB5	-0.54	0.61	Cytochrome b5, involved in the sterol and lipid biosynthesis pathways; acts as an electron donor to support sterol C5-6 desaturation
YDR116C	MRPL1	-0.54	0.38	Mitochondrial ribosomal protein of the large subunit
YEL011W	GLC3	-0.54	0.94	Glycogen branching enzyme, involved in glycogen accumulation; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm in a punctate pattern
YDR047W	HEM12	-0.53	0.36	Uroporphyrinogen decarboxylase, catalyzes the fifth step in the heme biosynthetic pathway; localizes to both the cytoplasm and nucleus; a hem12 mutant has phenotypes similar to patients with porphyria cutanea tarda
YLR312W-A	MRPL15	-0.53	0.65	Mitochondrial ribosomal protein of the large subunit
YLR077W	FMP25	-0.53	0.38	Putative protein of unknown function; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies
YBR251W	MRPS5	-0.53	0.63	Mitochondrial ribosomal protein of the small subunit
YML127W	RSC9	-0.52	0.78	Component of the RSC chromatin remodeling complex; DNA-binding protein involved in the synthesis of rRNA and in transcriptional repression and activation of genes regulated by the Target of Rapamycin (TOR) pathway
YHR117W	TOM71	-0.52	0.48	Mitochondrial outer membrane protein with similarity to Tom70p; probable minor component of the TOM (translocase of outer membrane) complex responsible for recognition and import of mitochondrially directed proteins
YML007W	YAP1	-0.52	0.42	Basic leucine zipper (bZIP) transcription factor required for oxidative stress tolerance; activated by H2O2 through the multistep formation of disulfide bonds and transit from the cytoplasm to the nucleus; mediates resistance to cadmium

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion				
Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YHL035C	VMR1	-0.52	0.72	Protein of unknown function that may interact with ribosomes, based on co-purification experiments; member of the ATP-binding cassette (ABC) family; potential Cdc28p substrate; detected in purified mitochondria in high-throughput studies
YKL152C	GPM1	-0.52	0.16	Tetrameric phosphoglycerate mutase, mediates the conversion of 3-phosphoglycerate to 2-phosphoglycerate during glycolysis and the reverse reaction during gluconeogenesis
YJL094C	KHA1	-0.52	0.70	Putative K+/H+ antiporter with a probable role in intracellular cation homeostasis, localized to Golgi vesicles and detected in highly purified mitochondria in high-throughput studies
YGR199W	PMT6	-0.51	0.49	Protein O-mannosyltransferase, transfers mannose from dolichyl phosphate-D-mannose to protein serine/threonine residues of secretory proteins; reaction is essential for cell wall rigidity; member of a family of mannosyltransferases
YJR121W	ATP2	-0.51	0.23	Beta subunit of the F1 sector of mitochondrial F1F0 ATP synthase, which is a large, evolutionarily conserved enzyme complex required for ATP synthesis; phosphorylated
YLR163C	MAS1	-0.51	0.66	Smaller subunit of the mitochondrial processing protease (MPP), essential processing enzyme that cleaves the N-terminal targeting sequences from mitochondrially imported proteins
YJL051W	IRC8	-0.51	0.57	Bud tip localized protein of unknown function; mRNA is targeted to the bud by a She2p dependent transport system; mRNA is cell cycle regulated via Fkh2p, peaking in G2/M phase; null mutant displays increased levels of spontaneous Rad52p foc
YDR226W	ADK1	-0.51	0.35	Adenylate kinase, required for purine metabolism; localized to the cytoplasm and the mitochondria; lacks cleavable signal sequence
YKL035W	UGP1	-0.50	0.40	UDP-glucose pyrophosphorylase (UGPase), catalyses the reversible formation of UDP-Glc from glucose 1-phosphate and UTP, involved in a wide variety of metabolic pathways, expression modulated by Pho85p through Pho4p
YDL178W	DLD2	-0.50	0.86	D-lactate dehydrogenase, located in the mitochondrial matrix

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YPL260W		-0.50	0.38	Putative substrate of cAMP-dependent protein kinase (PKA); green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus; YPL260W is not an essential gene
YOL011W	PLB3	-0.49	0.41	Phospholipase B (lysophospholipase) involved in phospholipid metabolism; hydrolyzes phosphatidylinositol and phosphatidylserine and displays transacylase activity in vitro
YDL020C	RPN4	-0.48	0.68	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
YMR186W	HSC82	-0.47	0.35	Cytoplasmic chaperone of the Hsp90 family, redundant in function and nearly identical with Hsp82p, and together they are essential; expressed constitutively at 10-fold higher basal levels than HSP82 and induced 2-3 fold by heat shock
YNL137C	NAM9	-0.47	0.39	Mitochondrial ribosomal component of the small subunit
YLR056W	ERG3	-0.47	0.66	C-5 sterol desaturase, catalyzes the introduction of a C-5(6) double bond into episterol, a precursor in ergosterol biosynthesis; mutants are viable, but cannot grow on non-fermentable carbon sources
YPL117C	IDI1	-0.47	0.32	Isopentenyl diphosphate:dimethylallyl diphosphate isomerase (IPP isomerase), catalyzes an essential activation step in the isoprenoid biosynthetic pathway; required for viability
YMR311C	GLC8	-0.47	0.35	Regulatory subunit of protein phosphatase 1 (Glc7p), involved in glycogen metabolism and chromosome segregation; proposed to regulate Glc7p activity via conformational alteration; ortholog of the mammalian protein phosphatase inhibitor 2
YLR177W		-0.47	0.78	Putative protein of unknown function; phosphorylated by Dbf2p-Mob1p in vitro; some strains contain microsatellite polymophisms at this locus; YLR177W is not an essential gene

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YFL045C	SEC53	-0.47	0.38	Phosphomannomutase, involved in synthesis of GDP-mannose and dolichol-phosphate-mannose; required for folding and glycosylation of secretory proteins in the ER lumen
YGR234W	YHB1	-0.46	0.26	Nitric oxide oxidoreductase, flavohemoglobin involved in nitric oxide detoxification; plays a role in the oxidative and nitrosative stress responses
YMR012W	CLU1	-0.46	0.29	eIF3 component of unknown function; deletion causes defects in mitochondrial organization but not in growth or translation initiation, can rescue cytokinesis and mitochondrial organization defects of the Dictyostelium cluA- mutant
YNL100W	AIM37	-0.46	0.39	Putative protein of unknown function; non-tagged protein is detected in purified mitochondria; null mutant is viable and displays reduced respiratory growth and reduced frequency of mitochondrial genome loss
YJL054W	TIM54	-0.45	0.45	Component of the mitochondrial TIM22 complex involved in insertion of polytopic proteins into the inner membrane
YBR126C	TPS1	-0.45	0.33	Synthase subunit of trehalose-6-phosphate synthase/phosphatase complex, which synthesizes the storage carbohydrate trehalose; also found in a monomeric form; expression is induced by the stress response and repressed by the Ras-cAMP pathway
YDR516C	EMI2	-0.45	0.67	Non-essential protein of unknown function required for transcriptional induction of the early meiotic-specific transcription factor IME1; required for sporulation; expression is regulated by glucose-repression transcription factors Mig1/2p
YNL183C	NPR1	-0.45	0.47	Protein kinase that stabilizes several plasma membrane amino acid transporters by antagonizing their ubiquitin-mediated degradation
YCL064C	CHA1	-0.45	1.24	Catabolic L-serine (L-threonine) deaminase, catalyzes the degradation of both L-serine and L-threonine; required to use serine or threonine as the sole nitrogen source, transcriptionally induced by serine and threonine

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion				
Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YEL050C	RML2	-0.45	0.29	Mitochondrial ribosomal protein of the large subunit, has similarity to E. coli L2 ribosomal protein; fat21 mutant allele causes inability to utilize oleate and may interfere with activity of the Adr1p transcription factor
YLR214W	FRE1	-0.45	0.61	Ferric reductase and cupric reductase, reduces siderophore-bound iron and oxidized copper prior to uptake by transporters; expression induced by low copper and iron levels
YNL177C	MRPL22	-0.45	0.60	Mitochondrial ribosomal protein of the large subunit
YBL066C	SEF1	-0.45	0.59	Putative transcription factor, has homolog in Kluyveromyces lactis
YDR214W	AHA1	-0.44	0.53	Co-chaperone that binds to Hsp82p and activates its ATPase activity; similar to Hch1p; expression is regulated by stresses such as heat shock
YDR529C	QCR7	-0.44	0.51	Subunit 7 of the ubiquinol cytochrome-c reductase complex, which is a component of the mitochondrial inner membrane electron transport chain; oriented facing the mitochondrial matrix; N-terminus appears to play a role in complex assembly
YOR093C		-0.44	0.53	Putative protein of unknown function; deletion causes sensitivity to unfolded protein response-inducing agents
YNL241C	ZWF1	-0.44	0.40	Glucose-6-phosphate dehydrogenase (G6PD), catalyzes the first step of the pentose phosphate pathway; involved in adapting to oxidatve stress; homolog of the human G6PD which is deficient in patients with hemolytic anemia
YPL013C	MRPS16	-0.44	0.35	Mitochondrial ribosomal protein of the small subunit
YOR354C	MSC6	-0.43	0.35	Protein of unknown function; mutant is defective in directing meiotic recombination events to homologous chromatids; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies
YGL256W	ADH4	-0.43	0.63	Alcohol dehydrogenase isoenzyme type IV, dimeric enzyme demonstrated to be zinc-dependent despite sequence similarity to iron-activated alcohol dehydrogenases; transcription is induced in response to zinc deficiency

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YDR175C	RSM24	-0.42	0.66	Mitochondrial ribosomal protein of the small subunit
YDR334W	SWR1	-0.42	0.32	Swi2/Snf2-related ATPase that is the structural component of the SWR1 complex, which exchanges histone variant H2AZ (Htz1p) for chromatin-bound histone H2A
YKL195W	MIA40	-0.41	0.38	Essential protein of the mitochondrial intermembrane space (IMS); promotes retention of newly imported proteins; may do so by stabilizing client protein folding as part of a disulfide relay system or transferring metal to client proteins
YPL075W	GCR1	-0.41	0.50	Transcriptional activator of genes involved in glycolysis; DNA-binding protein that interacts and functions with the transcriptional activator Gcr2p
YDR155C	CPR1	-0.41	0.43	Cytoplasmic peptidyl-prolyl cis-trans isomerase (cyclophilin), catalyzes the cis-trans isomerization of peptide bonds N-terminal to proline residues; binds the drug cyclosporin A
YDR430C	CYM1	-0.41	0.77	Lysine-specific metalloprotease of the mitochondrial intermembrane space, member of the pitrilysin family; degrades proteins and presequence peptides cleaved from imported proteins; required for normal mitochondrial morphology
YEL038W	UTR4	-0.40	0.39	Protein with sequence similarity to 2,3-diketo-5-methylthiopentyl-1-phosphate enolase-phosphatases, involved in methionine salvage; found in both the cytoplasm and nucleus
YDR224C	HTB1	-0.40	0.35	Histone H2B, core histone protein required for chromatin assembly and chromosome function; nearly identical to HTB2; Rad6p-Bre1p-Lge1p mediated ubiquitination regulates transcriptional activation, meiotic DSB formation and H3 methylation
YPL206C	PGC1	-0.40	0.43	Phosphatidyl Glycerol phospholipase C; regulates the phosphatidylglycerol (PG) content via a phospholipase C-type degradation mechanism; contains glycerophosphodiester phosphodiesterase motifs

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YBL058W	SHP1	-0.40	0.51	UBX (ubiquitin regulatory X) domain-containing protein that regulates Glc7p phosphatase activity and interacts with Cdc48p; interacts with ubiquitylated proteins in vivo and is required for degradation of a ubiquitylated model substrate
YIL070C	MAM33	-0.40	0.68	Acidic protein of the mitochondrial matrix involved in oxidative phosphorylation; related to the human complement receptor gC1q-R
YPL029W	SUV3	-0.40	0.48	ATP-dependent RNA helicase, component of the mitochondrial degradosome along with the RNase Dss1p; the degradosome associates with the ribosome and mediates RNA turnover; also required during splicing of the COX1 AI5_beta intron
YKL053C-A	MDM35	-0.40	0.46	Mitochondrial intermembrane space protein; mutation affects mitochondrial distribution and morphology; contains twin cysteine-x9-cysteine motifs
YER001W	MNN1	-0.39	0.57	Alpha-1,3-mannosyltransferase, integral membrane glycoprotein of the Golgi complex, required for addition of alpha1,3-mannose linkages to N-linked and O-linked oligosaccharides, one of five S. cerevisiae proteins of the MNN1 family
YPR169W	JIP5	-0.39	0.50	Essential protein required for biogenesis of the large ribosomal subunit; interacts with proteins involved in RNA processing, ribosome biogenesis, ubiquitination and demethylation; similar to WDR55, a human WD repeat protein
YLR069C	MEF1	-0.39	0.40	Mitochondrial elongation factor involved in translational elongation
YHL047C	ARN2	-0.39	0.37	Transporter, member of the ARN family of transporters that specifically recognize siderophore-iron chelates; responsible for uptake of iron bound to the siderophore triacetylfusarinine C
YHL030W	ECM29	-0.39	0.37	Major component of the proteasome; tethers the proteasome core particle to the regulatory particle, and enhances the stability of the proteasome
YLR216C	CPR6	-0.38	0.45	Peptidyl-prolyl cis-trans isomerase (cyclophilin), catalyzes the cis-trans isomerization of peptide bonds N-terminal to proline residues; binds to Hsp82p and contributes to chaperone activity

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YMR145C	NDE1	-0.38	0.45	Mitochondrial external NADH dehydrogenase, a type II NAD(P)H:quinone oxidoreductase that catalyzes the oxidation of cytosolic NADH; Nde1p and Nde2p provide cytosolic NADH to the mitochondrial respiratory chain
YCR042C	TAF2	-0.37	0.62	TFIID subunit (150 kDa), involved in RNA polymerase II transcription initiation
YER172C	BRR2	-0.36	0.48	RNA-dependent ATPase RNA helicase (DEIH box); required for disruption of U4/U6 base-pairing in native snRNPs to activate the spliceosome for catalysis; homologous to human U5-200kD
YOR136W	IDH2	-0.35	0.82	Subunit of mitochondrial NAD(+)-dependent isocitrate dehydrogenase, which catalyzes the oxidation of isocitrate to alpha-ketoglutarate in the TCA cycle; phosphorylated
YKL085W	MDH1	-0.34	0.41	Mitochondrial malate dehydrogenase, catalyzes interconversion of malate and oxaloacetate; involved in the tricarboxylic acid (TCA) cycle; phosphorylated
YFR004W	RPN11	-0.34	0.28	Metalloprotease subunit of the 19S regulatory particle of the 26S proteasome lid; couples the deubiquitination and degradation of proteasome substrates; involved, independent of catalytic activity, in fission of mitochondria and peroxisomes
YKL176C	LST4	-0.33	0.56	Protein possibly involved in a post-Golgi secretory pathway; required for the transport of nitrogen-regulated amino acid permease Gap1p from the Golgi to the cell surface
YMR302C	YME2	-0.33	0.59	Integral inner mitochondrial membrane protein with a role in maintaining mitochondrial nucleoid structure and number; mutants exhibit an increased rate of mitochondrial DNA escape; shows some sequence similarity to exonucleases
YML110C	COQ5	-0.32	0.77	2-hexaprenyl-6-methoxy-1,4-benzoquinone methyltransferase, involved in ubiquinone (Coenzyme Q) biosynthesis; localizes to the matrix face of the mitochondrial inner membrane in a large complex with other ubiquinone biosynthetic enzymes

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YGR231C	PHB2	-0.31	0.33	Subunit of the prohibitin complex (Phb1p-Phb2p), a 1.2 MDa ring-shaped inner mitochondrial membrane chaperone that stabilizes newly synthesized proteins; determinant of replicative life span; involved in mitochondrial segregation
YIR035C		-0.31	0.42	Putative cytoplasmic protein of unknown function
YGR254W	ENO1	-0.30	0.53	Enolase I, a phosphopyruvate hydratase that catalyzes the conversion of 2-phosphoglycerate to phosphoenolpyruvate during glycolysis and the reverse reaction during gluconeogenesis; expression is repressed in response to glucose
YDR211W	GCD6	-0.30	0.41	Catalytic epsilon subunit of the translation initiation factor eIF2B, the guanine-nucleotide exchange factor for eIF2; activity subsequently regulated by phosphorylated eIF2; first identified as a negative regulator of GCN4 expression
YMR092C	AIP1	-0.29	0.44	Actin cortical patch component, interacts with the actin depolymerizing factor cofilin; required to restrict cofilin localization to cortical patches; contains WD repeats
YGR209C	TRX2	-0.29	0.42	Cytoplasmic thioredoxin isoenzyme of the thioredoxin system which protects cells against oxidative and reductive stress, forms LMA1 complex with Pbi2p, acts as a cofactor for Tsa1p, required for ER-Golgi transport and vacuole inheritance
YJL143W	TIM17	-0.28	0.21	Essential subunit of the Translocase of the Inner Mitochondrial membrane (TIM23 complex); with Tim23p, contributes to the architecture and function of the import channel; may link the import motor to the core TIM23 complex
YOR167C	RPS28A	-0.26	0.24	Protein component of the small (40S) ribosomal subunit; nearly identical to Rps28Bp and has similarity to rat S28 ribosomal protein
YLR304C	ACO1	-0.26	0.36	Aconitase, required for the tricarboxylic acid (TCA) cycle and also independently required for mitochondrial genome maintenance; phosphorylated; component of the mitochondrial nucleoid; mutation leads to glutamate auxotrophy
YHR143W	DSE2	-0.25	0.42	Daughter cell-specific secreted protein with similarity to glucanases, degrades cell wall from the daughter side causing daughter to separate from mother; expression is repressed by cAMP

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YLR388W	RPS29A	-0.25	0.24	Protein component of the small (40S) ribosomal subunit; nearly identical to Rps29Bp and has similarity to rat S29 and E. coli S14 ribosomal proteins
YNL037C	IDH1	-0.25	0.45	Subunit of mitochondrial NAD(+)-dependent isocitrate dehydrogenase, which catalyzes the oxidation of isocitrate to alpha-ketoglutarate in the TCA cycle
YHR024C	MAS2	-0.23	0.45	Larger subunit of the mitochondrial processing protease (MPP), essential processing enzyme that cleaves the N-terminal targeting sequences from mitochondrially imported proteins
YPR103W	PRE2	-0.23	0.38	Beta 5 subunit of the 20S proteasome, responsible for the chymotryptic activity of the proteasome
YMR089C	YTA12	-0.23	0.25	Component, with Afg3p, of the mitochondrial inner membrane m-AAA protease that mediates degradation of misfolded or unassembled proteins and is also required for correct assembly of mitochondrial enzyme complexes
YHR007C	ERG11	-0.22	0.22	Lanosterol 14-alpha-demethylase, catalyzes the C-14 demethylation of lanosterol to form 4,4''-dimethyl cholesta-8,14,24-triene-3-beta-ol in the ergosterol biosynthesis pathway; member of the cytochrome P450 family
YGL012W	ERG4	-0.22	0.32	C-24(28) sterol reductase, catalyzes the final step in ergosterol biosynthesis; mutants are viable, but lack ergosterol
YIL043C	CBR1	-0.22	0.35	Microsomal cytochrome b reductase, not essential for viability; also detected in mitochondria; mutation in conserved NADH binding domain of the human ortholog results in type I methemoglobinemia
YDR345C	HXT3	-0.22	0.47	Low affinity glucose transporter of the major facilitator superfamily, expression is induced in low or high glucose conditions
YDL075W	RPL31A	-0.20	0.25	Protein component of the large (60S) ribosomal subunit, nearly identical to Rpl31Bp and has similarity to rat L31 ribosomal protein; associates with the karyopherin Sxm1p; loss of both Rpl31p and Rpl39p confers lethality

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YDR194C	MSS116	-0.19	0.47	DEAD-box protein required for efficient splicing of mitochondrial Group I and II introns; non-polar RNA helicase that also facilities strand annealing
YGR132C	PHB1	-0.18	0.19	Subunit of the prohibitin complex (Phb1p-Phb2p), a 1.2 MDa ring-shaped inner mitochondrial membrane chaperone that stabilizes newly synthesized proteins; determinant of replicative life span; involved in mitochondrial segregation
YKL145W	RPT1	-0.18	0.64	One of six ATPases of the 19S regulatory particle of the 26S proteasome involved in the degradation of ubiquitinated substrates; required for optimal CDC20 transcription; interacts with Rpn12p and the E3 ubiquitin-protein ligase Ubr1p
YPL154C	PEP4	-0.17	0.45	Vacuolar aspartyl protease (proteinase A), required for the posttranslational precursor maturation of vacuolar proteinases; important for protein turnover after oxidative damage; synthesized as a zymogen, self-activates
YNL178W	RPS3	-0.13	0.13	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
YAL061W	BDH2	-1.40	-0.51	Putative medium-chain alcohol dehydrogenase with similarity to BDH1; transcription induced by constitutively active PDR1 and PDR3
YBL047C	PDR5	-1.05	-0.07	Plasma membrane ATP-binding cassette (ABC) transporter, multidrug transporter actively regulated by Pdr1p; also involved in steroid transport, cation resistance, and cellular detoxification during exponential growth
YBR015C	ECM38	-0.86	-0.46	Gamma-glutamyltranspeptidase, major glutathione-degrading enzyme; involved in detoxification of electrophilic xenobiotics; expression induced mainly by nitrogen starvation
YBR158W	ALD6	-0.83	-1.78	Cytosolic aldehyde dehydrogenase, activated by Mg2+ and utilizes NADP+ as the preferred coenzyme; required for conversion of acetaldehyde to acetate; constitutively expressed; locates to the mitochondrial outer surface upon oxidative stress

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YCR012W	HAT2	-0.77	-0.76	Subunit of the Hat1p-Hat2p histone acetyltransferase complex; required for high affinity binding of the complex to free histone H4, thereby enhancing Hat1p activity; similar to human RbAp46 and 48; has a role in telomeric silencing
YCR046C	GYP8	-0.76	-0.99	GTPase-activating protein for yeast Rab family members; Ypt1p is the preferred in vitro substrate but also acts on Sec4p, Ypt31p and Ypt32p; involved in the regulation of ER to Golgi vesicle transport
YDL055C	GPA1	-0.75	-1.71	GTP-binding alpha subunit of the heterotrimeric G protein that couples to pheromone receptors; negatively regulates the mating pathway by sequestering G(beta)gamma and by triggering an adaptive response; activates Vps34p at the endosome
YDL128W	AMN1	-0.74	-0.40	Protein required for daughter cell separation, multiple mitotic checkpoints, and chromosome stability; contains 12 degenerate leucine-rich repeat motifs; expression is induced by the Mitotic Exit Network (MEN)
YDL174C	ERG5	-0.74	-0.33	C-22 sterol desaturase, a cytochrome P450 enzyme that catalyzes the formation of the C-22 (23) double bond in the sterol side chain in ergosterol biosynthesis; may be a target of azole antifungal drugs
YDL195W	YOR1	-0.74	-0.44	Plasma membrane ATP-binding cassette (ABC) transporter, multidrug transporter mediates export of many different organic anions including oligomycin; similar to human cystic fibrosis transmembrane receptor (CFTR)
YDR011W	DLD1	-0.74	-0.31	D-lactate dehydrogenase, oxidizes D-lactate to pyruvate, transcription is heme-dependent, repressed by glucose, and derepressed in ethanol or lactate; located in the mitochondrial inner membrane
YDR033W	VCX1	-0.69	-0.33	Vacuolar H+/Ca2+ exchanger involved in control of cytosolic Ca2+ concentration; has similarity to sodium/calcium exchangers, including the bovine Na+/Ca2+,K+ antiporter

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YDR170C	SEC7	-0.66	-0.33	Guanine nucleotide exchange factor (GEF) for ADP ribosylation factors involved in proliferation of the Golgi, intra-Golgi transport and ER-to-Golgi transport; found in the cytoplasm and on Golgi-associated coated vesicles
YDR502C	CWP1	-0.62	-0.57	Cell wall mannoprotein that localizes specifically to birth scars of daughter cells, linked to a beta-1,3- and beta-1,6-glucan heteropolymer through a phosphodiester bond; required for propionic acid resistance
YDR508C	CHO1	-0.61	-0.33	Phosphatidylserine synthase, functions in phospholipid biosynthesis; catalyzes the reaction CDP-diaclyglycerol + L-serine = CMP + L-1-phosphatidylserine, transcriptionally repressed by myo-inositol and choline
YEL056W	HMX1	-0.58	-0.37	ER localized heme oxygenase, involved in heme degradation during iron starvation and in the oxidative stress response; expression is regulated by AFT1 and oxidative stress; relocates to the perinuclear region in the presence of oxidants
YEL058W	FAA1	-0.56	-0.27	Long chain fatty acyl-CoA synthetase, activates imported fatty acids with a preference for C12:0-C16:0 chain lengths; functions in long chain fatty acid import; accounts for most acyl-CoA synthetase activity; localized to lipid particles
YER026C	TPO1	-0.55	-0.36	Polyamine transporter that recognizes spermine, putrescine, and spermidine; catalyzes uptake of polyamines at alkaline pH and excretion at acidic pH; phosphorylation enhances activity and sorting to the plasma membrane
YER056C	ARE2	-0.54	-0.28	Acyl-CoA:sterol acyltransferase, isozyme of Are1p; endoplasmic reticulum enzyme that contributes the major sterol esterification activity in the presence of oxygen
YER070W	STE2	-0.53	-3.12	Receptor for alpha-factor pheromone; seven transmembrane-domain GPCR that interacts with both pheromone and a heterotrimeric G protein to initiate the signaling response that leads to mating between haploid a and alpha cells

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YFL026W	TDH2	-0.51	-0.12	Glyceraldehyde-3-phosphate dehydrogenase, isozyme 2, involved in glycolysis and gluconeogenesis; tetramer that catalyzes the reaction of glyceraldehyde-3-phosphate to 1,3 bis-phosphoglycerate; detected in the cytoplasm and cell wall
YFL027C	PGK1	-0.50	-0.18	3-phosphoglycerate kinase, catalyzes transfer of high-energy phosphoryl groups from the acyl phosphate of 1,3-bisphosphoglycerate to ADP to produce ATP; key enzyme in glycolysis and gluconeogenesis
YGL008C	HXK2	-0.48	-0.46	Hexokinase isoenzyme 2 that catalyzes phosphorylation of glucose in the cytosol; predominant hexokinase during growth on glucose; functions in the nucleus to repress expression of HXK1 and GLK1 and to induce expression of its own gene
YGL040C	STE6	-0.46	-2.66	Plasma membrane ATP-binding cassette (ABC) transporter required for the export of a-factor, catalyzes ATP hydrolysis coupled to a-factor transport; contains 12 transmembrane domains and two ATP binding domains; expressed only in MATa cells
YGL253W		-0.45	-1.13	TyB Gag-Pol protein; proteolytically processed to make the Gag, RT, PR, and IN proteins that are required for retrotransposition
YGR130C	SSA2	-0.44	-0.33	ATP binding protein involved in protein folding and vacuolar import of proteins; member of heat shock protein 70 (HSP70) family; associated with the chaperonin-containing T-complex; present in the cytoplasm, vacuolar membrane and cell wall
YGR192C	TAT2	-0.43	-0.47	High affinity tryptophan and tyrosine permease, overexpression confers FK506 and FTY720 resistance
YGR240C	ERG27	-0.43	-0.36	3-keto sterol reductase, catalyzes the last of three steps required to remove two C-4 methyl groups from an intermediate in ergosterol biosynthesis; mutants are sterol auxotrophs
YGR281W	CHS1	-0.41	-0.53	Chitin synthase I, requires activation from zymogenic form in order to catalyze the transfer of N-acetylglucosamine (GlcNAc) to chitin; required for repairing the chitin septum during cytokinesis; transcription activated by mating factor

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YHR005C		-0.39	-0.37	Putative protein of unknown function; GFP-fusion protein localizes to the cytoplasm; possible component of the eisosome; specifically phosphorylated in vitro by mammalian diphosphoinositol pentakisphosphate (IP7)
YHR174W	RHR2	-0.38	-0.51	Constitutively expressed isoform of DL-glycerol-3-phosphatase; involved in glycerol biosynthesis, induced in response to both anaerobic and, along with the Hor2p/Gpp2p isoform, osmotic stress
YHR179W	GNP1	-0.37	-0.28	High-affinity glutamine permease, also transports Leu, Ser, Thr, Cys, Met and Asn; expression is fully dependent on Grr1p and modulated by the Ssy1p-Ptr3p-Ssy5p (SPS) sensor of extracellular amino acids
YIL053W	FAR1	-0.36	-1.15	Cyclin-dependent kinase inhibitor that mediates cell cycle arrest in response to pheromone; also forms a complex with Cdc24p, Ste4p, and Ste18p that may specify the direction of polarized growth during mating; potential Cdc28p substrate
YIL169C	MRH1	-0.36	-0.29	Protein that localizes primarily to the plasma membrane, also found at the nuclear envelope; the authentic, non-tagged protein is detected in mitochondria in a phosphorylated state; has similarity to Hsp30p and Yro2p
YJL063C	MNN2	-0.35	-0.29	Alpha-1,2-mannosyltransferase, responsible for addition of the first alpha-1,2-linked mannose to form the branches on the mannan backbone of oligosaccharides, localizes to an early Golgi compartment
YJL157C	TCB2	-0.35	-0.50	Bud-specific protein with a potential role in membrane trafficking; GFP-fusion protein migrates from the cell surface to intracellular vesicles near vacuole; contains 3 calcium and lipid binding domains; mRNA is targeted to the bud
YJR009C	SAM2	-0.33	-1.22	S-adenosylmethionine synthetase, catalyzes transfer of the adenosyl group of ATP to the sulfur atom of methionine; one of two differentially regulated isozymes (Sam1p and Sam2p)

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion				
Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YKL096W	FAS1	-0.31	-0.39	Beta subunit of fatty acid synthetase, which catalyzes the synthesis of long-chain saturated fatty acids; contains acetyltransacylase, dehydratase, enoyl reductase, malonyl transacylase, and palmitoyl transacylase activities
YKL182W	SNQ2	-0.31	-0.41	Plasma membrane ATP-binding cassette (ABC) transporter, multidrug transporter involved in multidrug resistance and resistance to singlet oxygen species
YKL209C	HEM2	-0.30	-0.29	Aminolevulinate dehydratase, a homo-octameric enzyme, catalyzes the conversion of 5-aminolevulinate to porphobilinogen, the second step in heme biosynthesis; enzymatic activity is zinc-dependent; localizes to the cytoplasm and nucleus
YKR039W	MRPL8	-0.30	-0.32	Mitochondrial ribosomal protein of the large subunit
YLL024C	ENT2	-0.29	-0.25	Epsin-like protein required for endocytosis and actin patch assembly and functionally redundant with Ent1p; contains clathrin-binding motif at C-terminus
YLL028W	PMA1	-0.29	-0.45	Plasma membrane H+-ATPase, pumps protons out of the cell; major regulator of cytoplasmic pH and plasma membrane potential; part of the P2 subgroup of cation-transporting ATPases
YLR100W	IMG1	-0.29	-0.59	Mitochondrial ribosomal protein of the large subunit, required for respiration and for maintenance of the mitochondrial genome
YLR150W	FCY2	-0.28	-0.19	Purine-cytosine permease, mediates purine (adenine, guanine, and hypoxanthine) and cytosine accumulation
YLR153C	EXG1	-0.28	-0.11	Major exo-1,3-beta-glucanase of the cell wall, involved in cell wall beta-glucan assembly; exists as three differentially glycosylated isoenzymes
YLR205C	RNR1	-0.28	-0.30	Major isoform of the large subunit of ribonucleotide-diphosphate reductase; the RNR complex catalyzes rate-limiting step in dNTP synthesis, regulated by DNA replication and DNA damage checkpoint pathways via localization of small subunits

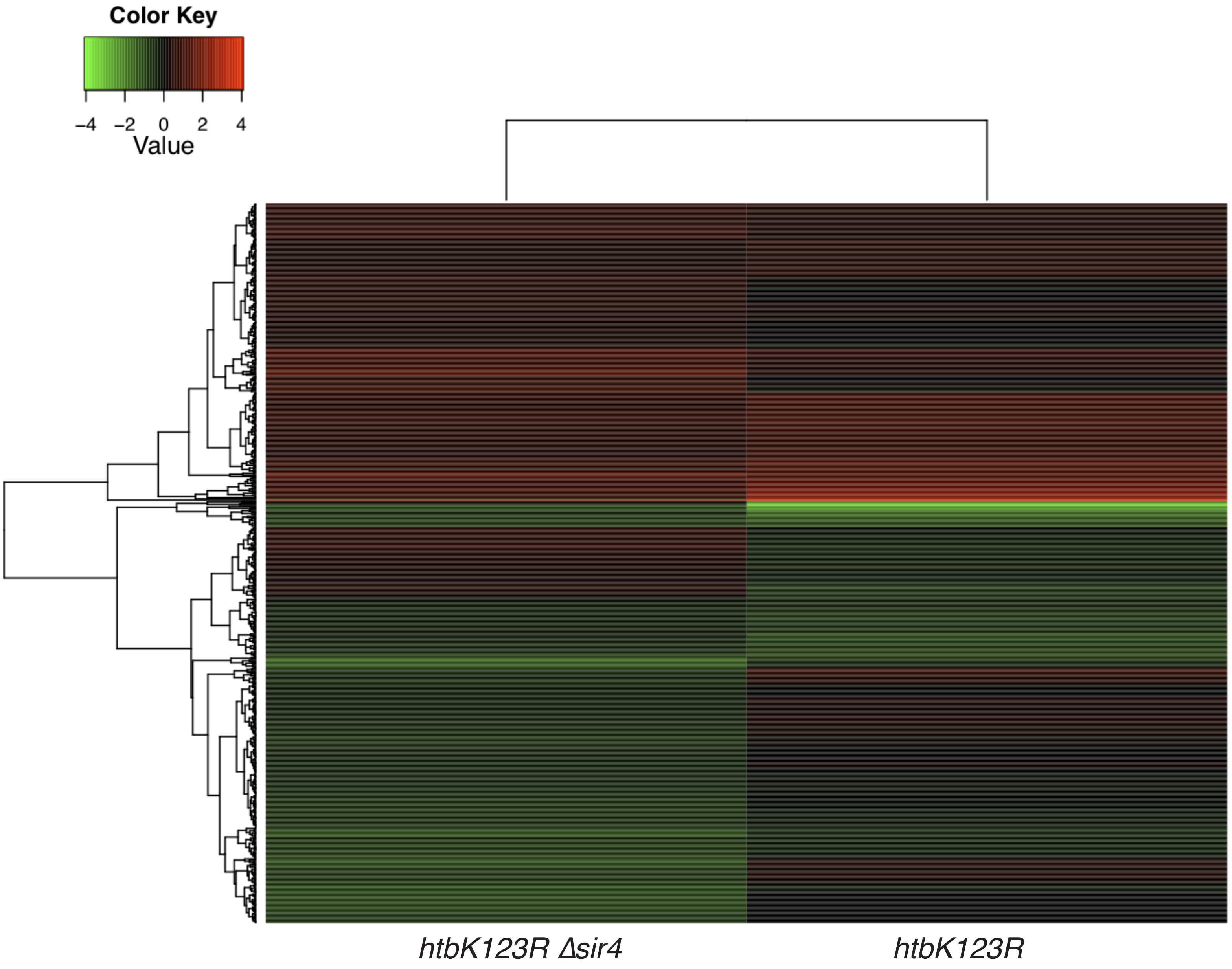
Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	Standard Name	Log2 (Fold change *htbK123R/WT*)	Log2 (Fold change *htbK123RΔsir4/ htbK123R*)	Gene Ontology Annotation
YLR206W	ERG10	-0.28	-0.28	Acetyl-CoA C-acetyltransferase (acetoacetyl-CoA thiolase), cytosolic enzyme that transfers an acetyl group from one acetyl-CoA molecule to another, forming acetoacetyl-CoA; involved in the first step in mevalonate biosynthesis
YLR259C	ACS2	-0.26	-0.79	Acetyl-coA synthetase isoform which, along with Acs1p, is the nuclear source of acetyl-coA for histone acetylation; mutants affect global transcription; required for growth on glucose; expressed under anaerobic conditions
YLR299W	HPF1	-0.26	-0.33	Haze-protective mannoprotein that reduces the particle size of aggregated proteins in white wines
YLR300W	PSA1	-0.26	-0.20	GDP-mannose pyrophosphorylase (mannose-1-phosphate guanyltransferase), synthesizes GDP-mannose from GTP and mannose-1-phosphate in cell wall biosynthesis; required for normal cell wall structure
YLR355C	EGT2	-0.26	-0.17	Glycosylphosphatidylinositol (GPI)-anchored cell wall endoglucanase required for proper cell separation after cytokinesis, expression is activated by Swi5p and tightly regulated in a cell cycle-dependent manner
YMR015C	EDE1	-0.25	-0.44	Key endocytic protein involved in a network of interactions with other endocytic proteins, binds membranes in a ubiquitin-dependent manner, may also bind ubiquitinated membrane-associated proteins
YNL054W-B	MEP3	-0.25	-0.44	Ammonium permease of high capacity and low affinity; belongs to a ubiquitous family of cytoplasmic membrane proteins that transport only ammonium (NH4+); expression is under the nitrogen catabolite repression regulation ammonia permease
YNL087W	PFK1	-0.24	-0.28	Alpha subunit of heterooctameric phosphofructokinase involved in glycolysis, indispensable for anaerobic growth, activated by fructose-2,6-bisphosphate and AMP, mutation inhibits glucose induction of cell cycle-related genes
YNL192W	SEC31	-0.23	-0.36	Component of the Sec13p-Sec31p complex of the COPII vesicle coat, required for vesicle formation in ER to Golgi transport

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion

Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YNL327W	PCM1	-0.19	-0.25	Essential N-acetylglucosamine-phosphate mutase; converts GlcNAc-6-P to GlcNAc-1-P, which is a precursor for the biosynthesis of chitin and for the formation of N-glycosylated mannoproteins and glycosylphosphatidylinositol anchors
YNR016C	FAS2	-0.19	-0.92	Alpha subunit of fatty acid synthetase, which catalyzes the synthesis of long-chain saturated fatty acids; contains the acyl-carrier protein domain and beta-ketoacyl reductase, beta-ketoacyl synthase and self-pantetheinylation activities
YNR019W	TDH3	-0.19	-0.35	Glyceraldehyde-3-phosphate dehydrogenase, isozyme 3, involved in glycolysis and gluconeogenesis; tetramer that catalyzes the reaction of glyceraldehyde-3-phosphate to 1,3 bis-phosphoglycerate; detected in the cytoplasm and cell wall
YOL020W	OYE2	-0.18	-0.50	Conserved NADPH oxidoreductase containing flavin mononucleotide (FMN), homologous to Oye3p with different ligand binding and catalytic properties; may be involved in sterol metabolism, oxidative stress response, and programmed cell death
YOL155C	HSP60	-0.17	-0.19	Tetradecameric mitochondrial chaperonin required for ATP-dependent folding of precursor polypeptides and complex assembly; prevents aggregation and mediates protein refolding after heat shock; role in mtDNA transmission; phosphorylated
YOR153W	GAP1	-0.16	-2.28	General amino acid permease; localization to the plasma membrane is regulated by nitrogen source
YOR317W	ILV5	-0.13	-0.12	Acetohydroxyacid reductoisomerase, mitochondrial protein involved in branched-chain amino acid biosynthesis, also required for maintenance of wild-type mitochondrial DNA and found in mitochondrial nucleoids
YPL028W	ACC1	-0.13	-0.31	Acetyl-CoA carboxylase, biotin containing enzyme that catalyzes the carboxylation of acetyl-CoA to form malonyl-CoA; required for de novo biosynthesis of long-chain fatty acids

Supplemental Table S4: Genes differentially expressed in the *htbK123R* mutant and responsive to subsequent *SIR4* deletion				
Systematic name	**Standard Name**	**Log2 (Fold change *htbK123R/WT*)**	**Log2 (Fold change *htbK123RΔsir4/ htbK123R*)**	**Gene Ontology Annotation**
YPL061W	STM1	-0.13	-0.10	Protein required for optimal translation under nutrient stress; perturbs association of Yef3p with ribosomes; involved in TOR signaling; binds G4 quadruplex and purine motif triplex nucleic acid; helps maintain telomere structure
YPL231W		-0.13	-0.81	Putative protein of unknown function; serine/ threonine rich and highly similar to YOL155C, a putative glucan alpha-1,4-glucosidase; transcript is induced in both high and low pH environments; YIL169C is a non-essential gene
YPR138C	ENO2	-0.12	-0.27	Enolase II, a phosphopyruvate hydratase that catalyzes the conversion of 2-phosphoglycerate to phosphoenolpyruvate during glycolysis and the reverse reaction during gluconeogenesis; expression is induced in response to glucose



SUPPLEMENTAL FIGURE S1. Heat Map representing the fold changes of the Category 4 genes in *htbK123R* and *htbK123R Δsir4* cells relative to congenic WT yeast.