

Supplementary material

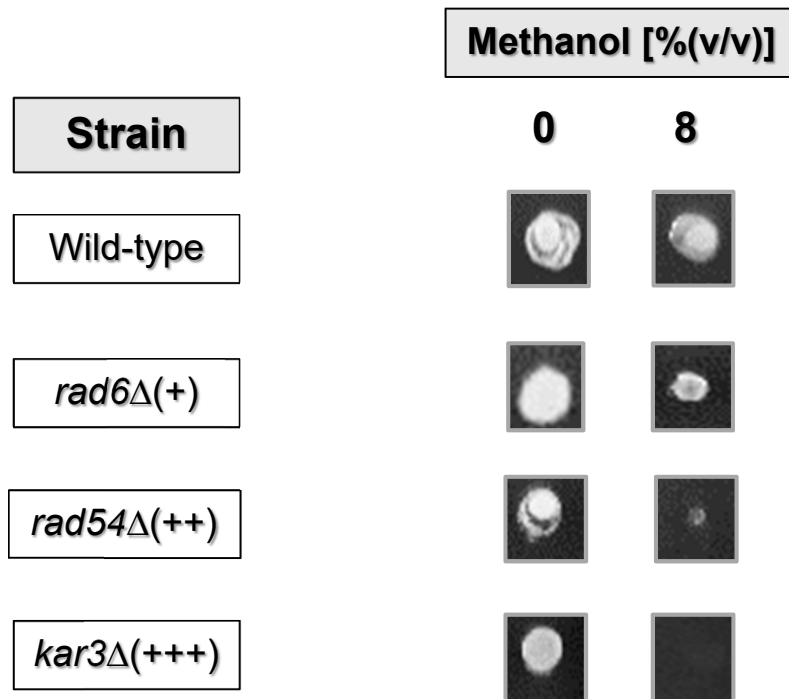


Figure S1. Visual description of the criteria used to define the different levels of susceptibility to methanol of the deletion mutant strains tested. Wild-type and deletion mutant strains were spotted onto solid YPD medium (pH 4.5) supplemented with 8%(v/v) of methanol. Three levels of susceptibility were defined when the growth of the single mutant strains was slightly diminished compared to wild type (+), significantly reduced (++), or abolished (+++).

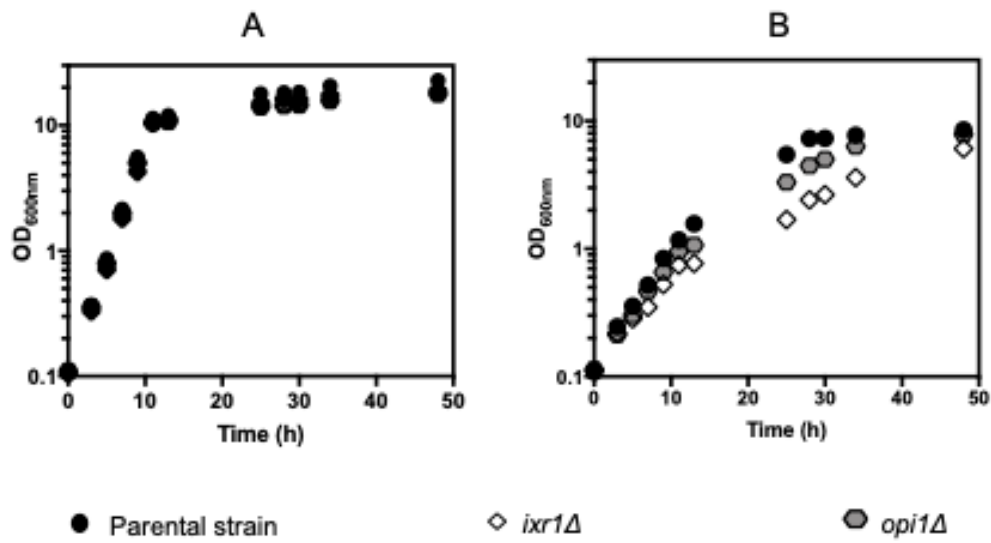


Figure S2. Effect of methanol in the growth curves of the parental strain BY4741 (circles), and derived *ixr1Δ* (hexagons) and *opi1Δ* (squares) mutants in YPD liquid medium, (A) or in this medium supplemented with 8%(v/v) methanol(B) at 35°C with orbital agitation (250 rpm). The growth curves are representative of at least three independent experiments.

Table S1. List of genes whose expression increases *S. cerevisiae* tolerance to 8%(v/v) methanol based on the screening of the Euroscarf deletion mutant collection; the elimination of the indicated genes increases yeast susceptibility to methanol. Biological functions are based on the information available in SGD (www.yeastgenome.org). The symbols '+++', '++' and '+' refer to phenotypes as shown in Figure S1.

Ammonium and vitamin metabolism

Genes	Function	Susceptibility to methanol
<i>BNA1</i>	3-hydroxyanthranilic acid dioxygenase. Bna1 is required for the <i>de novo</i> biosynthesis of NAD from tryptophan via kynurenine.	++
<i>ADO1</i>	Adenosine kinase. Ado1 is required for the utilization of S-adenosylmethionine.	+++
<i>MET7</i>	Folypolyglutamate synthetase. Met7 catalyses extension of the glutamate chains of the folate coenzymes, required for methionine synthesis and for maintenance of mitochondrial DNA.	+
<i>NPR3</i>	Subunit of the Iml1/SEACIT complex; SEACIT (Iml1-Npr2-Npr3) that is required for non-nitrogen-starvation-induced autophagy.	+
<i>PDX3</i>	Pyridoxine (pyridoxamine) phosphate oxidase.	++

Autophagy

Genes	Function	Susceptibility to methanol
<i>ATG11</i>	Adapter protein for pexophagy and the Cvt targeting pathway.	+++
<i>ATG15</i>	Phospholipase; Atg15 is required for lysis of autophagic and CVT bodies.	++
<i>MON1</i>	Subunit of a heterodimeric guanine nucleotide exchange factor (GEF). Mon1 is a subunit of the Mon1-Ccz1 GEF complex which stimulates nucleotide exchange and activation of Ypt7, a Rab family GTPase involved in membrane tethering and fusion events at the late endosome and vacuole.	++

Carbohydrate metabolism

Genes	Function	Susceptibility to methanol
<i>GPH1</i>	Glycogen phosphorylase required for the mobilization of glycogen.	+++
<i>LPD1</i>	Lipoamide dehydrogenase component (E3) of the pyruvate dehydrogenase and 2-oxoglutarate dehydrogenase multi-enzyme complexes.	+++
<i>MAN2</i>	Mannitol dehydrogenase.	+
<i>MLS1</i>	Malate synthase.	+
<i>PDA1</i>	E1 alpha subunit of the pyruvate dehydrogenase (PDH) complex.	+
<i>PDB1</i>	E1 beta subunit of the pyruvate dehydrogenase (PDH) complex.	+
<i>RPE1</i>	D-ribulose-5-phosphate 3-epimerase.	++
<i>TPS1</i>	Synthase subunit of trehalose-6-P synthase/phosphatase complex.	++
<i>TPS2</i>	Phosphatase subunit of the trehalose-6-P synthase/phosphatase complex.	+++

Cell cycle

Genes	Function	Susceptibility to methanol
<i>BNI5</i>	Linker protein responsible for recruitment of myosin to the bud neck.	+
<i>BUB3</i>	Kinetochore checkpoint WD40 repeat protein.	++
<i>CDC55</i>	Regulatory subunit B of protein phosphatase 2A (PP2A).	+++
<i>CIK1</i>	Kinesin-associated protein. Cik1 is required for both karyogamy and mitotic spindle organization.	+++
<i>CIN8</i>	Kinesin motor protein involved in mitotic spindle assembly and chromosome segregation.	++
<i>IBD2</i>	Component of the BUB2-dependent spindle checkpoint pathway.	+
<i>RTS1</i>	B-type regulatory subunit of protein phosphatase 2A (PP2A).	+
<i>SHS1</i>	Component of the septin ring that is required for cytokinesis.	+++
<i>SWM1</i>	Subunit of the anaphase-promoting complex (APC); APC is an E3 ubiquitin ligase that regulates the metaphase-anaphase transition and exit from mitosis.	+++

Cell wall function

Genes	Function	Susceptibility to methanol
<i>CCW12</i>	Cell wall mannoprotein. Ccw12 plays a role in maintenance of newly synthesized areas of cell wall.	++
<i>CWH41</i>	Processing alpha glucosidase I and ER type II integral membrane N-glycoprotein involved in assembly of cell wall beta 1,6 glucan and asparagine-linked protein glycosylation.	+
<i>FKS1</i>	Catalytic subunit of 1,3-beta-D-glucan synthase. Fks1 is involved in cell wall synthesis and maintenance.	+++
<i>GAS1</i>	Beta-1,3-glucanotransferase. Gas1 is required for cell wall assembly and also has a role in transcriptional silencing.	++
<i>KRE6</i>	Type II integral membrane protein. Kre6 is required for beta-1,6 glucan biosynthesis.	++
<i>MNN11</i>	Subunit of a Golgi mannosyltransferase complex that mediates elongation of the polysaccharide mannan backbone.	+++
<i>PEF1</i>	Penta-EF-hand protein, required for polar bud growth and cell wall abscission.	++
<i>ROT2</i>	Glucosidase II catalytic subunit. Rot2 is required to trim the final glucose in N-linked glycans and for normal cell wall synthesis.	+++
<i>SLG1</i>	Sensor-transducer of the stress-activated PKC1-MPK1 kinase pathway. Slg1 is involved in maintenance of cell wall integrity.	++
<i>SMI1</i>	Protein involved in the regulation of cell wall synthesis.	+++

Cellular signalling

Genes	Function	Susceptibility to methanol
<i>ASC1</i>	G-protein beta subunit and guanine dissociation inhibitor for Gpa2 required to prevent frameshifting at ribosomes stalled at repeated CGA codons.	+
<i>BCK1</i>	MAPKKK acting in the protein kinase C signalling pathway, controlling cell integrity.	++

<i>CLA4</i>	Cdc42-activated signal transducing kinase. Cla4 is involved in septin ring assembly, vacuole inheritance, cytokinesis, sterol uptake regulation.	++
<i>ELM1</i>	Serine/threonine protein kinase. Elm1 regulates the orientation checkpoint, the morphogenesis checkpoint and the metabolic switch from fermentative to oxidative metabolism.	++
<i>MKK1</i>	MAPKK involved in the protein kinase C signalling pathway, controlling of cell integrity.	+
<i>NBP2</i>	Protein involved in the HOG (high osmolarity glycerol) pathway; negatively regulates Hog1 by recruitment of phosphatase Ptc1 to the Pbs2-Hog1 complex.	++
<i>PCL6</i>	Pho85p cyclin of the Pho80p subfamily. Pcl6 is involved in the control of glycogen storage by Pho85.	+
<i>RAS2</i>	GTP-binding protein that regulates nitrogen starvation response, sporulation, and filamentous growth.	+++
<i>ROM2</i>	Guanine nucleotide exchange factor (GEF) for Rho1 and Rho2.	+
<i>SNF4</i>	Activating gamma subunit of the AMP-activated Snf1 kinase complex; activates glucose-repressed genes, represses glucose-induced genes; role in sporulation, and peroxisome biogenesis.	++
<i>SST2</i>	GTPase-activating protein for Gpa1. Sst2 regulates desensitization to alpha factor pheromone.	++
<i>TUS1</i>	Guanine nucleotide exchange factor (GEF) that modulates Rho1 activity. Tus1 is involved in the cell integrity signalling pathway.	++
<i>YPT7</i>	Rab family GTPase; GTP-binding protein of the rab family. Ypt7 is required for homotypic fusion event in vacuole inheritance, for endosome-endosome fusion.	++

Chromatin remodelling, nucleic acid metabolism and transcription

Genes	Function	Susceptibility to methanol
<i>ADA2</i>	Transcription coactivator; component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes.	++
<i>AMD1</i>	AMP deaminase that catalyses the deamination of AMP to form IMP and ammonia.	+
<i>ARP8</i>	Nuclear actin-related protein involved in chromatin remodelling.	+
<i>ASF1</i>	Nucleosome assembly factor. Asf1 is involved in chromatin assembly, disassembly and in the recovery after DSB repair.	++
<i>BRE1</i>	E3 ubiquitin ligase. Bre1 forms heterodimer with Rad6 to regulate K63 polyubiquitination in response to oxidative stress and to monoubiquitinate histone H2B-K123, which is required for the subsequent methylation of histone H3-K4 and H3-K79.	++
<i>CBP2</i>	Required for splicing of the group I intron bI5 of the COB pre-mRNA;	+
<i>CDC73</i>	Component of the Paf1 complex. Cdc73 binds to and modulates the activity of RNA polymerases I and II. Cdc73 is also involved in transcription elongation.	++
<i>CHZ1</i>	Histone chaperone for Htz1/H2A-H2B dimer.	+
<i>CSE2</i>	Subunit of the RNA polymerase II mediator complex.	++
<i>CSM1</i>	Nucleolar protein that mediates homolog segregation during meiosis I.	+++
<i>DIA2</i>	Origin-binding F-box protein that functions in ubiquitination of silent chromatin structural protein Sir4. Dia2 is required to target Cdc6 for destruction during G1 phase and is also required for deactivation of Rad53 checkpoint kinase, completion of DNA	++

	replication during recovery from DNA damage, assembly of RSC complex, RSC-mediated transcription regulation, and nucleosome positioning.	
<i>DST1</i>	General transcription elongation factor TFIIS. Dst1 enables RNA polymerase II to read through blocks to elongation by stimulating cleavage of nascent transcripts stalled at transcription arrest sites.	+
<i>ELP3</i>	Subunit of Elongator complex; Elongator is required for modification of wobble nucleosides in tRNA.	+
<i>GCN5</i>	Catalytic subunit of ADA and SAGA histone acetyltransferase complexes.	+
<i>GTF1</i>	Subunit of the trimeric GatFAB AmidoTransferase(AdT) complex. Gtf1 is involved in the formation of Q-tRNA ^Q .	+
<i>HIR3</i>	Subunit of the HIR complex, Hir3 is involved in regulation of histone gene transcription,	+
<i>HTA1</i>	Histone H2A. Hta1 is required for chromatin assembly and chromosome function.	++
<i>HTZ1</i>	Histone variant H2AZ. Htz1 is involved in transcriptional regulation through prevention of the spread of silent heterochromatin.	++
<i>IKI1</i>	Subunit of hexameric RecA-like ATPase Elp456 Elongator subcomplex. Iki1 is required for modification of wobble nucleosides in tRNA.	++
<i>LSM6</i>	Lsm (Like Sm) protein. Lsm6 is part of heteroheptameric complexes and it is involved in RNA decay.	+
<i>MAF1</i>	Negative regulator of RNA polymerase III that is involved in tRNA processing and stability.	++
<i>MED1</i>	Subunit of the RNA polymerase II mediator complex. Med1 is essential for transcriptional regulation.	++
<i>MED2</i>	Subunit of the RNA polymerase II mediator complex. Med2 is essential for transcriptional regulation.	++
<i>MFT1</i>	Subunit of the THO complex that is involved in transcription elongation and mitotic recombination.	++
<i>MOG1</i>	Nuclear protein that interacts with GTP-Gsp1, Mog1 stimulates nucleotide release from Gsp1 and is also involved in nuclear protein import.	+++
<i>NCL1</i>	S-adenosyl-L-methionine-dependent tRNA.	++
<i>NPP1</i>	Nucleotide pyrophosphatase/phosphodiesterase; Npp1 mediates extracellular nucleotide phosphate hydrolysis along with Npp2 and Pho5.	++
<i>NPT1</i>	Nicotinate phosphoribosyltransferase. Npt1 is required for silencing at rDNA and telomeres and has a role in silencing at mating-type loci.	++
<i>NUT1</i>	Component of the RNA polymerase II mediator complex that is required for transcriptional activation and also has a role in basal transcription.	++
<i>PAP2</i>	Non-canonical poly(A) polymerase. Pap2 is involved in nuclear RNA degradation as a component of TRAMP.	+
<i>PAT1</i>	Deadenylation-dependent mRNA-decapping factor.	+
<i>POL32</i>	Third subunit of DNA polymerase delta; Pol32 is involved in chromosomal DNA replication.	+
<i>RCO1</i>	Essential component of the Rpd3S histone deacetylase complex.	++
<i>RFM1</i>	Component of the Sum1-Rfm1-Hst1 complex. Rfm1 is involved in transcriptional repression of middle sporulation genes and in initiation of DNA replication.	+
<i>RMI1</i>	Subunit of the RecQ (Sgs1) - Top3 complex Rmi1 stimulates	++

	superhelical relaxing, DNA catenation/decatenation and ssDNA binding activities of Top3. Rmi1 is also involved in response to DNA damage;	
<i>RRN10</i>	Protein involved in promoting high level transcription of rDNA; subunit of UAF (upstream activation factor) for RNA polymerase I.	++
<i>RRP6</i>	Nuclear exosome exonuclease component that has 3'-5' exonuclease activity that is regulated by Lrp1.	+
<i>RSC1</i>	Component of the RSC chromatin remodelling complex. Rsc1 is required for expression of mid-late sporulation-specific genes.	++
<i>RTT101</i>	Cullin subunit of a Roc1-dependent E3 ubiquitin ligase complex. Rtt101 plays a role in anaphase progression and is required for recovery after DSB repair.	++
<i>RTT109</i>	Histone acetyltransferase. Acetylates H3K56, H3K9.	+
<i>SGS1</i>	RecQ family nucleolar DNA helicase. Sgs1 play a role in genome integrity maintenance, chromosome synapsis, meiotic joint molecule/crossover formation.	++
<i>SIN3</i>	Component of both the Rpd3S and Rpd3L histone deacetylase complexes. Sin3 is involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis.	+
<i>SIR3</i>	Silencing protein. Sir3 is required for spreading of silenced chromatin.	++
<i>SNF6</i>	Subunit of the SWI/SNF chromatin remodelling complex. Snf6 is involved in transcriptional regulation,	++
<i>SPT21</i>	Protein with a role in transcriptional silencing.	++
<i>SPT3</i>	Subunit of the SAGA and SAGA-like transcriptional regulatory complexes.	+
<i>SPT4</i>	Spt4/5 (DSIF) transcription elongation factor complex subunit; the Spt4/5 complex binds to ssRNA in a sequence-specific manner, and along with RNAP I and II has multiple roles regulating transcriptional elongation, RNA processing, quality control, and transcription-coupled repair.	+
<i>SRB8</i>	Subunit of the RNA polymerase II mediator complex. Srb8 is essential for transcriptional regulation and is involved in glucose repression.	+
<i>SSN8</i>	Cyclin-like component of the RNA polymerase II holoenzyme. Ssn8 is involved in phosphorylation of the RNA polymerase II C-terminal domain.	+++
<i>TCD2</i>	tRNA threonylcarbamoyladenosine dehydratase.	+
<i>THO2</i>	Subunit of the THO complex.	+++
<i>THP2</i>	Subunit of the THO and TREX complexes.	+++
<i>THP3</i>	Protein that may have a role in transcription elongation.	+
<i>TOP1</i>	Topoisomerase I; relieves torsional strain in DNA by cleaving and re-sealing the phosphodiester backbone. Top1 relaxes both positively and negatively supercoiled DNA.	++
<i>TOP3</i>	DNA Topoisomerase III that relax single-stranded negatively-supercoiled DNA preferentially.	++
<i>TRF5</i>	Non-canonical poly(A) polymerase. Trf5 is involved in nuclear RNA degradation as a component of the TRAMP complex.	+
<i>UAF30</i>	Subunit of UAF (upstream activation factor) complex.	+++
<i>UBP8</i>	Ubiquitin-specific protease component of the SAGA acetylation complex; Ubp8 is required for SAGA (Spt-Ada-Gcn5-Acetyltransferase)-mediated deubiquitination of histone H2B.	+
<i>UPF3</i>	Component of the nonsense-mediated mRNA decay (NMD) pathway. Upf3 is involved in decay of mRNA containing nonsense codon.	+

YAF9	Subunit of NuA4 histone H4 acetyltransferase and SWR1 complexes.	+
YNG2	Subunit of NuA4, an essential histone acetyltransferase complex.	+++
YTA7	Protein that localizes to chromatin that plays a role in regulation of histone gene expression.	++

Cytoskeleton

Genes	Functions	Susceptibility to methanol
<i>ARP6</i>	Actin-related protein that binds nucleosomes.	+++
<i>BEM2</i>	Rho GTPase activating protein (RhoGAP) that involved in the control of cytoskeleton organization and cellular morphogenesis.	+++
<i>BEM4</i>	Protein involved in establishment of cell polarity and bud emergence.	++
<i>BER1</i>	Protein involved in microtubule-related processes.	++
<i>BIK1</i>	Microtubule-associated protein. Bik1 is a component of the interface between microtubules and kinetochore and is involved in sister chromatid separation.	+
<i>BIM1</i>	Microtubule plus end-tracking protein.	++
<i>BNI1</i>	Formin; polarisome component; nucleates the formation of linear actin filaments, involved in cell processes such as budding and mitotic spindle orientation which require the formation of polarized actin cables.	++
<i>GIN4</i>	Protein kinase involved in bud growth and assembly of the septin ring.	+
<i>HOF1</i>	Protein that regulates actin cytoskeleton organization.	+
<i>KAR3</i>	Minus-end-directed microtubule motor.	+++
<i>LDB18</i>	Component of the dynactin complex; dynactin is required for dynein activity.	++
<i>PAC11</i>	Dynein intermediate chain, microtubule motor protein.	++
<i>SLA1</i>	Cytoskeletal protein binding protein.	+++
<i>SPC72</i>	Gamma-tubulin small complex (gamma-TuSC) receptor.	++
<i>VRP1</i>	Verprolin, proline-rich actin-associated protein; involved in cytoskeletal organization and cytokinesis.	++
<i>YKE2</i>	Subunit of the heterohexameric Gim/prefoldin protein complex; involved in the folding of alpha-tubulin, beta-tubulin, and actin.	+++

DNA repair

Genes	Function	Susceptibility to methanol
<i>MET18</i>	Component of cytosolic iron-sulfur protein assembly (CIA) machinery. Met18 acts at a late step of Fe-S cluster assembly and it is also involved in DNA replication and repair, transcription, and telomere maintenance.	+++
<i>MMS22</i>	Subunit of E3 ubiquitin ligase complex involved in replication repair.	+++
<i>MRE11</i>	Nuclease subunit of the MRX complex with Rad50 and Xrs2; MRX complex functions in repair of DNA double-strand breaks and in telomere stability.	+++
<i>MTF1</i>	Mitochondrial RNA polymerase specificity factor.	++
<i>RAD18</i>	E3 ubiquitin ligase; forms heterodimer with Rad6 to	++

	monoubiquitinate PCNA-K164; Rad18 is required for postreplication repair.	
<i>RAD27</i>	5' to 3' exonuclease, 5' flap endonuclease. Rad27 is required for Okazaki fragment processing and maturation, for long-patch base-excision repair.	+++
<i>RAD33</i>	Protein involved in nucleotide excision repair.	+
<i>RAD5</i>	DNA helicase/Ubiquitin ligase. Rad5 is involved in error-free DNA damage tolerance (DDT), replication fork regression during postreplication repair by template switching, error-prone translesion synthesis.	++
<i>RAD51</i>	Strand exchange protein. Rad51 is involved in the recombinational repair of double-strand breaks in DNA during vegetative growth and meiosis.	+++
<i>RAD54</i>	DNA-dependent ATPase that stimulates strand exchange. Rad54 is involved in the recombinational repair of double-strand breaks in DNA during vegetative growth and meiosis	++
<i>RAD57</i>	Protein that stimulates strand exchange by stabilizing the binding of Rad51 to single-stranded DNA. Rad57 is involved in the recombinational repair of double-strand breaks in DNA during vegetative growth and meiosis.	++
<i>RAD6</i>	Ubiquitin-conjugating enzyme (E2). Rad6 is involved in postreplication repair as a heterodimer with Rad18, regulation of K63 polyubiquitination in response to oxidative stress, DSB and checkpoint control and as a heterodimer with Bre1.	+
<i>TOF1</i>	Subunit of a replication-pausing checkpoint complex. Tof1-Mrc1-Csm3 complex acts at the stalled replication fork to promote sister chromatid cohesion after DNA damage, facilitating gap repair of damaged DNA.	+

Internal pH homeostasis

Genes	Function	Susceptibility to methanol
<i>PMP1</i>	Regulatory subunit for the plasma membrane H ⁽⁺⁾ -ATPase Pma1.	++
<i>VMA1</i>	Subunit A of the V1 peripheral membrane domain of V-ATPase.	+++
<i>VMA13</i>	Subunit H of the V1 peripheral membrane domain of V-ATPase.	+++
<i>VMA2</i>	Subunit B of V1 peripheral membrane domain of vacuolar H ⁺ -ATPase.	+++
<i>VMA7</i>	Subunit F of the V1 peripheral membrane domain of V-ATPase.	+++
<i>VPH1</i>	Subunit a of vacuolar-ATPase V0 domain.	+
<i>VPH2</i>	Integral membrane protein required for V-ATPase function.	++

Intracellular trafficking and protein sorting

Genes	Function	Susceptibility to methanol
<i>ACB1</i>	Acyl-CoA-binding protein that transports newly synthesized acyl-CoA esters from fatty acid synthetase (Fas1-Fas2) to acyl-CoA-consuming processes.	+
<i>ARF1</i>	ADP-ribosylation factor; GTPase of the Ras superfamily involved in regulation of coated vesicle formation in intracellular trafficking within the Golgi.	++
<i>ARV1</i>	Cortical ER protein. Arv1 is implicated in the membrane insertion of	+++

	tail-anchored C-terminal single transmembrane domain proteins.	
<i>BMH1</i>	14-3-3 protein, major isoform. Bmh1 controls proteome at post-transcriptional level, binds proteins and DNA and it is involved in regulation of exocytosis, vesicle transport, Ras/MAPK and rapamycin-sensitive signalling, aggresome formation, spindle position checkpoint.	+
<i>BRO1</i>	Cytoplasmic class E vacuolar protein sorting (VPS) factor. Bro1 coordinates deubiquitination in the multivesicular body (MVB) pathway by recruiting Doa4 to endosomes.	++
<i>BUG1</i>	Cis-Golgi localized protein involved in ER to Golgi transport.	++
<i>CCR4</i>	Component of the CCR4-NOT transcriptional complex. CCR4-NOT is involved in regulation of gene expression.	++
<i>CLC1</i>	Clathrin light chain and a subunit of the major coat protein involved in intracellular protein transport and endocytosis. Clc1 regulates endocytic progression.	+++
<i>DID2</i>	Class E protein of the vacuolar protein-sorting (Vps) pathway. Did2 binds Vps4p and directs it to dissociate ESCRT-III complexes.	++
<i>DID4</i>	Class E Vps protein of the ESCRT-III complex. Did4 is required for sorting of integral membrane proteins into luminal vesicles of multivesicular bodies, and for delivery of newly synthesized vacuolar enzymes to the vacuole.	+
<i>DOA4</i>	Ubiquitin hydrolase. Doa4 dephosphorylates intraluminal vesicle (ILVs) cargo proteins and is required for recycling ubiquitin from proteasome-bound ubiquitinated intermediates.	++
<i>END3</i>	EH domain-containing protein involved in endocytosis.	+
<i>GCS1</i>	ADP-ribosylation factor GTPase activating protein (ARF GAP); involved in ER-Golgi transport.	+++
<i>GLO3</i>	ADP-ribosylation factor GTPase activating protein (ARF GAP) that is involved in ER-Golgi transport.	+
<i>GSF2</i>	Endoplasmic reticulum (ER) localized integral membrane protein that may promote secretion of certain hexose transporters.	++
<i>GTR1</i>	Subunit of a TORC1-stimulating GTPase and the EGO/GSE complex. Gtr1 is also a subunit of Gtr1-Gtr2, a GTPase that activates TORC1 in response to amino acid stimulation.	+
<i>LDB19</i>	Alpha-arrestin involved in ubiquitin-dependent endocytosis.	++
<i>PEP12</i>	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.	++
<i>RAV1</i>	Subunit of RAVE complex (Rav1, Rav2, Skp1). The RAVE complex promotes assembly of the V-ATPase holoenzyme.	+++
<i>RCY1</i>	F-box protein involved in recycling endocytosed proteins.	++
<i>RRT2</i>	Methylesterase performing penultimate step of diphthamide biosynthesis; Rrt2 is involved in endosomal recycling; forms complex with Rtt10p that functions in retromer-mediated pathway for recycling internalized cell-surface proteins.	++
<i>RVS167</i>	Calmodulin-binding actin-associated protein with roles in endocytic membrane tabulation and constriction, and exocytosis.	+
<i>SEC28</i>	Epsilon-COP subunit of the coatamer. Sec28 regulates retrograde Golgi-to-ER protein traffic.	++
<i>SEC66</i>	Non-essential subunit of Sec63 complex.	+++
<i>SEC72</i>	Non-essential subunit of Sec63 complex.	+++
<i>SNF7</i>	One of four subunits of the ESCRT-III complex. Snf1 is involved in the sorting of transmembrane proteins into the multivesicular body (MVB) pathway.	+++
<i>SNF8</i>	Component of the ESCRT-II complex.	+++

<i>STP22</i>	Component of the ESCRT-I complex.	++
<i>SXM1</i>	Nuclear transport factor (karyopherin) that is involved in protein transport between the cytoplasm and nucleoplasm.	+
<i>SYO1</i>	Transport adaptor or symportin that facilitates synchronized nuclear coimport of the two 5S-rRNA binding proteins Rpl5 and Rpl11. Syo1 is required for biogenesis of the large ribosomal subunit.	++
<i>TIM18</i>	Component of the mitochondrial TIM22 complex that is involved in insertion of polytopic proteins into the inner membrane.	+
<i>TRS65</i>	Component of transport protein particle (TRAPP) complex II; TRAPP II is a multimeric guanine nucleotide-exchange factor for the GTPase Ypt1, regulating intra-Golgi and endosome-Golgi traffic.	+++
<i>VAM10</i>	Protein involved in vacuole morphogenesis and acts at an early step of homotypic vacuole fusion that is required for vacuole tethering.	+
<i>VAM3</i>	Syntaxin-like vacuolar t-SNARE. Vam3 mediates docking/fusion of late transport intermediates with the vacuole.	+
<i>VAM6</i>	Guanine nucleotide exchange factor for the GTPase Gtr1. Vam6 is a Rab GTPase effector, interacting with both GTP- and GDP-bound conformations of Ypt7.	+
<i>VAM7</i>	Vacuolar SNARE protein; Vam7 functions with Vam3 in vacuolar protein trafficking.	+++
<i>VPS1</i>	Dynammin-like GTPase required for vacuolar sorting.	+++
<i>VPS20</i>	Myristoylated subunit of the ESCRT-III complex.	++
<i>VPS21</i>	Endosomal Rab family GTPase required for endocytic transport and sorting of vacuolar hydrolases. Vps21 is also required for endosomal localization of the CORVET complex.	++
<i>VPS24</i>	One of four subunits of the ESCRT-III complex. Vps24 is involved in the sorting of transmembrane proteins into the multivesicular body (MVB) pathway.	+++
<i>VPS25</i>	Component of the ESCRT-II complex.	+++
<i>VPS27</i>	Endosomal protein that forms a complex with Hse1. Vps27 is required for recycling Golgi proteins, forming luminal membranes and sorting ubiquitinated proteins destined for degradation.	+++
<i>VPS28</i>	Component of the ESCRT-I complex.	++
<i>VPS3</i>	Component of CORVET membrane tethering complex. VPS is required for the sorting and processing of soluble vacuolar proteins, acidification of the vacuolar lumen, and assembly of the vacuolar H ⁺ -ATPase.	+++
<i>VPS33</i>	ATP-binding protein that is a subunit of the HOPS and CORVET complexes. Vps33 is essential for protein sorting, vesicle docking, and fusion at the vacuole.	+++
<i>VPS36</i>	Component of the ESCRT-II complex.	+++
<i>VPS4</i>	AAA-ATPase involved in multivesicular body (MVB) protein sorting.	++
<i>VPS5</i>	Nexin-1 homolog required for localizing membrane proteins from a prevacuolar/late endosomal compartment back to late Golgi.	+
<i>VPS52</i>	Component of the GARP (Golgi-associated retrograde protein) complex. GARP is required for the recycling of proteins from endosomes to the late Golgi, and for mitosis after DNA damage induced checkpoint arrest.	++
<i>VPS64</i>	Protein required for cytoplasm to vacuole targeting of proteins.	++
<i>VPS72</i>	Htz1-binding component of the SWR1 complex. Vps72 is required for vacuolar protein sorting.	+
<i>VPS74</i>	Golgi phosphatidylinositol-4-kinase effector and PtdIns4P sensor. Vps74 interacts with the cytosolic domains of cis and medial glycosyltransferases, and in the PtdIns4P-bound state mediates the	+

	targeting of these enzymes to the Golgi.	
<i>YPT6</i>	Rab family GTPase required for endosome-to-Golgi, intra-Golgi retrograde, and retrograde Golgi-to-ER transport.	+++

Ion homeostasis

Genes	Function	Susceptibility to methanol
<i>FRE8</i>	Protein with sequence similarity to iron/copper reductases; involved in iron homeostasis.	++

Lipid synthesis

Genes	Function	Susceptibility to methanol
<i>ELO2</i>	Fatty acid elongase, involved in sphingolipid biosynthesis.	+++
<i>ELO3</i>	Elongase involved in fatty acid and sphingolipid biosynthesis.	++
<i>ERG2</i>	C-8 sterol isomerase; catalyses isomerization of delta-8 double bond to delta-7 position at an intermediate step in ergosterol biosynthesis.	+
<i>ERG3</i>	C-5 sterol desaturase. Erg3 is glycoprotein that catalyses the introduction of a C-5(6) double bond into episterol, a precursor in ergosterol biosynthesis.	++
<i>ISC1</i>	Inositol phosphosphingolipid phospholipase C. Isc1 hydrolyzes complex sphingolipids to produce ceramide.	+
<i>KCS1</i>	Inositol hexakisphosphate and inositol heptakisphosphate kinase.	++
<i>LIP5</i>	Protein involved in biosynthesis of the coenzyme lipoic acid.	+
<i>SAC1</i>	Phosphatidylinositol phosphate (PtdInsP) phosphatase. Sac1 is involved in hydrolysis of PtdIns[4]P in the early and medial Golgi.	+
<i>SPO7</i>	Putative regulatory subunit of Nem1-Spo7 phosphatase holoenzyme. Spo7 regulates nuclear growth by controlling phospholipid biosynthesis.	++
<i>TGL3</i>	Bifunctional triacylglycerol lipase and LPE acyltransferase; major lipid particle-localized triacylglycerol (TAG) lipase; catalyses acylation of lysophosphatidylethanolamine (LPE), a function which is essential for sporulation.	+

Mitochondrial function

Genes	Function	Susceptibility to methanol
<i>AIF1</i>	Mitochondrial cell death effector.	+
<i>ATP10</i>	Mitochondrial inner membrane protein that is an assembly factor for the F0 sector of mitochondrial F1F0 ATP synthase	++
<i>ATP11</i>	Molecular chaperone that is required for the assembly of alpha and beta subunits into the F1 sector of mitochondrial F1F0 ATP synthase.	+
<i>CEM1</i>	Mitochondrial beta-keto-acyl synthase required for mitochondrial respiration.	++
<i>COA3</i>	Mitochondrial protein required for cytochrome c oxidase assembly.	+
<i>COQ1</i>	Hexaprenyl pyrophosphate synthetase. Coq1 catalyses the first step in ubiquinone (coenzyme Q) biosynthesis.	+
<i>COQ10</i>	Coenzyme Q (ubiquinone) binding protein that functions in the	+

	delivery of Q6 to its proper location for electron transport during respiration.	
<i>COQ4</i>	Protein with a role in ubiquinone (Coenzyme Q) biosynthesis.	+
<i>COX17</i>	Copper metallochaperone that transfers copper to Sco1 and Cox11.	+
<i>COX18</i>	Mitochondrial integral inner membrane protein required for membrane insertion of C-terminus of Cox2,	++
<i>COX19</i>	Protein required for cytochrome c oxidase assembly.	+
<i>COX9</i>	Subunit VIIa of cytochrome c oxidase (Complex IV).	++
<i>GEP4</i>	Mitochondrial phosphatidylglycerophosphatase (PGP phosphatase). Gep4 dephosphorylates phosphatidylglycerolphosphate to generate phosphatidylglycerol, an essential step during cardiolipin biosynthesis.	++
<i>HFA1</i>	Mitochondrial acetyl-coenzyme A carboxylase that catalyses the production of malonyl-CoA in mitochondrial fatty acid biosynthesis.	+
<i>ICP55</i>	Mitochondrial aminopeptidase. Icp55 cleaves the N termini of at least 38 imported proteins after cleavage by the mitochondrial processing peptidase (MPP), thereby increasing their stability.	++
<i>IMP1</i>	Catalytic subunit of mitochondrial inner membrane peptidase complex; required for maturation of mitochondrial proteins of the intermembrane space	+
<i>ISA1</i>	Protein required for maturation of mitochondrial [4Fe-4S] proteins.	+
<i>MDM12</i>	Mitochondrial outer membrane protein, required for transmission of mitochondria to daughter cells and for mitophagy.	+
<i>MDM20</i>	Non-catalytic subunit of the NatB N-terminal acetyltransferase. Mdm20 is involved in mitochondrial inheritance and actin assembly.	++
<i>MEF1</i>	Mitochondrial elongation factor involved in translational elongation.	+
<i>MGM1</i>	Mitochondrial GTPase required for mitochondrial morphology, fusion, and genome maintenance.	++
<i>MIR1</i>	Mitochondrial phosphate carrier that imports inorganic phosphate into mitochondria.	+++
<i>MMR1</i>	Phosphorylated protein of the mitochondrial outer membrane.	++
<i>MRF1</i>	Mitochondrial translation release factor that is involved in stop codon recognition and hydrolysis of the peptidyl-tRNA bond during mitochondrial translation.	+
<i>MRM1</i>	Ribose methyltransferase that modifies a functionally critical, conserved nucleotide in mitochondrial 21S rRNA	+
<i>MRM2</i>	Mitochondrial 2' O-ribose methyltransferase that is required for methylation of U(2791) in 21S rRNA.	+
<i>MSE1</i>	Mitochondrial glutamyl-tRNA synthetase.	+
<i>MSY1</i>	Mitochondrial tyrosyl-tRNA synthetase.	+
<i>PET54</i>	Mitochondrial inner membrane protein that binds to the 5' UTR of the COX3 mRNA to activate its translation together with Pet122 and Pet494.	+++
<i>POR1</i>	Mitochondrial porin (voltage-dependent anion channel) required for maintenance of mitochondrial osmotic stability and mitochondrial membrane permeability.	+
<i>POS5</i>	Mitochondrial NADH kinase that phosphorylates NADH.	+
<i>PRX1</i>	Mitochondrial peroxiredoxin with thioredoxin peroxidase activity. Prx1 has a role in reduction of hydroperoxides.	++
<i>RMD9</i>	Mitochondrial protein required for respiratory growth.	+
<i>SHE9</i>	Mitochondrial inner membrane protein required for normal mitochondrial morphology.	+

<i>SHY1</i>	Mitochondrial inner membrane protein required for complex IV assembly,	+
<i>SLM5</i>	Mitochondrial asparaginyl-tRNA synthetase.	+++
<i>TIM13</i>	Mitochondrial intermembrane space protein that forms a complex with Tim8 that delivers a subset of hydrophobic proteins to the TIM22 complex for insertion into the inner membrane.	+++
<i>TIM8</i>	Mitochondrial intermembrane space protein. Tim8 forms a complex with Tim13 that delivers a subset of hydrophobic proteins to the TIM22 complex for inner membrane insertion.	+
<i>TOM6</i>	Component of the TOM (translocase of outer membrane) complex. Tom6 is responsible for recognition and initial import steps for all mitochondrially directed proteins.	+
<i>TOM70</i>	Component of the TOM (translocase of outer membrane) complex that is involved in the recognition and initial import steps for all mitochondrially directed proteins.	++
<i>TUF1</i>	Mitochondrial translation elongation factor Tu (EF-Tu). Tuf1 is involved in fundamental pathway of mtDNA homeostasis.	+

Protein folding

Genes	Function	Susceptibility to methanol
<i>BUD27</i>	Unconventional prefoldin protein involved in translation initiation; required for correct assembly of RNAP I, II, and III in an Rpb5-dependent manner.	++
<i>GIM3</i>	Subunit of the heterohexameric cochaperone prefoldin complex; prefoldin binds specifically to cytosolic chaperonin and transfers target proteins to it.	+++
<i>IRC25</i>	Component of a heterodimeric Poc4-Irc25 chaperone. Irc25 is involved in assembly of alpha subunits into the 20S proteasome.	+
<i>PAC10</i>	Part of the heteromeric co-chaperone GimC/prefoldin complex - promotes efficient protein folding.	++
<i>PIH1</i>	Component of the conserved R2TP complex (Rvb1-Rvb2-Tah1-Pih1). The R2TP complex interacts with Hsp90 (Hsp82 and Hsc82) to mediate assembly large protein complexes such as box C/D snoRNPs and RNA polymerase II.	+++
<i>SSE1</i>	ATPase component of heat shock protein Hsp90 chaperone complex. Sse1 binds unfolded proteins.	+
<i>SSZ1</i>	Hsp70 protein that interacts with Zuo1. Ssz1 is also involved in pleiotropic drug resistance via sequential activation of <i>PDR1</i> and <i>PDR5</i> .	++
<i>UMP1</i>	Chaperone required for correct maturation of the 20S proteasome.	++
<i>VPS75</i>	NAP family histone chaperone. Vps75 binds to histones and Rtt109, stimulating histone acetyltransferase activity	++

Protein modification

Genes	Functions	Susceptibility to methanol
<i>AKR1</i>	Palmitoyl transferase involved in protein palmitoylation.	+++
<i>ALG3</i>	Dolichol-P-Man dependent alpha (1-3) mannosyltransferase that is involved in synthesis of dolichol-linked oligosaccharide donor for N-linked glycosylation of proteins.	++

<i>ALG5</i>	UDP-glucose:dolichyl-phosphate glucosyltransferase that is involved in asparagine-linked glycosylation in the endoplasmic reticulum.	++
<i>ALG6</i>	Alpha 1,3 glucosyltransferase that is involved in transfer of oligosaccharides from dolichyl pyrophosphate to asparagine residues of proteins during N-linked protein glycosylation.	+
<i>ALG8</i>	Glucosyl transferase that is involved in N-linked glycosylation.	++
<i>ARG82</i>	Inositol polyphosphate multikinase (IPMK); sequentially phosphorylates Ins(1,4,5)P3 to form Ins(1,3,4,5,6)P5.	++
<i>CKB2</i>	Beta' regulatory subunit of casein kinase 2 (CK2). Ckb2 is a Ser/Thr protein kinase with roles in cell growth and proliferation.	+
<i>DUF1</i>	Ubiquitin-binding protein of unknown function.	+
<i>MCK1</i>	Dual-specificity Ser/Thr and tyrosine protein kinase. Mck1 participates in chromosome segregation, meiotic entry, genome stability.	+
<i>MTQ2</i>	Adenosylmethionine-dependent methyltransferase.	+
<i>NAT1</i>	Subunit of protein N-terminal acetyltransferase NatA.	++
<i>OST6</i>	Subunit of the oligosaccharyltransferase complex of the ER lumen complex. This complex catalyses asparagine-linked glycosylation of newly synthesized proteins.	+
<i>PER1</i>	Protein of the endoplasmic reticulum required for GPI-phospholipase A2 activity that remodels the GPI anchor as a prerequisite for association of GPI-anchored proteins with lipid rafts.	++
<i>PPT2</i>	Phosphopantetheine:protein transferase (PPTase). Ppt2 activates mitochondrial acyl carrier protein (Acp1).	++
<i>SAP155</i>	Protein required for function of the Sit4 protein phosphatase.	++
<i>SEM1</i>	19S proteasome regulatory particle lid subcomplex component.	++
<i>SLX8</i>	Subunit of Slx5-Slx8 SUMO-targeted ubiquitin ligase (STUbL) complex. Slx plays a role in proteolysis of spindle positioning protein Kar9, DNA repair proteins Rad52 and Rad57.	++
<i>UFO1</i>	F-box receptor protein; subunit of the Skp1-Cdc53-F-box receptor (SCF) E3 ubiquitin ligase complex.	++
<i>VID22</i>	Glycosylated integral membrane protein that plays a role in fructose-1,6-bisphosphatase degradation.	++
<i>YME1</i>	Catalytic subunit of i-AAA protease complex. Yme1 is responsible for degradation of unfolded or misfolded mitochondrial gene products.	++

Protein synthesis

Genes	Function	Susceptibility to methanol
<i>DOM34</i>	Protein that facilitates ribosomal subunit dissociation.	+
<i>GEP3</i>	Protein required for mitochondrial ribosome small subunit biogenesis.	+
<i>IMG2</i>	Mitochondrial ribosomal protein of the large subunit.	+++
<i>MRP7</i>	Mitochondrial ribosomal protein of the large subunit.	++
<i>MRPL10</i>	Mitochondrial ribosomal protein of the large subunit.	+
<i>MRPL17</i>	Mitochondrial ribosomal protein of the large subunit.	+
<i>MRPL20</i>	Mitochondrial ribosomal protein of the large subunit.	++
<i>MRPL22</i>	Mitochondrial ribosomal protein of the large subunit.	+
<i>MRPL24</i>	Mitochondrial ribosomal protein of the large subunit.	+

<i>MRPL25</i>	Mitochondrial ribosomal protein of the large subunit.	+
<i>MRPL27</i>	Mitochondrial ribosomal protein of the large subunit.	+
<i>MRPL7</i>	Mitochondrial ribosomal protein of the large subunit.	++
<i>MRPS28</i>	Mitochondrial ribosomal protein of the small subunit.	+
<i>MRPS35</i>	Mitochondrial ribosomal protein of the small subunit.	++
<i>RPL12B</i>	Ribosomal 60S subunit protein L12B.	+
<i>RPL14A</i>	Ribosomal 60S subunit protein L14A	++
<i>RPL16B</i>	Ribosomal 60S subunit protein L16B.	+
<i>RPL19B</i>	Ribosomal 60S subunit protein L19B.	++
<i>RPL21A</i>	Ribosomal 60S subunit protein L21A.	++
<i>RPL36A</i>	Ribosomal 60S subunit protein L36A.	+++
<i>RPL43A</i>	Ribosomal 60S subunit protein L43A.	++
<i>RPL8A</i>	Ribosomal 60S subunit protein L8A.	+
<i>RPS0B</i>	Protein component of the small (40S) ribosomal subunit.	++
<i>RPS11A</i>	Protein component of the small (40S) ribosomal subunit.	+
<i>RPS17A</i>	Ribosomal protein 51 (rp51) of the small (40s) subunit.	+
<i>RPS19A</i>	Protein component of the small (40S) ribosomal subunit.	+
<i>RPS22B</i>	Protein component of the small (40S) ribosomal subunit.	++
<i>RPS24A</i>	Protein component of the small (40S) ribosomal subunit.	+
<i>RPS27B</i>	Protein component of the small (40S) ribosomal subunit.	+
<i>RSM18</i>	Mitochondrial ribosomal protein of the small subunit.	+
<i>RSM23</i>	Mitochondrial ribosomal protein of the small subunit.	+
<i>RSM7</i>	Mitochondrial ribosomal protein of the small subunit.	+++
<i>TEF4</i>	Gamma subunit of translational elongation factor eEF1B.	+++
<i>IFM1</i>	Mitochondrial translation initiation factor 2.	++

Response to stress

Genes	Function	Susceptibility to methanol
<i>GSH1</i>	Gamma glutamylcysteine synthetase. Gsh1 catalyses the first step in glutathione (GSH) biosynthesis.	++
<i>MXR1</i>	Methionine-S-sulfoxide reductase that is involved in the response to oxidative stress, Mxr1 also protects iron-sulfur clusters from oxidative inactivation along with <i>MXR2</i> .	+
<i>RMD8</i>	Cytosolic protein required for sporulation.	++
<i>SOD1</i>	Cytosolic copper-zinc superoxide dismutase; detoxifies superoxide.	+++

Transcription factors

Gene	Function	Susceptibility to methanol
<i>CBF1</i>	Transcription factor that associates with kinetochore proteins, required for chromosome segregation. Basic helix-loop-helix (bHLH) protein; forms homodimer to bind E-box consensus sequence CACGTG present at MET gene promoters and centromere DNA element I (CDEI); affects nucleosome positioning at this motif; associates with other transcription factors such as Met4 and Isw1 to mediate transcriptional activation or repression;	+
<i>GLN3</i>	Transcriptional activator of genes regulated by nitrogen catabolite repression; localization and activity regulated by quality of nitrogen source and Ure2.	+
<i>IXR1</i>	Transcriptional repressor that regulates hypoxic genes during	+++

	normoxia; involved in the aerobic repression of genes such as <i>COX5b</i> , <i>TIR1</i> , and <i>HEM13</i> .	
<i>NGG1</i>	Transcriptional regulator involved in glucose repression of Gal4-regulated genes. Subunit of chromatin modifying histone acetyltransferase complexes; member of the ADA complex, the SAGA complex, and the SLIK complex.	++
<i>OPI1</i>	Transcriptional regulator of a variety of genes; its phosphorylation by protein kinase A stimulates Opi1 function in negative regulation of phospholipid biosynthetic genes; involved in telomere maintenance.	+++
<i>RPH1</i>	Transcription factor with JmjC domain-containing histone demethylase. Rph1 targets tri- and dimethylated H3K36 and associates with actively transcribed regions and promotes elongation. Rph1 acts as a repressor of autophagy-related genes in nutrient-replete conditions.	+
<i>RPN4</i>	Transcription factor that stimulates expression of proteasome encoding genes being regulated by the 26S proteasome in a negative feedback control mechanism; <i>RPN4</i> is transcriptionally regulated by various stress response.	+
<i>SFL1</i>	Transcriptional repressor and activator; involved in repression of flocculation-related genes, and activation of stress responsive genes; has direct role in <i>INO1</i> transcriptional memory; negatively regulated by cAMP-dependent protein kinase A subunit Tpk2.	++
<i>SOK2</i>	Transcription factor that negatively regulates pseudohyphal differentiation. Sok2 also plays a regulatory role in the cyclic AMP (cAMP)-dependent protein kinase (PKA) signal transduction pathway.	++
<i>SFP1</i>	Transcription factor that regulates ribosomal protein and biogenesis genes. Sfp1 also regulates response to nutrients and stress, G2/M transitions during mitotic cell cycle and DNA-damage response and modulates cell size.	++
<i>STB5</i>	Transcription factor involved in the regulation multidrug resistance and oxidative stress response; forms a heterodimer with Pdr1; contains a Zn(II) ₂ Cys ₆ zinc finger domain that interacts with a pleiotropic drug resistance element <i>in vitro</i> .	++
<i>UME6</i>	Transcriptional regulator of early meiotic genes; involved in chromatin remodelling and transcriptional repression via DNA looping; binds URS1 upstream regulatory sequence, represses transcription by recruiting conserved histone deacetylase Rpd3 (through co-repressor Sin3) and chromatin-remodelling factor Isw2; couples metabolic responses to nutritional cues with initiation and progression of meiosis.	++

Transporters

Gene	Function	Susceptibility to methanol
<i>AGP2</i>	General amino acid permease with broad substrate specificity. Can also transport carnitine.	++
<i>FEN2</i>	Plasma membrane H ⁺ -pantothenate symporter.	+++
<i>MCH4</i>	Probable transporter. Does not act in the transport of monocarboxylic acids across the plasma membrane.	+
<i>MCH5</i>	Riboflavin transporter involved in riboflavin (vitamin B2) uptake. monocarboxylic acids across the plasma membrane.	+++
<i>MUP1</i>	High affinity methionine permease that is also involved in cysteine	++

	uptake.	
<i>PET8</i>	S-adenosyl-L-methionine transport.	+
<i>SPF1</i>	Mediates manganese transport into the endoplasmic reticulum. The ATPase activity is required for cellular manganese homeostasis.	+++
<i>TPN1</i>	Thiamine-regulated, high affinity import carrier of pyridoxine, pyridoxal and pyridoxamine.	++
<i>VMR1</i>	ATP-binding cassette (ABC) family member involved in multiple drug resistance and metal sensitivity.	+

Unknown function

Gene	Function	Susceptibility to methanol
<i>AIM22</i>	Putative lipoate-protein ligase.	++
<i>AIM26</i>	Protein of unknown function.	+++
<i>DIA1</i>	Protein of unknown function; involved in invasive and pseudohyphal growth.	++
<i>EMI1</i>	Non-essential protein of unknown function; required for transcriptional induction of the early meiotic-specific transcription factor IME1, also required for sporulation.	+
<i>ERD1</i>	Predicted membrane protein required for luminal ER protein retention.	+
<i>FSH3</i>	Putative serine hydrolase.	+
<i>FYV1</i>	Dubious open reading frame; unlikely to encode a functional protein.	+
<i>ILM1</i>	Protein of unknown function; may be involved in mitochondrial DNA maintenance; required for slowed DNA synthesis-induced filamentous growth.	+++
<i>IRC13</i>	Putative protein of unknown function.	+
<i>MCT1</i>	Predicted malonyl-CoA:ACP transferase.	+
<i>NRP1</i>	Putative RNA binding protein of unknown function.	++
<i>OPI8</i>	Dubious open reading frame; unlikely to encode a functional protein,	++
<i>OPI9</i>	Dubious open reading frame; unlikely to encode a functional protein	+++
<i>RBK1</i>	Putative ribokinase.	++
<i>RRG9</i>	Protein of unknown function.	+
<i>SWS2</i>	Putative mitochondrial ribosomal protein of the small subunit.	+
<i>TAN1</i>	Putative tRNA acetyltransferase;	+++
<i>VPS61</i>	Dubious open reading frame; unlikely to encode a functional protein.	**
<i>VPS63</i>	Putative protein of unknown function.	+++
<i>VPS65</i>	Dubious open reading frame; unlikely to encode a functional protein.	+++
<i>YBL083C</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YBL094C</i>	Dubious open reading frame; unlikely to encode a functional protein.	+++
<i>YBR085C-A</i>	Protein of unknown function.	+
<i>YBR225W</i>	Putative protein of unknown function.	+
<i>YBR226C</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YCR025C</i>	Putative protein of unknown function.	++
<i>YDL062W</i>	Dubious open reading frame; unlikely to encode a functional	++

	protein.	
<i>YDL199C</i>	Putative transporter; member of the sugar porter family.	++
<i>YDR008C</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YDR203W</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YDR230W</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YDR417C</i>	Dubious open reading frame; unlikely to encode a functional protein.	+
<i>YDR431W</i>	Dubious open reading frame; unlikely to encode a functional protein.	+
<i>YER156C</i>	Putative protein of unknown function.	+
<i>YGL007C-A</i>	Putative protein of unknown function.	+++
<i>YGL149W</i>	Putative protein of unknown function.	+
<i>YGL235W</i>	Putative protein of unknown function.	++
<i>YGR011W</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YGR064W</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YGR182C</i>	Dubious open reading frame; unlikely to encode a functional protein.	+++
<i>YHL005C</i>	Putative protein of unknown function.	+
<i>YIM2</i>	Dubious open reading frame; unlikely to encode a functional protein.	+
<i>YJL120W</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YJR011C</i>	Putative protein of unknown function.	++
<i>YJR120W</i>	Protein of unknown function.	+
<i>YLR111W</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YLR202C</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YLR235C</i>	Dubious open reading frame; unlikely to encode a functional protein,	++
<i>YLR269C</i>	Dubious open reading frame; unlikely to encode a functional protein.	+++
<i>YLR366W</i>	Dubious open reading frame; unlikely to encode a functional protein.	+
<i>YML009W-B</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YML012C-A</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YMR031W-A</i>	Dubious open reading frame; unlikely to encode a functional protein,	+++
<i>YMR075C-A</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YNL140C</i>	Protein of unknown function.	+
<i>YNL165W</i>	Putative protein of unknown function.	+
<i>YNL319W</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YNR005C</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YOR139C</i>	Dubious open reading frame; unlikely to encode a functional protein.	++
<i>YOR199W</i>	Dubious open reading frame; unlikely to encode a functional	+

	protein.	
<i>YOR200W</i>	Dubious open reading frame; unlikely to encode a functional protein.	+
<i>YOR331C</i>	Dubious open reading frame; unlikely to encode a functional protein.	+

Table S2. List of genes whose expression increases *S. cerevisiae* tolerance to 5.5%(v/v) ethanol based on the screening of the Euroscarf deletion mutant collection; the elimination of the indicated genes increases yeast susceptibility to ethanol. Biological functions are based on the information available in SGD (www.yeastgenome.org). The symbols '+++', '++' and '+' correspond to phenotypes as shown in Figure S1.

Autophagy

Gene	Function	Susceptibility level
<i>ATG10</i>	Conserved E2-like conjugating enzyme; mediates formation of the Atg12-Atg5 conjugate, which is a critical step in autophagy.	+
<i>ATG11</i>	Adapter protein for pexophagy and the Cvt targeting pathway; directs receptor-bound cargo to the phagophore assembly site (PAS) for packaging into vesicles; required for recruiting other proteins to the PAS; recruits Dnm1p to facilitate fission of mitochondria that are destined for removal by mitophagy.	++
<i>ATG17</i>	Scaffold protein responsible for phagophore assembly site organization; regulatory subunit of an autophagy-specific complex that includes Atg1 and Atg13; stimulates Atg1 kinase activity.	+
<i>ATG2</i>	Peripheral membrane protein required for autophagic vesicle formation; also required for vesicle formation during pexophagy and the cytoplasm-to-vacuole targeting (Cvt) pathway; involved in Atg9p cycling between the phagophore assembly site and mitochondria; contains an APT1 domain that binds phosphatidylinositol-3-phosphate; essential for cell cycle progression from G2/M to G1 under nitrogen starvation; forms cytoplasmic foci upon DNA replication stress.	+
<i>ATG20</i>	Sorting nexin family member; required for the cytoplasm-to-vacuole targeting (Cvt) pathway and for endosomal sorting; has a Phox homology domain that binds phosphatidylinositol-3-phosphate; interacts with Snx4; potential Cdc28 substrate.	+++
<i>ATG4</i>	Conserved cysteine protease required for autophagy; cleaves Atg8p to a form required for autophagosome and Cvt vesicle generation.	+
<i>MEH1</i>	Component of the EGO and GSE complexes; EGO is involved in the regulation of microautophagy and GSE is required for proper sorting of amino acid permease Gap1.	+

Carbohydrate metabolism

Gene	Function	Susceptibility level
<i>ADH3</i>	Mitochondrial alcohol dehydrogenase isozyme III; involved in the shuttling of mitochondrial NADH to the cytosol under anaerobic conditions and ethanol production.	++

<i>ARO1</i>	Pentafunctional arom protein; catalyzes steps 2 through 6 in the biosynthesis of chorismate, which is a precursor to aromatic amino acids.	+
<i>ARO2</i>	Bifunctional chorismate synthase and flavin reductase; catalyzes the conversion of 5-enolpyruvylshikimate 3-phosphate (EPSP) to form chorismate, which is a precursor to aromatic amino acids; protein abundance increases in response to DNA replication stress.	++
<i>ARO7</i>	Chorismate mutase; catalyzes the conversion of chorismate to prephenate to initiate the tyrosine/phenylalanine-specific branch of aromatic amino acid biosynthesis.	+++
<i>BNA1</i>	3-hydroxyanthranilic acid dioxygenase; required for the <i>de novo</i> biosynthesis of NAD from tryptophan via kynurenine; expression regulated by Hst1.	++
<i>FUM1</i>	Fumarase; converts fumaric acid to L-malic acid in the TCA cycle; cytosolic and mitochondrial distribution determined by the N-terminal targeting sequence, protein conformation, and status of glyoxylate shunt; phosphorylated in mitochondria.	++
<i>GCN5</i>	Catalytic subunit of ADA and SAGA histone acetyltransferase complexes; modifies N-terminal lysines on histones H2B and H3; acetylates Rsc4p, a subunit of the RSC chromatin-remodeling complex, altering replication stress tolerance; relocates to the cytosol in response to hypoxia; mutant displays reduced transcription elongation in the G-less-based run-on (GLRO).	++
<i>GPH1</i>	Glycogen phosphorylase required for the mobilization of glycogen; non-essential; regulated by cyclic AMP-mediated phosphorylation; phosphorylation by Cdc28 may coordinately regulate carbohydrate metabolism and the cell cycle; expression is regulated by stress-response elements and by the HOG MAP kinase pathway.	++
<i>KGD2</i>	Dihydrolipoyl transsuccinylase; component of the mitochondrial alpha-ketoglutarate dehydrogenase complex, which catalyzes the oxidative decarboxylation of alpha-ketoglutarate to succinyl-CoA in the TCA cycle.	+
<i>MET7</i>	Folypolyglutamate synthetase; catalyzes extension of the glutamate chains of the folate coenzymes, required for methionine synthesis and for maintenance of mitochondrial DNA.	+
<i>PCL7</i>	Pho85p cyclin of the Pho80 subfamily; forms a functional kinase complex with Pho85 which phosphorylates Mmr1 and is regulated by Pho81; involved in glycogen metabolism, expression is cell-cycle regulated; <i>PCL7</i> has a paralog, <i>PCL6</i> , that arose from the whole genome duplication.	+
<i>PDC1</i>	Major of three pyruvate decarboxylase isozymes; key enzyme in alcoholic fermentation; decarboxylates pyruvate to acetaldehyde; involved in amino acid catabolism.	+
<i>PRS3</i>	5-phospho-ribosyl-1(alpha)-pyrophosphate synthetase; synthesizes PRPP, which is required for nucleotide, histidine, and tryptophan biosynthesis; one of five related enzymes, which are active as heteromultimeric complexes.	+++
<i>REG1</i>	Regulatory subunit of type 1 protein phosphatase Glc7; involved in negative regulation of glucose-repressible genes; involved in regulation of the nucleocytoplasmic shuttling of Hxk2; <i>REG1</i> has a paralog, <i>REG2</i> , that arose from the whole genome duplication.	+++

<i>REG2</i>	Regulatory subunit of the Glc7 type-1 protein phosphatase; involved with Reg1, Glc7, and Snf1 in regulation of glucose-repressible genes.	+
<i>RIB4</i>	Lumazine synthase (DMRL synthase); catalyzes synthesis of immediate precursor to riboflavin; DMRL synthase stands for 6,7-dimethyl-8-ribityllumazine synthase.	+++

Cell cycle

Gene	Function	Susceptibility level
<i>CIK1</i>	Kinesin-associated protein; required for both karyogamy and mitotic spindle organization, interacts stably and specifically with Kar3 and may function to target this kinesin to a specific cellular role; locus encodes a long and short transcript with differing functions; <i>CIK1</i> has a paralog, <i>VIK1</i> , that arose from the whole genome duplication.	+++
<i>CLN1</i>	G1 cyclin involved in regulation of the cell cycle; activates Cdc28 kinase to promote the G1 to S phase transition; late G1 specific expression depends on transcription factor complexes, MBF (Swi-Mbp1) and SBF (Swi6-Swi4).	+
<i>HOS4</i>	Subunit of the Set3 complex; complex is a meiotic-specific repressor of sporulation specific genes that contains deacetylase activity.	+
<i>IRC19</i>	Protein of unknown function; <i>YLL033W</i> is not an essential gene but mutant is defective in spore formation; null mutant displays increased levels of spontaneous Rad52 foci.	++
<i>SPO22</i>	Meiosis-specific protein essential for chromosome synapsis; involved in completion of nuclear divisions during meiosis.	+

Cell wall function

Gene	Function	Susceptibility level
<i>CHS1</i>	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.	+++
<i>CWH43</i>	GPI lipid remodelase; responsible for introducing ceramides into GPI anchors having a C26:0 fatty acid in sn-2 of the glycerol moiety; can also use lyso-GPI protein anchors and various base resistant lipids as substrates.	+
<i>FKS1</i>	Catalytic subunit of 1,3-beta-D-glucan synthase; functionally redundant with alternate catalytic subunit Gsc2; binds to regulatory subunit Rho1p; involved in cell wall synthesis and maintenance; localizes to sites of cell wall remodeling.	+++
<i>MNN11</i>	Subunit of a Golgi mannosyltransferase complex; this complex also contains Anp1, Mnn9, Mnn10, and Hoc1, and mediates elongation of the polysaccharide mannan backbone; has homology to Mnn10.	+++

<i>PUN1</i>	Plasma membrane protein with a role in cell wall integrity; co-localizes with Sur7 in punctate membrane patches.	+
<i>ROM2</i>	Guanine nucleotide exchange factor (GEF) for Rho1 and Rho2; mutations are synthetically lethal with mutations in <i>rom1</i> , which also encodes a GEF; Rom2 localization to the bud surface is dependent on Ack1p; <i>ROM2</i> has a paralog, <i>ROM1</i> , that arose from the whole genome duplication.	+
<i>ROT2</i>	Glucosidase II catalytic subunit; required to trim the final glucose in N-linked glycans; required for normal cell wall synthesis; mutations in <i>rot2</i> suppress <i>tor2</i> mutations, and are synthetically lethal with <i>rot1</i> mutations.	++
<i>SAG1</i>	Alpha-agglutinin of alpha-cells; binds to Aga1 during agglutination, N-terminal half is homologous to the immunoglobulin superfamily and contains binding site for a-agglutinin, C-terminal half is highly glycosylated and contains GPI anchor.	++
<i>SLG1</i>	Sensor-transducer of the stress-activated PKC1-MPK1 kinase pathway; involved in maintenance of cell wall integrity; required for mitophagy; involved in organization of the actin cytoskeleton; secretory pathway Wsc1 is required for the arrest of secretion response.	+++
<i>SMI1</i>	Protein involved in the regulation of cell wall synthesis; proposed to be involved in coordinating cell cycle progression with cell wall integrity.	++
<i>YEH2</i>	Steryl ester hydrolase; catalyzes steryl ester hydrolysis at the plasma membrane; involved in sterol metabolism; <i>YEH2</i> has a paralog, <i>YEH1</i> , that arose from the whole genome duplication.	++

Chromatin remodelling and transcriptional control

Gene	Function	Susceptibility level
<i>ADA2</i>	Transcription coactivator; component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes.	++
<i>APA1</i>	AP4A phosphorylase; catalyzes phosphorolysis of dinucleoside oligophosphates, cleaving substrates' alpha/beta-anhydride bond and introducing Pi into the beta-position of the corresponding NDP formed.	+
<i>ADO1</i>	Adenosine kinase; required for the utilization of S-adenosylmethionine (AdoMet); may be involved in recycling adenosine produced through the methyl cycle.	+++
<i>APT1</i>	Adenine phosphoribosyltransferase; catalyzes the formation of AMP from adenine and 5-phosphoribosylpyrophosphate; involved in the salvage pathway of purine nucleotide biosynthesis; <i>APT1</i> has a paralog, <i>APT2</i> , that arose from the whole genome duplication.	++
<i>BUD13</i>	Subunit of the RES complex; RES complex is required for nuclear pre-mRNA retention and splicing; involved in bud-site selection; diploid mutants display a unipolar budding pattern instead of the wild-type bipolar pattern due to a specific defect in MATa1 pre-mRNA splicing which leads to haploid gene expression in diploids.	+++

<i>CBP2</i>	Required for splicing of the group I intron bI5 of the COB pre-mRNA; nuclear-encoded mitochondrial protein that binds to the RNA to promote splicing; also involved in but not essential for splicing of the COB bI2 intron and the intron in the 21S rRNA gene.	++
<i>CBS1</i>	Mitochondrial translational activator of the COB mRNA; membrane protein that interacts with translating ribosomes, acts on the COB mRNA 5'-untranslated leader.	+
<i>CBS2</i>	Mitochondrial translational activator of the COB mRNA; interacts with translating ribosomes, acts on the COB mRNA 5'-untranslated leader.	++
<i>CCR4</i>	Component of the <i>CCR4-NOT</i> transcriptional complex; <i>CCR4-NOT</i> is involved in regulation of gene expression; component of the major cytoplasmic deadenylase, which is involved in mRNA poly(A) tail shortening.	+
<i>CDC50</i>	Endosomal protein that interacts with phospholipid flippase Drs2; interaction with Cdc50 is essential for Drs2 catalytic activity; mutations affect cell polarity and polarized growth; similar to Lem3; <i>CDC50</i> has a paralog, <i>YNR048W</i> , that arose from the whole genome duplication.	+++
<i>COQ4</i>	Protein with a role in ubiquinone (Coenzyme Q) biosynthesis; possibly functioning in stabilization of Coq7; located on matrix face of mitochondrial inner membrane.	+
<i>COQ10</i>	Coenzyme Q (ubiquinone) binding protein; functions in the delivery of Q6 to its proper location for electron transport during respiration; START domain protein with homologs in bacteria and eukaryotes; respiratory growth defect of the null mutant is functionally complemented by human <i>COQ10A</i> .	++
<i>CSE2</i>	Subunit of the RNA polymerase II mediator complex; associates with core polymerase subunits to form the RNA polymerase II holoenzyme; component of the Middle domain of mediator; required for regulation of RNA polymerase II activity; relocates to the cytosol in response to hypoxia.	++
<i>DEP1</i>	Component of the Rpd3L histone deacetylase complex; required for diauxic shift-induced histone H2B deposition onto rDNA genes; transcriptional modulator involved in regulation of structural phospholipid biosynthesis genes and metabolically unrelated genes, as well as maintenance of telomeres, mating efficiency, and sporulation.	+
<i>DHH1</i>	Cytoplasmic DEAD-box helicase, stimulates mRNA decapping; coordinates distinct steps in mRNA function and decay, interacting with both decapping and deadenylase complexes; role in translational repression, mRNA decay, and possibly mRNA export; interacts and cooperates with Ngr1 to promote specific mRNA decay; ATP- and RNA-bound form promotes processing body (PB) assembly, while ATPase stimulation by Not1p promotes PB disassembly; forms cytoplasmic <i>foci</i> on replication stress.	+++
<i>DST1</i>	General transcription elongation factor TFIIS; enables RNA polymerase II to read through blocks to elongation by stimulating cleavage of nascent transcripts stalled at transcription arrest sites; maintains RNAPII elongation activity on ribosomal protein genes during conditions of transcriptional stress.	+++

<i>ELP3</i>	Subunit of Elongator complex; Elongator 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 <i>K. lactis</i> zymotoxin; human homolog <i>ELP3</i> can partially complement yeast <i>elp3</i> null mutant.	++
<i>GTF1</i>	Subunit of the trimeric GatFAB AmidoTransferase(AdT) complex; involved in the formation of Q-tRNAQ; transposon insertion mutant is salt sensitive and null mutant has growth defects; non-tagged protein is detected in purified mitochondria.	++
<i>HDA2</i>	Subunit of the HDA1 histone deacetylase complex; possibly tetrameric trichostatin A-sensitive class II histone deacetylase complex contains Hda1p homodimer and an Hda2-Hda3 heterodimer; involved in telomere maintenance; relocalizes to the cytosol in response to hypoxia.	++
<i>HIT1</i>	Protein involved in C/D snoRNP assembly; regulates abundance of Rsa1p; required for growth at high temperature; similar to human <i>ZNHIT</i> .	++
<i>HMI1</i>	Mitochondrial inner membrane localized ATP-dependent DNA helicase; required for the maintenance of the mitochondrial genome; not required for mitochondrial transcription; has homology to <i>E. coli</i> helicase <i>uvrD</i> .	++
<i>HMO1</i>	Chromatin associated high mobility group (HMG) family member; involved in compacting, bending, bridging and looping DNA; rDNA-binding component that regulates transcription from RNA polymerase I promoters; regulates start site selection of ribosomal protein genes via RNA polymerase II promoters.	+++
<i>HPR1</i>	Subunit of <i>THO/TREX</i> complexes; this complex couple transcription elongation with mitotic recombination and with mRNA metabolism and export, subunit of an RNA Pol II complex; regulates lifespan; involved in telomere maintenance; similar to Top1.	+++
<i>HTL1</i>	Component of the RSC chromatin remodeling complex; RSC functions in transcriptional regulation and elongation, chromosome stability, and establishing sister chromatid cohesion; involved in telomere maintenance.	+++
<i>HTZ1</i>	Histone variant H2AZ; exchanged for histone H2A in nucleosomes by the SWR1 complex; involved in transcriptional regulation through prevention of the spread of silent heterochromatin; Htz1-containing nucleosomes facilitate RNA Pol II passage by affecting correct assembly and modification status of RNA Pol II elongation complexes and by favoring efficient nucleosome remodeling.	+++
<i>IME4</i>	mRNA N6-adenosine methyltransferase required for entry into meiosis; mediates N6-adenosine methylation of bulk mRNA during the induction of sporulation which includes the meiotic regulators <i>IME1</i> , <i>IME2</i> and <i>IME4</i> itself; repressed in haploids via production of antisense <i>IME4</i> transcripts.	+
<i>IST3</i>	Component of the U2 snRNP; required for the first catalytic step of splicing and for spliceosomal assembly; interacts with Rds3 and is required for Mer1p-activated splicing; diploid mutants have a specific defect in MATA1 pre-mRNA splicing which leads to haploid gene expression in diploids.	+
<i>LEA1</i>	Component of U2 snRNP complex; disruption causes reduced U2 snRNP levels; physically interacts with Msl1p; putative homolog of human U2A' snRNP protein.	+
<i>LDB7</i>	Component of the RSC chromatin remodeling complex; interacts	+

	with Rsc3, Rsc30, Npl6, and Htl1 to form a module important for a broad range of RSC functions.	
<i>MAF1</i>	Highly conserved negative regulator of RNA polymerase III; involved in tRNA processing and stability; inhibits tRNA degradation via rapid tRNA decay (RTD) pathway; binds N-terminal domain of Rpc160 subunit of Pol III to prevent closed-complex formation; regulated by phosphorylation mediated by <i>TORC1</i> , protein kinase A, Sch9, casein kinase 2; localizes to cytoplasm during vegetative growth and translocates to nucleus and nucleolus under stress conditions.	+++
<i>MED1</i>	Subunit of the RNA polymerase II mediator complex; associates with core polymerase subunits to form the RNA polymerase II holoenzyme; essential for transcriptional regulation.	++
<i>MFT1</i>	Subunit of the THO complex; <i>THO</i> is a nuclear complex comprised of Hpr1, Mft1, Rlr1, and Thp2, that is involved in transcription elongation and mitotic recombination; involved in telomere maintenance.	+
<i>MRF1</i>	Mitochondrial translation release factor; involved in stop codon recognition and hydrolysis of the peptidyl-tRNA bond during mitochondrial translation; lack of <i>MRF1</i> causes mitochondrial genome instability.	+++
<i>MSE1</i>	Mitochondrial glutamyl-tRNA synthetase; predicted to be palmitoylated.	++
<i>NPT1</i>	Nicotinate phosphoribosyltransferase; acts in the salvage pathway of NAD ⁺ biosynthesis; required for silencing at rDNA and telomeres and has a role in silencing at mating-type <i>loci</i> .	+
<i>NPL3</i>	RNA-binding protein; promotes elongation, regulates termination, and carries poly(A) mRNA from nucleus to cytoplasm; represses translation initiation by binding eIF4G; required for pre-mRNA splicing; interacts with E3 ubiquitin ligase Bre1, linking histone ubiquitination to mRNA processing; may have role in telomere maintenance; dissociation from mRNAs promoted by Mtr10; phosphorylated by Sky1 in cytoplasm; protein abundance increases in response to DNA replication stress.	++
<i>NRP1</i>	Putative RNA binding protein of unknown function; localizes to stress granules induced by glucose deprivation; predicted to be involved in ribosome biogenesis.	++
<i>PHO23</i>	Component of the Rpd3L histone deacetylase complex; involved in transcriptional regulation of <i>PHO5</i> ; affects termination of snoRNAs and cryptic unstable transcripts (CUTs).	+
<i>POP2</i>	RNase of the DEDD superfamily; subunit of the Ccr4-Not complex that mediates 3' to 5' mRNA deadenylation.	++
<i>REF2</i>	RNA-binding protein; involved in the cleavage step of mRNA 3'-end formation prior to polyadenylation, and in snoRNA maturation; part of holo-CPF subcomplex APT, which associates with 3'-ends of snoRNA- and mRNA-encoding genes; putative regulatory subunit of type 1 protein phosphatase Glc7p, required for actomyosin ring formation, and for timely dephosphorylation and release of Bnr1p from the division site; relocalizes to the cytosol in response to hypoxia.	++
<i>RXT2</i>	Component of the histone deacetylase Rpd3L complex; possibly involved in cell fusion and invasive growth.	+
<i>RXT3</i>	Component of the Rpd3L histone deacetylase complex; involved in histone deacetylation.	+

<i>RMI1</i>	Subunit of the RecQ (Sgs1) - Topo III (Top3p) complex; stimulates superhelical relaxing, DNA catenation/decatenation and ssDNA binding activities of Top3; involved in response to DNA damage; functions in S phase-mediated cohesion establishment via a pathway involving the Ctf18-RFC complex and Mrc1; stimulates Top3 DNA catenation/decatenation activity; null mutants display increased rates of recombination and delayed S phase.	++
<i>RPB9</i>	RNA polymerase II subunit B12.6; contacts DNA; mutations affect transcription start site selection and fidelity of transcription.	+++
<i>RRN10</i>	Protein involved in promoting high level transcription of rDNA; subunit of UAF (upstream activation factor) for RNA polymerase I.	++
<i>RRP6</i>	Nuclear exosome exonuclease component; has 3'-5' exonuclease activity that is regulated by Lrp1; involved in RNA processing, maturation, surveillance, degradation, tethering, and export; role in sn/snoRNAs precursor degradation; forms a stable heterodimer with Lrp1; has similarity to <i>E. coli</i> RNase D and to human PM-Sc1 100 (<i>EXOSC10</i>).	++
<i>RSC2</i>	Component of the RSC chromatin remodeling complex; required for expression of mid-late sporulation-specific genes; involved in telomere maintenance; <i>RSC2</i> has a paralog, <i>RSC1</i> , that arose from the whole genome duplication.	+++
<i>SHE2</i>	RNA-binding protein that binds specific mRNAs and interacts with She3; part of the mRNA localization machinery that restricts accumulation of certain proteins to the bud.	+
<i>SDS23</i>	Protein involved in cell separation during budding; one of two <i>S. cerevisiae</i> homologs (Sds23p and Sds24p) of the <i>S. pombe</i> Sds23 protein, which is implicated in APC/cyclosome regulation; <i>SDS23</i> has a paralog, <i>SDS24</i> , that arose from the whole genome duplication.	+++
<i>SGS1</i>	RecQ family nucleolar DNA helicase; role in genome integrity maintenance, chromosome synapsis, meiotic joint molecule/crossover formation; stimulates activity of Top3; rapidly lost in response to rapamycin in Rrd1p-dependent manner; forms nuclear foci upon DNA replication stress; yeast <i>SGS1</i> complements mutations in human homolog BLM implicated in Bloom syndrome; also similar to human WRN implicated in Werner syndrome; human BLM and WRN can each complement yeast null mutant.	++
<i>SIN3</i>	Component of both the Rpd3S and Rpd3L histone deacetylase complexes; involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis; involved in the maintenance of chromosomal integrity.	+
<i>SRB2</i>	Subunit of the RNA polymerase II mediator complex; associates with core polymerase subunits to form the RNA polymerase II holoenzyme; general transcription factor involved in telomere maintenance.	+++
<i>SRB8</i>	Subunit of the RNA polymerase II mediator complex; associates with core polymerase subunits to form the RNA polymerase II holoenzyme; essential for transcriptional regulation; involved in glucose repression.	++

<i>SSN2</i>	Subunit of the RNA polymerase II mediator complex; associates with core polymerase subunits to form the RNA polymerase II holoenzyme; required for stable association of Srb10-Srb11 kinase; essential for transcriptional regulation.	+++
<i>SSN8</i>	Cyclin-like component of the RNA polymerase II holoenzyme; involved in phosphorylation of the RNA polymerase II C-terminal domain; forms a kinase-cyclin pair in the RNAPII holoenzyme with Ssn3p; required for both entry into and execution of the meiotic program; involved in glucose repression and telomere maintenance; cyclin homolog 35% identical to human cyclin C.	+++
<i>SSO2</i>	Plasma membrane t-SNARE; involved in fusion of secretory vesicles at the plasma membrane; syntaxin homolog that is functionally redundant with Sso1; <i>SSO2</i> has a paralog, <i>SSO1</i> , that arose from the whole genome duplication.	+
<i>SWC5</i>	Component of the SWR1 complex; complex exchanges histone variant H2AZ (Htz1) for chromatin-bound histone H2A; protein abundance increases in response to DNA replication stress; relocalizes to the cytosol in response to hypoxia.	++
<i>TCD2</i>	tRNA threonylcarbamoyladenosine dehydratase; required for the ct6A tRNA base modification, where an adenosine at position 37 is modified to form a cyclized active ester with an oxazolone ring; localized to the mitochondrial outer membrane; <i>TCD2</i> has a paralog, <i>TCD1</i> , that arose from the whole genome duplication.	++
<i>TDA5</i>	Putative protein of unknown function; detected in highly purified mitochondria in high-throughput studies; proposed to be involved in resistance to mechlorethamine and streptozotocin.	++
<i>THO2</i>	Subunit of the THO complex; <i>THO2</i> is required for efficient transcription elongation and involved in transcriptional elongation-associated recombination; required for LacZ RNA expression from certain plasmids.	+++
<i>THP3</i>	Protein that may have a role in transcription elongation; forms a complex with Csn12 that is recruited to transcribed genes; possibly involved in splicing based on pre-mRNA accumulation defect for many intron-containing genes.	++
<i>TOP1</i>	Topoisomerase I; nuclear enzyme that relieves torsional strain in DNA by cleaving and re-sealing the phosphodiester backbone; relaxes both positively and negatively supercoiled DNA; functions in replication, transcription, and recombination; role in processing ribonucleoside monophosphates in genomic DNA into irreversible single-strand breaks; enzymatic activity and interaction with Nsr1p are negatively regulated by polyphosphorylation.	++
<i>TOP3</i>	DNA Topoisomerase III; conserved protein that functions in a complex with Sgs1 and Rmi1 to relax single-stranded negatively-supercoiled DNA preferentially; DNA catenation/decatenation activity is stimulated by RPA and Sgs1-Top3-Rmi1; involved in telomere stability and regulation of mitotic recombination.	++

<i>TRM1</i>	tRNA methyltransferase; two forms of protein are made by alternative translation starts; localizes to both nucleus and mitochondrion to produce modified base N ² ,N ² -dimethylguanosine in tRNAs in both compartments; nuclear Trm1 is evenly distributed around inner nuclear membrane in WT, but mislocalizes as puncta near ER-nucleus junctions in spindle pole body (SPB) mutants; both Trm1 inner nuclear membrane targeting and maintenance depend upon SPB.	+++
<i>TRM10</i>	tRNA methyltransferase; methylates the N-1 position of guanine at position 9 in tRNAs; protein abundance increases in response to DNA replication stress; member of the SPOUT (SpoU-TrmD) methyltransferase family; human ortholog <i>TRMT10A</i> plays a role in the pathogenesis of microcephaly and early onset diabetes; an 18-mer originates from the <i>TRM10</i> locus; genetic analysis shows the 18-mer is the translation regulator.	++
<i>XRN1</i>	Evolutionarily-conserved 5'-3' exonuclease; component of cytoplasmic processing (P) bodies involved in mRNA decay; also enters the nucleus and positively regulates transcription initiation and elongation; plays a role in microtubule-mediated processes, filamentous growth, ribosomal RNA maturation, and telomere maintenance; activated by the scavenger decapping enzyme Dcs1.	+++
<i>YTA7</i>	Protein that localizes to chromatin; has a role in regulation of histone gene expression; has a bromodomain-like region that interacts with the N-terminal tail of histone H3, and an ATPase domain; relocalizes to the cytosol in response to hypoxia; potentially phosphorylated by Cdc28.	+

Cytoskeleton organization and morphogenesis

Gene	Function	Susceptibility level
<i>ALF1</i>	Alpha-tubulin folding protein; similar to mammalian cofactor B; Alf1p-GFP localizes to cytoplasmic microtubules; required for the folding of alpha-tubulin and may play an additional role in microtubule maintenance.	+++
<i>ARC18</i>	Subunit of the ARP2/3 complex; <i>ARP2/3</i> is required for the motility and integrity of cortical actin patches.	++
<i>ARP1</i>	Actin-related protein of the dynactin complex; required for spindle orientation and nuclear migration; forms actin-like short filament composed of 9 or 10 Arp1 monomers.	++
<i>AVO2</i>	Component of a complex containing the Tor2pkinase and other proteins; complex may have a role in regulation of cell growth.	+++
<i>BEM1</i>	Protein containing SH3-domains; involved in establishing cell polarity and morphogenesis; functions as a scaffold protein for complexes that include Cdc24, Ste5, Ste20, and Rsr1.	+++
<i>BEM2</i>	Rho GTPase activating protein (RhoGAP); involved in the control of cytoskeleton organization and cellular morphogenesis; required for bud emergence.	++
<i>BEM4</i>	Protein involved in establishment of cell polarity and bud emergence; interacts with the Rho1p small GTP-binding protein and with the Rho-type GTPase Cdc42; involved in maintenance of proper telomere length.	+++

<i>BUB3</i>	Kinetochore checkpoint WD40 repeat protein; localizes to kinetochores during prophase and metaphase, delays anaphase in the presence of unattached kinetochores; forms complexes with Mad1-Bub1 and with Cdc20, binds Mad2 and Mad3; functions at kinetochore to activate APC/C-Cdc20 for normal mitotic progression.	++
<i>KEL1</i>	Protein required for proper cell fusion and cell morphology; forms a complex with Bud14 and Kel2 that regulates Bnr1 (formin) to affect actin cable assembly, cytokinesis, and polarized growth.	+
<i>MDY2</i>	Protein involved in inserting tail-anchored proteins into ER membranes; forms a complex with Get4; required for efficient mating; involved in shmoo formation and nuclear migration in the pre-zygote; associates with ribosomes.	++
<i>MMR1</i>	Phosphorylated protein of the mitochondrial outer membrane; localizes only to mitochondria of the bud; interacts with Myo2 to mediate mitochondrial distribution to buds; mRNA is targeted to the bud via the transport system involving She2.	+
<i>NCL1</i>	S-adenosyl-L-methionine-dependent tRNA: m5C-methyltransferase; methylates cytosine to m5C at several positions in tRNAs and intron-containing pre-tRNAs; increases proportion of tRNA ^{Leu} (CAA) with m5C at wobble position in response to hydrogen peroxide, causing selective translation of mRNA from genes enriched in TTG codon; loss of <i>NCL1</i> confers hypersensitivity to oxidative stress; similar to Nop2 and human proliferation associated nucleolar protein p120.	++
<i>RTN1</i>	Reticulon protein; involved in nuclear pore assembly and maintenance of tubular ER morphology.	+
<i>RVS161</i>	Amphiphysin-like lipid raft protein; N-BAR domain protein that interacts with Rvs167p and regulates polarization of the actin cytoskeleton, endocytosis, cell polarity, cell fusion and viability following starvation or osmotic stress.	+
<i>SAC6</i>	Fimbrin, actin-bundling protein; cooperates with Scp1 in organization and maintenance of the actin cytoskeleton; phosphorylated by Cdc28/Clb2 in metaphase on T103, to regulate conformation, and modulate actin filament binding affinity and actin cable dynamics; relocates from the plasma membrane to the cytoplasm upon DNA replication stress; human homologs <i>PLS3</i> and <i>LCP1</i> implicated in spinocerebellar ataxia type 2 (SCA2) can each complement yeast null mutant.	+++
<i>SHS1</i>	Component of the septin ring that is required for cytokinesis; present at the ends of rod-like septin hetero-oligomers; C-terminal extension is important for recruitment of Bni5 to the mother-bud neck, which in turn is required for Myo1 recruitment and cytokinesis; undergoes sumoylation and phosphorylation during mitosis; protein abundance increases in response to DNA replication stress.	+++
<i>SLA1</i>	Cytoskeletal protein binding protein; required for assembly of the cortical actin cytoskeleton; interacts with proteins regulating actin dynamics and proteins required for endocytosis; found in the nucleus and cell cortex; has 3 SH3 domains.	+++

<i>SPC72</i>	Gamma-tubulin small complex (gamma-TuSC) receptor; recruits the gamma-TuSC complex to the cytoplasmic side of the SPB, connecting nuclear microtubules to the SPB; involved in astral microtubule formation, stabilization, and with Stu2, anchoring astral MTs at the cytoplasmic face of the SPB, and regulating plus-end MT dynamics; regulated by Cdc5 kinase.	++
<i>SSD1</i>	Translational repressor with a role in polar growth and wall integrity; regulated by Cbk1 phosphorylation to effect bud-specific translational control and localization of specific mRNAs; interacts with TOR pathway components; contains a functional N-terminal nuclear localization sequence and nucleocytoplasmic shuttling appears to be critical to Ssd1 function.	++
<i>VAC17</i>	Phosphoprotein involved in vacuole inheritance; degraded in late M phase of the cell cycle; acts as a vacuole-specific receptor for myosin Myo2.	+
<i>VRP1</i>	Verprolin, proline-rich actin-associated protein; involved in cytoskeletal organization and cytokinesis; promotes actin nucleation and endocytosis; related to mammalian Wiskott-Aldrich syndrome protein (WASP)-interacting protein (WIP).	+++

DNA repair

Gene	Function	Susceptibility level
<i>CTF3</i>	Outer kinetochore protein that forms a complex with Mcm16 and Mcm22; may bind the kinetochore to spindle microtubules; required for the spindle assembly checkpoint; orthologous to human centromere constitutive-associated network (CCAN) subunit CENP-I and fission yeast <i>mis6</i> .	+
<i>FZO1</i>	Mitofusin; integral membrane protein involved in mitochondrial outer membrane tethering and fusion; role in mitochondrial genome maintenance; efficient tethering and degradation of Fzo1p requires an intact N-terminal GTPase domain; targeted for destruction by the ubiquitin ligase SCF-Mdm30p and the cytosolic ubiquitin-proteasome system.	+++
<i>MET18</i>	Component of cytosolic iron-sulfur protein assembly (CIA) machinery; acts at a late step of Fe-S cluster assembly; forms the CIA targeting complex with Cia1 and Cia2 that directs Fe-S cluster incorporation into a subset of proteins involved in methionine biosynthesis, DNA replication and repair, transcription, and telomere maintenance; ortholog of human <i>MMS19</i> .	+
<i>MIP1</i>	Mitochondrial DNA polymerase gamma; single subunit of mitochondrial DNA polymerase in yeast, in contrast to metazoan complex of catalytic and accessory subunits; polymorphic in yeast, petites occur more frequently in some lab strains; human ortholog <i>POLG</i> complements yeast <i>mip1</i> mutant; mutations in human <i>POLG</i> associated with Alpers-Huttenlocher syndrome (AHS), progressive external ophthalmoplegia (PEO), parkinsonism, other mitochondrial diseases.	++
<i>MLH1</i>	Protein required for mismatch repair in mitosis and meiosis; also required for crossing over during meiosis; forms a complex with Pms1 and Msh2-Msh3 during mismatch repair; human homolog is associated with hereditary non-polyposis colon cancer.	++

<i>MTF1</i>	Mitochondrial RNA polymerase specificity factor; has structural similarity to S-adenosylmethionine-dependent methyltransferases and functional similarity to bacterial sigma-factors; Mtf1 interacts with and stabilizes the Rpo41-promoter complex, enhancing DNA bending and melting to facilitate pre-initiation open complex formation.	++
<i>MTF2</i>	Mitochondrial protein that interacts with mitochondrial RNA polymerase; interacts with an N-terminal region of mitochondrial RNA polymerase (Rpo41) and couples RNA processing and translation to transcription.	+

Ion homeostasis

Gene	Function	Susceptibility level
<i>FRE8</i>	Protein with sequence similarity to iron/copper reductases; involved in iron homeostasis; deletion mutant has iron deficiency/accumulation growth defects.	+
<i>ICE2</i>	Integral ER membrane protein with type-III transmembrane domains; required for maintenance of ER zinc homeostasis; necessary for efficient targeting of Trm1 tRNA methyltransferase to inner nuclear membrane; mutations cause defects in cortical ER morphology in both the mother and daughter cells.	+++
<i>LSO2</i>	Protein with a potential role in response to iron deprivation; localizes to nucleus and cytoplasm, and nuclear localization is enhanced under iron-replete conditions; null mutant exhibits slow growth during iron deprivation.	++
<i>TRK1</i>	Component of the Trk1-Trk2 potassium transport system; 180 kDa high affinity potassium transporter; phosphorylated <i>in vivo</i> and interacts physically with the phosphatase Ppz1, suggesting Trk1 activity is regulated by phosphorylation.	++

Internal pH homeostasis

Gene	Function	Susceptibility level
<i>VMA1</i>	Subunit A of the V1 peripheral membrane domain of V-ATPase; protein precursor undergoes self-catalyzed splicing to yield the extein Tfp1 and the intein Vde (PI-SceI), which is a site-specific endonuclease; the V1 peripheral membrane domain of the vacuolar H ⁺ -ATPase (V-ATPase) has eight subunits; involved in methionine restriction extension of chronological lifespan in an autophagy-dependent manner.	+++
<i>VMA10</i>	Subunit G of the V1 peripheral membrane domain of V-ATPase; part of the electrogenic proton pump found throughout the endomembrane system; involved in vacuolar acidification; the V1 peripheral membrane domain of the vacuolar H ⁺ -ATPase (V-ATPase) has eight subunits.	+++

<i>VMA13</i>	Subunit H of the V1 peripheral membrane domain of V-ATPase; part of the electrogenic proton pump found throughout the endomembrane system; serves as an activator or a structural stabilizer of the V-ATPase; the V1 peripheral membrane domain of the vacuolar H ⁺ -ATPase (V-ATPase) has eight subunits.	+++
<i>VMA16</i>	Subunit c" of the vacuolar ATPase; v-ATPase functions in acidification of the vacuole; one of three proteolipid subunits of the V0 domain.	+++
<i>VMA21</i>	Integral membrane protein required for V-ATPase function; not an actual component of the vacuolar H ⁺ -ATPase (V-ATPase) complex; diverged ortholog of human <i>XMEA</i> (X-linked Myopathy with Excessive Autophagy); functions in the assembly of the V-ATPase; localized to the yeast endoplasmic reticulum.	+++
<i>VMA5</i>	Subunit C of the V1 peripheral membrane domain of V-ATPase; part of the electrogenic proton pump found throughout the endomembrane system; required for the V1 domain to assemble onto the vacuolar membrane; the V1 peripheral membrane domain of vacuolar H ⁺ -ATPase (V-ATPase) has eight subunits.	+++
<i>VMA9</i>	Vacuolar H ⁺ ATPase subunit e of the V-ATPase V0 subcomplex; essential for vacuolar acidification; interacts with the V-ATPase assembly factor Vma21p in the ER; involved in V0 biogenesis.	+++
<i>VPH2</i>	Integral membrane protein required for V-ATPase function; not an actual component of the vacuolar H ⁺ -ATPase (V-ATPase) complex; functions in the assembly of the V-ATPase; localized to the endoplasmic reticulum (ER); involved in methionine restriction extension of chronological lifespan in an autophagy-dependent manner.	++

Intracellular trafficking

Gene	Function	Susceptibility level
<i>ARL3</i>	ARF-like small GTPase of the RAS superfamily; required for recruitment of Arl1, a GTPase that regulates membrane traffic, to the Golgi apparatus; NatC-catalyzed N-terminal acetylation regulates Golgi membrane association mediated by interaction with membrane receptor, Sys1; similar to ADP-ribosylation factor and orthologous to mammalian <i>ARFRP1</i> .	+
<i>ARV1</i>	Cortical ER protein; implicated in the membrane insertion of tail-anchored C-terminal single transmembrane domain proteins; may function in transport of glycosylphosphatidylinositol intermediates into the ER lumen; required for normal intracellular sterol distribution; human <i>ARV1</i> , required for normal cholesterol and bile acid homeostasis, can complement yeast <i>arv1</i> null mutant; human variant causing early onset epileptic encephalopathy is unable to rescue the yeast null.	++
<i>AVL9</i>	Conserved protein involved in exocytic transport from the Golgi; mutation is synthetically lethal with <i>apl2 vps1</i> double mutation; member of a protein superfamily with orthologs in diverse organisms.	+

<i>CHS3</i>	Chitin synthase III; catalyzes the transfer of N-acetylglucosamine (GlcNAc) to chitin; required for synthesis of the majority of cell wall chitin, the chitin ring during bud emergence, and spore wall chitosan; contains overlapping dileucine and di-acidic signals that mediate, respectively, intracellular trafficking by AP-1 and trafficking to plasma membrane by exomer complex.	+
<i>CHS5</i>	Component of the exomer complex; the exomer which also contains Csh6p, Bch1p, Bch2p, and Bud7, is involved in the export of select proteins, such as chitin synthase Chs3p, from the Golgi to the plasma membrane.	+
<i>DID2</i>	Class E protein of the vacuolar protein-sorting (Vps) pathway; binds Vps4 and directs it to dissociate ESCRT-III complexes; forms a functional and physical complex with Ist1p; human ortholog may be altered in breast tumors.	++
<i>DID4</i>	Class E Vps protein of the ESCRT-III complex; required for sorting of integral membrane proteins into luminal vesicles of multivesicular bodies, and for delivery of newly synthesized vacuolar enzymes to the vacuole, involved in endocytosis.	++
<i>DOA1</i>	WD repeat protein required for ubiquitin-mediated protein degradation; ubiquitin binding cofactor that complexes with Cdc48; required for ribophagy; controls cellular ubiquitin concentration; promotes efficient NHEJ in postdiauxic/stationary phase; facilitates N-terminus-dependent proteolysis of centromeric histone H3 (Cse4) for faithful chromosome segregation.	+
<i>DOA4</i>	Ubiquitin hydrolase; deubiquitinates intraluminal vesicle (ILVs) cargo proteins; required for recycling ubiquitin from proteasome-bound ubiquitinated intermediates, acts at the late endosome/prevacuolar compartment to recover ubiquitin from ubiquitinated membrane proteins destined for the vacuole; <i>DOA4</i> has a paralog, <i>UBP5</i> , that arose from the whole genome duplication.	+++
<i>DRS2</i>	Trans-golgi network aminophospholipid translocase (flippase); maintains membrane lipid asymmetry in post-Golgi secretory vesicles; contributes to clathrin-coated vesicle formation, endocytosis, protein trafficking between the Golgi and endosomal system and the cellular response to mating pheromone; autoinhibited by its C-terminal tail; localizes to the trans-Golgi network; mutations in human homolog <i>ATP8B1</i> result in liver disease.	++
<i>END3</i>	EH domain-containing protein involved in endocytosis; actin cytoskeletal organization and cell wall morphogenesis; forms a complex with Sla1 and Pan1.	+++
<i>EPS1</i>	ER protein with chaperone and co-chaperone activity; involved in retention of resident ER proteins; has a role in recognizing proteins targeted for ER-associated degradation (ERAD), member of the protein disulfide isomerase family.	++
<i>FYV10</i>	Subunit of GID complex; involved in proteasome-dependent catabolite inactivation of gluconeogenic enzymes FBPase, PEPCCK, and c-MDH; forms dimer with Rmd5 that is then recruited to GID Complex by Gid8; contains a degenerate RING finger motif needed for GID complex ubiquitin ligase activity in vivo, as well as CTLH and CRA domains; plays role in anti-apoptosis; required for survival upon exposure to K1 killer toxin.	+

<i>GCS1</i>	ADP-ribosylation factor GTPase activating protein (ARF GAP); involved in ER-Golgi transport; required for prospore membrane formation; regulates phospholipase Spo14; shares functional similarity with Glo3; <i>GCS1</i> has a paralog, <i>SPS18</i> , that arose from the whole genome duplication.	+++
<i>GET1</i>	Subunit of the GET complex; involved in insertion of proteins into the ER membrane; required for the retrieval of HDEL proteins from the Golgi to the ER in an <i>ERD2</i> dependent fashion and for normal mitochondrial morphology and inheritance.	+
<i>GTR2</i>	Subunit of a TORC1-stimulating GTPase complex; subunit of the Gtr1-Gtr2 GTPase complex that stimulates TORC1 in response to amino acid stimulation; stimulates the GTPase activity of Gtr1p; negatively regulates the Ran/Tc4 GTPase cycle; activates transcription; tethered to the vacuolar membrane as part of the EGO complex (EGOC); required for sorting of Gap1p; activated by the the Lst4-Lst7 GAP complex; localizes to cytoplasm and to chromatin.	++
<i>GYP1</i>	Cis-golgi GTPase-activating protein (GAP) for yeast Rabs; the Rab family members are Ypt1 (<i>in vivo</i>) and for Ypt1, Sec4, Ypt7, and Ypt51 (<i>in vitro</i>); involved in vesicle docking and fusion.	++
<i>HSE1</i>	Subunit of the endosomal Vps27-Hse1 complex; complex is required for sorting of ubiquitinated membrane proteins into intraluminal vesicles prior to vacuolar degradation, as well as for recycling of Golgi proteins and formation of luminal membranes.	+++
<i>PKH2</i>	Serine/threonine protein kinase; involved in sphingolipid-mediated signaling pathway that controls endocytosis; activates Ypk1 and Ykr2, components of signaling cascade required for maintenance of cell wall integrity; contains a PH-like domain; redundant with Pkh1p; <i>PKH2</i> has a paralog, <i>PKH1</i> , that arose from the whole genome duplication.	++
<i>RAV1</i>	Subunit of RAVE complex (Rav1, Rav2, Skp1); the RAVE complex promotes assembly of the V-ATPase holoenzyme; required for transport between the early and late endosome/PVC and for localization of TGN membrane proteins; potential Cdc28 substrate.	++
<i>RAV2</i>	Subunit of RAVE complex (Rav1, Rav2, Skp1); the RAVE complex associates with the V1 domain of the vacuolar membrane (H ⁺)-ATPase (V-ATPase) and promotes assembly and reassembly of the holoenzyme.	++
<i>RER1</i>	Protein involved in retention of membrane proteins; including Sec12, in the ER; localized to Golgi.	+
<i>RGP1</i>	Subunit of a Golgi membrane exchange factor (Ric1-Rgp1); this complex catalyzes nucleotide exchange on Ypt6.	+++
<i>SEC22</i>	R-SNARE protein; assembles into SNARE complex with Bet1p, Bos1 and Sed5; cycles between the ER and Golgi complex; involved in anterograde and retrograde transport between the ER and Golgi.	+
<i>SEC28</i>	Epsilon-COP subunit of the coatomer; regulates retrograde Golgi-to-ER protein traffic; stabilizes Cop1, the alpha-COP and the coatomer complex; non-essential for cell growth; protein abundance increases in response to DNA replication stress.	++

<i>SEC66</i>	Non-essential subunit of Sec63 complex; with Sec61 complex, Kar2/BiP and Lhs1 forms a channel competent for SRP-dependent and post-translational SRP-independent protein targeting and import into the ER; other members are Sec63, Sec62, and Sec72.	+++
<i>SLM4</i>	Component of the EGO and GSE complexes; essential for integrity and function of EGO; EGO is involved in the regulation of microautophagy and GSE is required for proper sorting of amino acid permease Gap1; gene exhibits synthetic genetic interaction with <i>MSS4</i> .	++
<i>SLM5</i>	Mitochondrial asparaginyl-tRNA synthetase.	++
<i>SNF2</i>	Catalytic subunit of the SWI/SNF chromatin remodeling complex; involved in transcriptional regulation; contains DNA-stimulated ATPase activity; functions interdependently in transcriptional activation with Snf5p and Snf6p.	+
<i>SNF7</i>	One of four subunits of the ESCRT-III complex; involved in the sorting of transmembrane proteins into the multivesicular body (MVB) pathway; recruited from the cytoplasm to endosomal membranes; ESCRT-III stands for endosomal sorting complex required for transport III.	+++
<i>SNF8</i>	Component of the ESCRT-II complex; ESCRT-II is involved in ubiquitin-dependent sorting of proteins into the endosome; appears to be functionally related to <i>SNF7</i> ; involved in glucose derepression.	+++
<i>STP22</i>	Component of the ESCRT-I complex; ESCRT-I is involved in ubiquitin-dependent sorting of proteins into the endosome; prevents polyubiquitination of the arrestin-related protein Rim8p, thereby directing its monoubiquitination by Rsp5; homologous to the mouse and human Tsg101 tumor susceptibility gene; mutants exhibit a Class E Vps phenotype.	+++
<i>TIM18</i>	Component of the mitochondrial <i>TIM22</i> complex; involved in insertion of polytopic proteins into the inner membrane; may mediate assembly or stability of the complex.	++
<i>TLG2</i>	Syntaxin-like t-SNARE; forms a complex with Tlg1 and Vti1 and mediates fusion of endosome-derived vesicles with the late Golgi; required along with <i>VPS45</i> for an early step of the constitutive CVT pathway.	+
<i>TRS33</i>	Core component of TRAPP complexes I, II and IV; transport protein particle (TRAPP) complexes are related multimeric guanine nucleotide-exchange factor for the GTPase Ypt1, regulating ER-Golgi traffic (TRAPPI), intra-Golgi traffic (TRAPPPII), endosome-Golgi traffic (TRAPPPII and III) and autophagy (TRAPPPIII, and IV); proposed subunit of a novel complex, TRAPPPIV, that may function redundantly with TRAPPPIII as a GEF that activates Ypt1 during autophagy.	++
<i>TRS85</i>	Component of transport protein particle (TRAPP) complex III; TRAPPPIII is a multimeric guanine nucleotide-exchange factor for the GTPase Ypt1, regulating endosome-Golgi traffic and required for membrane expansion during autophagy and the CVT pathway; directs Ypt1 to the PAS; late post-replication meiotic role.	++
<i>VAM10</i>	Protein involved in vacuole morphogenesis; acts at an early step of homotypic vacuole fusion that is required for vacuole tethering.	++

VAM3	Syntaxin-like vacuolar t-SNARE; functions with Vam7 in vacuolar protein trafficking; mediates docking/fusion of late transport intermediates with the vacuole; has an acidic dileucine sorting signal and C-terminal transmembrane region.	++
VAM6	Guanine nucleotide exchange factor for the GTPase Gtr1; subunit of the HOPS endocytic tethering complex; vacuole membrane protein; functions as a Rab GTPase effector, interacting with both GTP- and GDP-bound conformations of Ypt7; facilitates tethering and promotes membrane fusion events at the late endosome and vacuole; required for both membrane and protein trafficking; component of vacuole-mitochondrion contacts (vCLAMPs) important for lipid transfer between organelles.	++
VPS1	Dynamin-like GTPase required for vacuolar sorting; also involved in actin cytoskeleton organization, endocytosis, late Golgi-retention of some proteins, regulation of peroxisome biogenesis.	+++
VPS16	Subunit of the HOPS and the CORVET complexes; part of the Class C Vps complex essential for membrane docking and fusion at Golgi-to-endosome and endosome-to-vacuole protein transport stages.	++
VPS17	Subunit of the membrane-associated retromer complex; essential for endosome-to-Golgi retrograde protein transport; peripheral membrane protein that assembles onto the membrane with Vps5 to promote vesicle formation; required for recruiting the retromer complex to the endosome membranes.	++
VPS21	Endosomal Rab family GTPase; required for endocytic transport and sorting of vacuolar hydrolases; required for endosomal localization of the CORVET complex; required with YPT52 for MVB biogenesis and sorting; involved in autophagy and ionic stress tolerance; geranylgeranylation required for membrane association; protein abundance increases in response to DNA replication stress; mammalian Rab5 homolog; VPS21 has a paralog, YPT53, that arose from the whole genome duplication.	++
VPS24	One of four subunits of the ESCRT-III complex; forms an endosomal sorting complex required for transport III (ESCRT-III) subcomplex with Did4; involved in the sorting of transmembrane proteins into the multivesicular body (MVB) pathway.	+++
VPS25	Component of the ESCRT-II complex; ESCRT-II is involved in ubiquitin-dependent sorting of proteins into the endosome.	++
VPS27	Endosomal protein that forms a complex with Hse1; required for recycling Golgi proteins, forming lumenal membranes and sorting ubiquitinated proteins destined for degradation; has Ubiquitin Interaction Motifs which bind ubiquitin (Ubi4).	++
VPS28	Component of the ESCRT-I complex; complex is involved in ubiquitin-dependent sorting of proteins into the endosome; conserved C-terminal domain interacts with ESCRT-III subunit Vps20p; other members include Stp22, Srn2, Vps28, and Mvb12.	+++
VPS33	ATP-binding protein that is a subunit of the HOPS and CORVET complexes; essential for protein sorting, vesicle docking, and fusion at the vacuole; binds to SNARE domain.	+++

<i>VPS36</i>	Component of the ESCRT-II complex; contains the GLUE (GRAM Like Ubiquitin binding in EAP45) domain which is involved in interactions with ESCRT-I and ubiquitin-dependent sorting of proteins into the endosome; plays a role in the formation of mutant huntingtin (Htt) aggregates in yeast.	+++
<i>VPS4</i>	AAA-ATPase involved in multivesicular body (MVB) protein sorting; ATP-bound Vps4p localizes to endosomes and catalyzes ESCRT-III disassembly and membrane release; ATPase activity is activated by Vta1; regulates cellular sterol metabolism.	+
<i>VPS41</i>	Subunit of the HOPS endocytic tethering complex; vacuole membrane protein that functions as a Rab GTPase effector, interacting specifically with the GTP-bound conformation of Ypt7p, facilitating tethering, docking and promoting membrane fusion events at the late endosome and vacuole; required for both membrane and protein trafficking; Yck3-mediated phosphorylation regulates the organization of vacuolar fusion sites.	++
<i>VPS5</i>	Nexin-1 homolog; required for localizing membrane proteins from a prevacuolar/late endosomal compartment back to late Golgi; structural component of retromer membrane coat complex; forms a retromer subcomplex with Vps17; required for recruiting the retromer complex to the endosome membranes; <i>VPS5</i> has a paralog, <i>YKR078W</i> , that arose from the whole genome duplication.	++
<i>VPS52</i>	Component of the GARP (Golgi-associated retrograde protein) complex; GARP is required for the recycling of proteins from endosomes to the late Golgi, and for mitosis after DNA damage induced checkpoint arrest; involved in localization of actin and chitin; members of the GARP complex are Vps51-Vps52-Vps53-Vps54.	++
<i>VPS61</i>	Dubious open reading frame; unlikely to encode a functional protein, based on available experimental and comparative sequence data; not conserved in closely related <i>Saccharomyces</i> species; 4% of ORF overlaps the verified gene <i>RGP1</i> ; deletion causes a vacuolar protein sorting defect.	+++
<i>VPS63</i>	Putative protein of unknown function; not conserved in closely related <i>Saccharomyces</i> species; 98% of ORF overlaps the verified gene <i>YPT6</i> ; deletion causes a vacuolar protein sorting defect; decreased levels of protein in enolase deficient mutant.	+++
<i>VPS74</i>	Golgi phosphatidylinositol-4-kinase effector and PtdIns4P sensor; interacts with the cytosolic domains of cis and medial glycosyltransferases, and in the PtdIns4P-bound state mediates the targeting of these enzymes to the Golgi; interacts with the catalytic domain of Sac1, the major cellular PtdIns4P phosphatase, to direct dephosphorylation of the Golgi pool of PtdIns4P; tetramerization required for function; ortholog of human <i>GOLPH3/GPP34/GMx33</i> .	++
<i>YPT6</i>	Rab family GTPase; required for endosome-to-Golgi, intra-Golgi retrograde, and retrograde Golgi-to-ER transport; temporarily at the Golgi, dissociating into the cytosol on arrival of the late Golgi GTPase Ypt32; Golgi-localized form is GTP bound, while cytosolic form is GDP-bound; required for delivery of Atg9 to the phagophore assembly site during autophagy under heat stress, with Ypt6p for starvation induced autophagy and for the CVT pathway.	+++

Lipid synthesis

Gene	Function	Susceptibility level
<i>ELO2</i>	Fatty acid elongase, involved in sphingolipid biosynthesis; acts on fatty acids of up to 24 carbons in length; mutations have regulatory effects on 1,3-beta-glucan synthase, vacuolar ATPase, and the secretory pathway; <i>ELO2</i> has a paralog, <i>ELO1</i> , that arose from the whole genome duplication; lethality of the <i>elo2 elo3</i> double null mutation is functionally complemented by human <i>ELOVL1</i> and weakly complemented by human <i>ELOVL3</i> or <i>ELOV7</i> .	+++
<i>ELO3</i>	Elongase; involved in fatty acid and sphingolipid biosynthesis; synthesizes very long chain 20-26-carbon fatty acids from C18-CoA primers; involved in regulation of sphingolipid biosynthesis; lethality of the <i>elo2 elo3</i> double null mutation is functionally complemented by human <i>ELOVL1</i> and weakly complemented by human <i>ELOVL3</i> or <i>ELOV7</i> .	++
<i>ERG2</i>	C-8 sterol isomerase; catalyzes isomerization of delta-8 double bond to delta-7 position at an intermediate step in ergosterol biosynthesis; transcriptionally down-regulated when ergosterol is in excess.	+++
<i>ERG24</i>	C-14 sterol reductase; acts in ergosterol biosynthesis; mutants accumulate the abnormal sterol ignosterol (ergosta-8,14 dienol), and are viable under anaerobic growth conditions but inviable on rich medium under aerobic condition.	++
<i>ERG28</i>	Endoplasmic reticulum membrane protein; may facilitate protein-protein interactions between the Erg26 dehydrogenase and the Erg27p 3-ketoreductase and/or tether these enzymes to the ER, also interacts with Erg6.	+++
<i>ERG3</i>	C-5 sterol desaturase; glycoprotein that catalyzes the introduction of a C-5(6) double bond into episterol, a precursor in ergosterol biosynthesis; transcriptionally down-regulated when ergosterol is in excess; mutants are viable, but cannot grow on non-fermentable carbon sources; substrate of HRD ubiquitin ligase; mutation is functionally complemented by human <i>SC5D</i> .	++
<i>ERG4</i>	C-24(28) sterol reductase; catalyzes the final step in ergosterol biosynthesis; mutants are viable, but lack ergosterol.	+
<i>ERG5</i>	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	+
<i>ETR1</i>	2-enoyl thioester reductase; member of the medium chain dehydrogenase/reductase family; localized to mitochondria, where it has a probable role in fatty acid synthesis; human MECR functionally complements the respiratory growth defect of the null mutant.	++
<i>HTD2</i>	Mitochondrial 3-hydroxyacyl-thioester dehydratase; involved in fatty acid biosynthesis, required for respiratory growth and for normal mitochondrial morphology.	++

<i>KCS1</i>	Inositol hexakisphosphate and inositol heptakisphosphate kinase; generation of high energy inositol pyrophosphates by Kcs1 is required for many processes such as vacuolar biogenesis, stress response, RNA polymerase I-mediated rRNA transcription and telomere maintenance; inositol hexakisphosphate is also known as IP6; inositol heptakisphosphate is also known as IP7.	+++
<i>LAM1</i>	Putative sterol transfer protein; localizes to puncta in the cortical ER; probable role in retrograde transport of sterols from the plasma membrane to the ER; one of six StART-like domain-containing proteins in yeast that may be involved in sterol transfer between intracellular membranes.	+
<i>LIP5</i>	Protein involved in biosynthesis of the coenzyme lipoic acid.	+
<i>LOA1</i>	Lysophosphatidic acid acyltransferase; involved in triacylglyceride homeostasis and lipid droplet formation; localized to lipid droplets and the ER; specificity for oleoyl-CoA.	+
<i>PDX3</i>	Pyridoxine (pyridoxamine) phosphate oxidase; has homologs in <i>E. coli</i> and <i>Myxococcus xanthus</i> ; transcription is under the general control of nitrogen metabolism.	+++
<i>SAC1</i>	Phosphatidylinositol phosphate (PtdInsP) phosphatase; involved in hydrolysis of PtdIns[4]P in the early and medial Golgi; regulated by interaction with Vps74p; ER localized transmembrane protein which cycles through the Golgi; involved in protein trafficking and processing, secretion, and cell wall maintenance; regulates sphingolipid biosynthesis through the modulation of PtdIns(4)P metabolism.	++
<i>SPO7</i>	Putative regulatory subunit of Nem1-Spo7 phosphatase holoenzyme; regulates nuclear growth by controlling phospholipid biosynthesis, required for normal nuclear envelope morphology, premeiotic replication, and sporulation.	+

Mitochondrial function

Gene	Function	Susceptibility level
<i>AEPI</i>	Protein required for expression of the mitochondrial <i>OLI1</i> gene; mitochondrial <i>OLI1</i> gene encodes subunit 9 of F1-F0 ATP synthase.	++
<i>AIF1</i>	Mitochondrial cell death effector; translocates to the nucleus in response to apoptotic stimuli, homolog of mammalian Apoptosis-Inducing Factor, putative reductase.	++
<i>ATP1</i>	Alpha subunit of the F1 sector of mitochondrial F1-F0 ATP synthase; which is a large, evolutionarily conserved enzyme complex required for ATP synthesis; F1 translationally regulates <i>ATP6</i> and <i>ATP8</i> expression to achieve a balanced output of ATP synthase genes encoded in nucleus and mitochondria; phosphorylated; N-terminally propionylated <i>in vivo</i> .	+++
<i>ATP10</i>	Assembly factor for the F0 sector of mitochondrial F1-F0 ATP synthase; mitochondrial inner membrane protein; interacts genetically with <i>ATP6</i> .	+++
<i>ATP11</i>	Molecular chaperone; required for the assembly of alpha and beta subunits into the F1 sector of mitochondrial F1-F0 ATP synthase; N-terminally propionylated <i>in vivo</i> .	++

<i>ATP23</i>	Putative metalloprotease of the mitochondrial inner membrane; required for processing of Atp6; has an additional role in assembly of the F0 sector of the F1-F0 ATP synthase complex; substrate of the Mia40p-Erv1p disulfide relay system, and folding is assisted by Mia40.	++
<i>CEM1</i>	Mitochondrial beta-keto-acyl synthase; possible role in fatty acid synthesis; required for mitochondrial respiration; human homolog <i>OXSM</i> can complement yeast <i>cem1</i> null mutant.	+++
<i>COA3</i>	Mitochondrial protein required for cytochrome c oxidase assembly; also involved in translational regulation of Cox1 and prevention of Cox1 aggregation before assembly; located in the mitochondrial inner membrane.	+++
<i>COQ1</i>	Hexaprenyl pyrophosphate synthetase; catalyzes the first step in ubiquinone (coenzyme Q) biosynthesis.	++
<i>COQ3</i>	O-methyltransferase; catalyzes two different O-methylation steps in ubiquinone (Coenzyme Q) biosynthesis; component of a mitochondrial ubiquinone-synthesizing complex; phosphoprotein.	+
<i>COX5B</i>	Subunit Vb of cytochrome c oxidase; cytochrome c oxidase is the terminal member of the mitochondrial inner membrane electron transport chain; Cox5B is predominantly expressed during anaerobic growth while its isoform Va (Cox5A) is expressed during aerobic growth.	+
<i>COX13</i>	Subunit VIa of cytochrome c oxidase; present in a subclass of cytochrome c oxidase complexes that may have a role in minimizing generation of reactive oxygen species; not essential for cytochrome c oxidase activity but may modulate activity in response to ATP	+
<i>COX17</i>	Copper metallochaperone that transfers copper to Sco1 and Cox11; eventual delivery to cytochrome c oxidase; contains twin cysteine-x9-cysteine motifs; interacts with the MICOS complex, and interaction is promoted by copper ions; human homolog <i>COX17</i> partially complements yeast null mutant.	++
<i>COX18</i>	Protein required for membrane insertion of C-terminus of Cox2; mitochondrial integral inner membrane protein; interacts genetically and physically with Mss2 and Pnt1; similar to <i>S. cerevisiae</i> Oxa1, <i>N. crassa</i> Oxa2, and <i>E. coli</i> YidC; respiratory defect of the null mutant is functionally complemented by human <i>COX18</i> carrying the N-terminal 54 amino acids of <i>S. cerevisiae</i> Cox18.	+++
<i>COX19</i>	Protein required for cytochrome c oxidase assembly; located in the cytosol and mitochondrial intermembrane space; putative copper metallochaperone that delivers copper to cytochrome c oxidase; contains twin cysteine-x9-cysteine motifs.	+
<i>COX6</i>	Subunit VI of cytochrome c oxidase (Complex IV); Complex IV is the terminal member of the mitochondrial inner membrane electron transport chain; expression is regulated by oxygen levels.	++
<i>FIS1</i>	Protein involved in mitochondrial fission and peroxisome abundance; may have a distinct role in tethering protein aggregates to mitochondria in order to retain them in the mother cell; required for localization of Dnm1 and Mdv1 during mitochondrial division; mediates ethanol-induced apoptosis and ethanol-induced mitochondrial fragmentation.	+

<i>FMC1</i>	Mitochondrial matrix protein; required for assembly or stability at high temperature of the F1 sector of mitochondrial F1-F0 ATP synthase; null mutant temperature sensitive growth on glycerol is suppressed by multicopy expression of <i>Odc1</i> .	+++
<i>GPD2</i>	NAD-dependent glycerol 3-phosphate dehydrogenase; expression is controlled by an oxygen-independent signaling pathway required to regulate metabolism under anoxic conditions; located in cytosol and mitochondria.	+
<i>GGC1</i>	Mitochondrial GTP/GDP transporter; essential for mitochondrial genome maintenance; has a role in mitochondrial iron transport; member of the mitochondrial carrier family.	+++
<i>MGM1</i>	Mitochondrial GTPase, present in complex with <i>Ugo1p</i> and <i>Fzo1p</i> ; required for mitochondrial morphology, fusion, and genome maintenance; promotes membrane bending.	+
<i>MCX1</i>	Non-proteolytic ATPase of the AAA family; stimulates incorporation of the pyridoxal phosphate cofactor into <i>Hem1p</i> (5-aminolevulinic acid synthase).	+
<i>MDM10</i>	Subunit of both the ERMES and the SAM complex; component of ERMES complex which acts as a molecular tether between the mitochondria and the ER, necessary for efficient phospholipid exchange between organelles and for mitophagy; SAM/TOB complex component that functions in the assembly of outer membrane beta-barrel proteins; involved in mitochondrial inheritance and morphology; ERMES complex is often co-localized with peroxisomes and concentrated areas of pyruvate dehydrogenase.	+
<i>MDM12</i>	Mitochondrial outer membrane protein, ERMES complex subunit; required for transmission of mitochondria to daughter cells; required for mitophagy; may influence import and assembly of outer membrane beta-barrel proteins; ERMES complex is often co-localized with peroxisomes and with concentrated areas of pyruvate dehydrogenase.	++
<i>MDM20</i>	Non-catalytic subunit of the <i>NatB</i> N-terminal acetyltransferase; <i>NatB</i> catalyzes N-acetylation of proteins with specific N-terminal sequences; involved in mitochondrial inheritance and actin assembly.	++
<i>MDM34</i>	Mitochondrial component of the ERMES complex; links the ER to mitochondria and may promote inter-organellar calcium and phospholipid exchange as well as coordinating mitochondrial DNA replication and growth; required for mitophagy; ERMES complex is often co-localized with peroxisomes and with concentrated areas of pyruvate dehydrogenase.	++
<i>MEF2</i>	Mitochondrial elongation factor involved in translational elongation.	++
<i>MHR1</i>	Mitochondrial ribosomal protein of the large subunit; also involved in homologous recombination in mitochondria; required for recombination-dependent mtDNA partitioning; involved in stimulation of mitochondrial DNA replication in response to oxidative stress.	++
<i>MRS1</i>	Splicing protein; required for splicing of two mitochondrial group I introns (<i>BI3</i> in <i>COB</i> and <i>AI5beta</i> in <i>COX1</i>); forms a splicing complex, containing four subunits of <i>Mrs1</i> and two subunits of the <i>BI3</i> -encoded maturase, that binds to the <i>BI3</i> RNA; <i>MRS1</i> has a paralog, <i>CCE1</i> , that arose from the whole genome duplication.	++

<i>MSF1</i>	Mitochondrial phenylalanyl-tRNA synthetase; active as a monomer, unlike the cytoplasmic subunit which is active as a dimer complexed to a beta subunit dimer; similar to the alpha subunit of <i>E. coli</i> phenylalanyl-tRNA synthetase.	+++
<i>MSK1</i>	Mitochondrial lysine-tRNA synthetase; required for import of both aminoacylated and deacylated forms of tRNA (Lys) into mitochondria and for aminoacylation of mitochondrially encoded tRNA (Lys).	+
<i>NAM2</i>	Mitochondrial leucyl-tRNA synthetase; also has direct role in splicing of several mitochondrial group I introns; indirectly required for mitochondrial genome maintenance; human homolog LARS2 can complement yeast null mutant and is implicated in Perrault syndrome.	++
<i>OAR1</i>	Mitochondrial 3-oxoacyl-[acyl-carrier-protein] reductase; may comprise a type II mitochondrial fatty acid synthase along with Mct1; human homolog <i>CBR4</i> complements yeast null mutant.	++
<i>PET100</i>	Chaperone that facilitates the assembly of cytochrome c oxidase; integral to the mitochondrial inner membrane; interacts with a subcomplex of subunits VII, VIIa, and VIII (Cox7, Cox9, and Cox8) but not with the holoenzyme.	++
<i>PET117</i>	Protein required for assembly of cytochrome c oxidase.	+
<i>PET54</i>	Mitochondrial inner membrane protein; binds to the 5' UTR of the COX3 mRNA to activate its translation together with Pet122 and Pet494p; also binds to the COX1 Group I intron AI5 beta to facilitate exon ligation during splicing.	++
<i>PRX1</i>	Mitochondrial peroxiredoxin with thioredoxin peroxidase activity; has a role in reduction of hydroperoxides; reactivation requires Trx2 and glutathione; induced during respiratory growth and oxidative stress; phosphorylated; protein abundance increases in response to DNA replication stress.	++
<i>PSD1</i>	Phosphatidylserine decarboxylase of the mitochondrial inner membrane; converts phosphatidylserine to phosphatidylethanolamine; regulates mitochondrial fusion and morphology by affecting lipid mixing in the mitochondrial membrane and by influencing the ratio of long to short forms of Mgm1p; partly exposed to the mitochondrial intermembrane space; autocatalytically processed.	++
<i>RRG9</i>	Protein of unknown function; null mutant lacks mitochondrial DNA and cannot grow on glycerol; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies.	++
<i>RSM23</i>	Mitochondrial ribosomal protein of the small subunit; has similarity to mammalian apoptosis mediator proteins; null mutation prevents induction of apoptosis by overproduction of metacaspase Mca1.	+++
<i>RSM24</i>	Mitochondrial ribosomal protein of the small subunit.	+
<i>RTC6</i>	Protein involved in translation; mutants have defects in biogenesis of nuclear ribosomes; sequence similar to prokaryotic ribosomal protein L36, may be a mitochondrial ribosomal protein; protein abundance increases in response to DNA replication stress.	++
<i>SCO1</i>	Copper-binding protein of mitochondrial inner membrane; required for cytochrome c oxidase activity and respiration; may function to deliver copper to cytochrome c oxidase.	+
<i>SCO2</i>	Protein anchored to mitochondrial inner membrane; may have a	+

	redundant function with Sco1p in delivery of copper to cytochrome c oxidase.	
<i>SOV1</i>	Mitochondrial protein of unknown function.	++
<i>YTA12</i>	Mitochondrial inner membrane m-AAA protease component; mediates degradation of misfolded or unassembled proteins; also required for correct assembly of mitochondrial enzyme complexes; overexpression of human <i>AFG3L2</i> complements respiratory defect of yeast <i>afg3 yta12</i> double null mutation, but overexpression of disease-associated <i>AFG3L2</i> variants does not; expression of both human <i>SPG7</i> (paraplegin) and <i>AFG3L2</i> complements yeast <i>yta12 afg3</i> double mutation.	+

Peroxisomal function

Gene	Function	Susceptibility level
<i>PEX12</i>	C3HC4-type RING-finger peroxin and E3 ubiquitin ligase; required for peroxisome biogenesis and peroxisomal matrix protein import.	+
<i>PEX27</i>	Peripheral peroxisomal membrane protein; involved in controlling peroxisome size and number.	+
<i>PEX34</i>	Protein that regulates peroxisome populations; peroxisomal integral membrane protein; interacts with Pex11p, Pex25p, and Pex27p to control both constitutive peroxisome division and peroxisome morphology and abundance during peroxisome proliferation.	+
<i>PEX19</i>	Chaperone and import receptor for newly-synthesized class I PMPs; binds peroxisomal membrane proteins (PMPs) in the cytoplasm and delivers them to the peroxisome for subsequent insertion into the peroxisomal membrane.	+
<i>PEX22</i>	Putative peroxisomal membrane protein; required for import of peroxisomal proteins.	+
<i>PEX6</i>	AAA-peroxin; heterodimerizes with AAA-peroxin Pex1 and participates in the recycling of peroxisomal signal receptor Pex5 from the peroxisomal membrane to the cytosol; mutations in human <i>PEX6</i> can lead to severe peroxisomal disorders and early death.	++

Protein modification

Gene	Function	Susceptibility level
<i>AIM22</i>	Putative lipoate-protein ligase; required along with Lip2 and Lip5 for lipoylation of Lat1 and Kgd2; similar to E. coli LplA; null mutant displays reduced frequency of mitochondrial genome loss.	++
<i>ARD1</i>	Subunit of protein N-terminal acetyltransferase NatA; NatA comprises Nat1, Ard1, Nat5; acetylates many proteins to influence telomeric silencing, cell cycle, heat-shock resistance, mating, sporulation, early stages of mitophagy; protein abundance increases under DNA replication stress.	+++

<i>BNI5</i>	Linker protein responsible for recruitment of myosin to the bud neck; interacts with the C-terminal extensions of septins Cdc11 and Shs1 and binds Myo1p to promote cytokinesis.	++
<i>BRE5</i>	Ubiquitin protease cofactor; forms deubiquitination complex with Ubp3 that coregulates anterograde and retrograde transport between the endoplasmic reticulum and Golgi compartments; null is sensitive to brefeldin A.	++
<i>CDC73</i>	Component of the Paf1 complex; binds to and modulates the activity of RNA polymerases I and II; required for expression of certain genes, modification of some histones, and telomere maintenance; involved in transcription elongation as demonstrated by the G-less-based run-on (GLRO) assay; protein abundance increases in response to DNA replication stress; human homolog, parafibromin, is a tumour suppressor linked to breast, renal and gastric cancer.	++
<i>CTK1</i>	Catalytic (alpha) subunit of C-terminal domain kinase I (CTDK-I); phosphorylates both RNA pol II subunit Rpo21 to affect transcription and pre-mRNA 3' end processing, and ribosomal protein Rps2 to increase translational fidelity; required for H3K36 trimethylation but not dimethylation by Set2; suggested stimulatory role in 80S formation during translation initiation.	+++
<i>DBF2</i>	Ser/Thr kinase involved in transcription and stress response; functions as part of a network of genes in exit from mitosis; localization is cell cycle regulated; activated by Cdc15 during the exit from mitosis; also plays a role in regulating the stability of <i>SWI5</i> and <i>CLB2</i> mRNAs; phosphorylates Chs2 to regulate primary septum formation and Hof1 to regulate cytokinesis.	+++
<i>EFM4</i>	Lysine methyltransferase; involved in the dimethylation of <i>eEF1A</i> (Tef1/Tef2) at lysine 316; sequence similarity to S-adenosylmethionine-dependent methyltransferases of the seven beta-strand family; role in vesicular transport.	+
<i>EFT2</i>	Elongation factor 2 (EF-2), also encoded by <i>EFT1</i> ; catalyzes ribosomal translocation during protein synthesis; contains diphthamide, the unique posttranslationally modified histidine residue specifically ADP-ribosylated by diphtheria toxin; <i>EFT2</i> has a paralog, <i>EFT1</i> , that arose from the whole genome duplication.	+
<i>FES1</i>	Hsp70 (Ssa1) nucleotide exchange factor; required for the release of misfolded proteins from the Hsp70 system to the Ub-proteasome machinery for destruction; cytosolic homolog of Sil1, which is the nucleotide exchange factor for BiP (Kar2) in the endoplasmic reticulum; protein abundance increases in response to DNA replication stress.	+++
<i>FPK1</i>	Ser/Thr protein kinase; phosphorylates several aminophospholipid translocase family members, regulating phospholipid translocation and membrane asymmetry; phosphorylates and inhibits upstream inhibitory kinase, Ypk1; localizes to the cytoplasm, early endosome/TGN compartments and thplasma membrane.	+
<i>GIM3</i>	Subunit of the heterohexameric cochaperone prefoldin complex; prefoldin binds specifically to cytosolic chaperonin and transfers target proteins to it; prefoldin complex also localizes to chromatin of actively transcribed genes in the nucleus and facilitates transcriptional elongation.	++

<i>HPM1</i>	AdoMet-dependent methyltransferase; involved in a novel 3-methylhistidine modification of ribosomal protein Rpl3p; seven beta-strand MTase family member	+
<i>KEX2</i>	Kexin, a subtilisin-like protease (proprotein convertase); a calcium-dependent serine protease involved in the activation of proproteins of the secretory pathway.	+++
<i>LIP2</i>	Lipoyl ligase; involved in the modification of mitochondrial enzymes by the attachment of lipoic acid groups.	+
<i>MCK1</i>	Dual-specificity ser/thr and tyrosine protein kinase; roles in chromosome segregation, meiotic entry, genome stability, phosphorylation-dependent protein degradation (Rcn1 and Cdc6), inhibition of protein kinase A, transcriptional regulation, inhibition of RNA pol III, calcium stress and inhibition of Clb2-Cdc28 after nuclear division; <i>MCK1</i> has a paralog, <i>YGK3</i> , that arose from the whole genome duplication.	+
<i>NAS2</i>	Evolutionarily conserved 19S regulatory particle assembly-chaperone; involved in assembly of the base subcomplex of the 19S proteasomal regulatory particle (RP); non-essential gene; interacts with Rpn4; protein abundance increases in response to DNA replication stress; ortholog of human p27.	++
<i>NAT1</i>	Subunit of protein N-terminal acetyltransferase NatA; NatA comprised of Nat1, Ard1, and Nat5; N-terminally acetylates many proteins to influence multiple processes such as cell cycle progression, heat-shock resistance, mating, sporulation, telomeric silencing and early stages of mitophagy; orthologous to human <i>NAA15</i> ; expression of both human <i>NAA10</i> and <i>NAA15</i> functionally complements <i>ard1 nat1</i> double mutant although single mutations are not complemented by their orthologs.	+++
<i>NAT3</i>	Catalytic subunit of the NatB N-terminal acetyltransferase; NatB catalyzes acetylation of the amino-terminal methionine residues of all proteins beginning with Met-Asp or Met-Glu and of some proteins beginning with Met-Asn or Met-M.	+++
<i>NAT4</i>	N alpha-acetyl-transferase; involved in acetylation of the N-terminal residues of histones H4 and H2A.	+++
<i>OST3</i>	Gamma subunit of the oligosaccharyltransferase complex of the ER lumen; complex catalyzes asparagine-linked glycosylation of newly synthesized proteins.	+
<i>OST4</i>	Subunit of the oligosaccharyltransferase complex of the ER lumen; complex catalyzes protein asparagine-linked glycosylation; type I membrane protein required for incorporation of Ost3 or Ost6 into the OST complex.	+++
<i>PMT1</i>	Protein O-mannosyltransferase of the ER membrane; transfers mannose from dolichyl phosphate-D-mannose to protein serine and threonine residues.	+
<i>PPM1</i>	Carboxyl methyltransferase; methylates the C terminus of the protein phosphatase 2A catalytic subunit (Pph21 or Pph22), which is important for complex formation with regulatory subunits; required for methionine to inhibit autophagy and promote growth.	++
<i>PPT2</i>	Phosphopantetheine:protein transferase (PPTase); activates mitochondrial acyl carrier protein (Acp1) by phosphopantetheinylation.	++
<i>PTK2</i>	Serine/threonine protein kinase; involved in regulation of ion transport across plasma membrane; carboxyl terminus is essential for glucose-dependent Pma1 activation via	++

	phosphorylation of Pma1-Ser899.	
<i>RAM1</i>	Beta subunit of the CAAX farnesyltransferase (FTase); this complex 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.	+
<i>SHR5</i>	Palmitoyltransferase subunit; this complex adds a palmitoyl lipid moiety to heterolipidated substrates such as Ras1 and Ras2 through a thioester linkage; palmitoylation is required for Ras2 membrane localization; Palmitoyltransferase is composed of Shr5 and Erf.	+++
<i>SWM1</i>	Subunit of the anaphase-promoting complex (APC); APC is an E3 ubiquitin ligase that regulates the metaphase-anaphase transition and exit from mitosis; required for activation of the daughter-specific gene expression and spore wall maturation.	+++
<i>TOS3</i>	Protein kinase; related to and functionally redundant with Elm1 and Sak1p for the phosphorylation and activation of Snf1; functionally orthologous to <i>LKB1</i> , a mammalian kinase associated with Peutz-Jeghers cancer-susceptibility syndrome; <i>TOS3</i> has a paralog, <i>SAK1</i> , that arose from the whole genome duplication.	++
<i>UBA4</i>	E1-like protein that activates Urm1 before urmylation; also acts in thiolation of the wobble base of cytoplasmic tRNAs by adenylating and then thiolating Urm1; receives sulfur from Tum1.	++
<i>UBI4</i>	Ubiquitin; becomes conjugated to proteins, marking them for selective degradation via the ubiquitin-26S proteasome system.	+
<i>UBP14</i>	Ubiquitin-specific protease; specifically disassembles unanchored ubiquitin chains; involved in fructose-1,6-bisphosphatase (Fbp1) degradation	+
<i>UBP6</i>	Ubiquitin-specific protease; situated in the base subcomplex of the 26S proteasome, releases free ubiquitin from branched polyubiquitin chains <i>en bloc</i> , rather than from the distal tip of the chain.	+
<i>VMS1</i>	Component of a Cdc48-complex involved in protein quality control; exhibits cytosolic and ER-membrane localization, with Cdc48p, during normal growth, and contributes to ER-associated degradation (ERAD) of specific substrates at a step after their ubiquitination; forms a mitochondrially-associated complex with Cdc48 and Npl4 under oxidative stress that is required for ubiquitin-mediated mitochondria-associated protein degradation (MAD); conserved in <i>C. elegans</i> and humans.	++
<i>YME1</i>	Catalytic subunit of i-AAA protease complex; complex is located in mitochondrial inner membrane; responsible for degradation of unfolded or misfolded mitochondrial gene products; serves as nonconventional translocation motor to pull PNPase into intermembrane space; also has role in intermembrane space protein folding; mutation causes elevated rate of mitochondrial turnover.	++

Protein synthesis

Gene	Function	Susceptibility level
<i>HCR1</i>	eIF3j component of translation initiation factor 3 (eIF3); dual function protein involved in translation initiation as a substoichiometric component (eIF3j) of eIF3; required for 20S pre-rRNA processing; required at post-transcriptional step for efficient retrotransposition; absence decreases Ty1 Gag:GFP protein levels.	+++
<i>IFM1</i>	Mitochondrial translation initiation factor.	++
<i>MRP17</i>	Mitochondrial ribosomal protein of the small subunit; <i>MRP17</i> exhibits genetic interactions with <i>PET122</i> , encoding a COX3-specific translational activator.	++
<i>MRP7</i>	Mitochondrial ribosomal protein of the large subunit.	++
<i>MRPL13</i>	Mitochondrial ribosomal protein of the large subunit; not essential for mitochondrial translation.	+
<i>MRPL20</i>	Mitochondrial ribosomal protein of the large subunit.	++
<i>MRPL22</i>	Mitochondrial ribosomal protein of the large subunit.	++
<i>MRPL24</i>	Mitochondrial ribosomal protein of the large subunit; two mitochondrial ribosomal proteins, <i>YmL14</i> and <i>YmL24</i> , have been assigned to the same gene.	+
<i>MRPL36</i>	Mitochondrial ribosomal protein of the large subunit; overproduction suppresses mutations in the COX2 leader peptide-encoding region.	++
<i>MRPL49</i>	Mitochondrial ribosomal protein of the large subunit.	++
<i>MRPS12</i>	Mitochondrial protein; may interact with ribosomes based on co-purification experiments; similar to <i>E. coli</i> and human mitochondrial S12 ribosomal proteins.	++
<i>MRX14</i>	Putative mitochondrial ribosomal protein of the large subunit; similar to <i>E. coli</i> L34 ribosomal protein; required for respiratory growth, as are most mitochondrial ribosomal proteins; protein increases in abundance and relocalizes to the plasma membrane upon DNA replication stress.	+
<i>RML2</i>	Mitochondrial ribosomal protein of the large subunit (L2); has similarity to <i>E. coli</i> L2 ribosomal protein; mutant allele (<i>fat21</i>) causes inability to utilize oleate, and induce oleic acid oxidation; may interfere with activity of the Adr1 transcription factor.	+++
<i>RPB4</i>	RNA polymerase II subunit B32; forms dissociable heterodimer with Rpb7; Rpb4/7 dissociates from RNAPII as Ser2 CTD phosphorylation increases; Rpb4/7 regulates cellular lifespan via mRNA decay process; involved in recruitment of 3'-end processing factors to transcribing RNAPII complex, export of mRNA to cytoplasm under stress conditions; also involved in translation initiation.	+++
<i>RPL20B</i>	Ribosomal 60S subunit protein L20B; homologous to mammalian ribosomal protein L18A, no bacterial homolog; <i>RPL20B</i> has a paralog, <i>RPL20A</i> , that arose from the whole genome duplication.	+++
<i>RPL21A</i>	Ribosomal 60S subunit protein L21A.	+

<i>RPL21B</i>	Ribosomal 60S subunit protein L21B; homologous to mammalian ribosomal protein L21, no bacterial homolog; <i>RPL21B</i> has a paralog, <i>RPL21A</i> , that arose from the whole genome duplication.	+
<i>RPL39</i>	Ribosomal 60S subunit protein L39; required for ribosome biogenesis; loss of both Rpl31p and Rpl39p confers lethality; also exhibits genetic interactions with <i>SIS1</i> and <i>PAB1</i> ; homologous to mammalian ribosomal protein L39, no bacterial homolog.	+++
<i>RPL40A</i>	Ubiquitin-ribosomal 60S subunit protein L40A fusion protein; cleaved to yield ubiquitin and ribosomal protein L40A; ubiquitin may facilitate assembly of the ribosomal protein into ribosomes; homologous to mammalian ribosomal protein L40, no bacterial homolog; <i>RPL40A</i> has a paralog, <i>RPL40B</i> , that arose from the whole genome duplication; relative distribution to the nucleus increases upon DNA replication stress.	+
<i>RPL42B</i>	Ribosomal 60S subunit protein L42B; required for propagation of the killer toxin-encoding M1 double-stranded RNA satellite of the L-A double-stranded RNA virus; homologous to mammalian ribosomal protein L36A, no bacterial homolog; <i>RPL42B</i> has a paralog, <i>RPL42A</i> .	++
<i>RPP1A</i>	Ribosomal stalk protein P1 alpha; involved in the interaction between translational elongation factors and the ribosome; free (non-ribosomal) P1 stimulates the phosphorylation of the <i>eIF2</i> alpha subunit (Sui2) by Gcn2; accumulation of P1 in the cytoplasm is regulated by phosphorylation and interaction with the P2 stalk component.	++
<i>RPS10A</i>	Protein component of the small (40S) ribosomal subunit; homologous to mammalian ribosomal protein S10, no bacterial homolog; <i>RPS10A</i> has a paralog, <i>RPS10B</i> , that arose from the whole genome duplication; mutations in the human homolog associated with Diamond-Blackfan anemia.	+
<i>RPS11B</i>	Protein component of the small (40S) ribosomal subunit; homologous to mammalian ribosomal protein S11 and bacterial S17; <i>RPS11B</i> has a paralog, <i>RPS11A</i> , that arose from the whole genome duplication.	+
<i>RPS16A</i>	Protein component of the small (40S) ribosomal subunit	+
<i>RPS21A</i>	Protein component of the small (40S) ribosomal subunit; homologous to mammalian ribosomal protein S21, no bacterial homolog.	+
<i>RPS21B</i>	Protein component of the small (40S) ribosomal subunit; homologous to mammalian ribosomal protein S21, no bacterial homolog; <i>RPS21B</i> has a paralog, <i>RPS21A</i> , that arose from the whole genome duplication.	++
<i>RPS24A</i>	Protein component of the small (40S) ribosomal subunit; homologous to mammalian ribosomal protein S24, no bacterial homolog; <i>RPS24A</i> has a paralog, <i>RPS24B</i> , that arose from the whole genome duplication.	+
<i>RPS27B</i>	Protein component of the small (40S) ribosomal subunit; homologous to mammalian ribosomal protein S27, no bacterial homolog; <i>RPS27B</i> has a paralog, <i>RPS27A</i> , that arose from the whole genome duplication.	+++
<i>RPS6A</i>	Protein component of the small (40S) ribosomal subunit; homologous to mammalian ribosomal protein S6, no bacterial homolog; phosphorylated on S233 by Ypk3 in a TORC1-dependent manner, and on S232 in a TORC1/2-dependent manner by Ypk1/2/3; <i>RPS6A</i> has a paralog, <i>RPS6B</i> , that arose from the whole genome duplication.	++

<i>RPS6B</i>	Protein component of the small (40S) ribosomal subunit;	+
<i>RSM19</i>	Mitochondrial ribosomal protein of the small subunit; has similarity to <i>E. coli</i> S19 ribosomal protein.	++
<i>RSM26</i>	Mitochondrial ribosomal protein of the small subunit.	+
<i>SEM1</i>	19S proteasome regulatory particle lid subcomplex component; role in Ub-dependent proteolysis and proteasome stability; involved in TREX-2 mediated mRNA export, and in the prevention of transcription-associated genome instability; ubiquitinated by Nedd4-like E3-ligase, Rsp5; human ortholog <i>DSS1</i> , a <i>BRCA1</i> binding protein implicated in cancer, complements the yeast null; drives trinucleotide repeat expansion; protein abundance increases in response to DNA replication stress.	+
<i>TIF3</i>	Translation initiation factor eIF-4B; contains an RNA recognition motif and binds to single-stranded RNA; has RNA annealing activity; interacts with Rps20 at the head of the 40S ribosomal subunit and alters the structure of the mRNA entry channel.	++
<i>TIF4631</i>	Translation initiation factor <i>eIF4G</i> ; subunit of the mRNA cap-binding protein complex (eIF4F) that also contains eIF4E (Cdc33); interacts with Pab1 and with eIF4A (Tif1).	+

Response to stress

Gene	Function	Susceptibility level
<i>CCS1</i>	Copper chaperone for superoxide dismutase Sod1; involved in oxidative stress protection; Met-X-Cys-X2-Cys motif within N-terminus is involved in insertion of copper into Sod1 under conditions of copper deprivation; required for regulation of yeast copper genes in response to DNA-damaging agents; protein abundance increases in response to DNA replication stress; human homolog CCS can complement yeast <i>ccs1</i> null mutant.	++
<i>MXR2</i>	Methionine-R-sulfoxide reductase; involved in the response to oxidative stress; protects iron-sulfur clusters from oxidative inactivation along with <i>MXR1</i> .	+
<i>SYM1</i>	Protein required for ethanol metabolism; induced by heat shock and localized to the inner mitochondrial membrane; homologous to mammalian peroxisomal membrane protein Mpv17; human homolog MPV17 is implicated in hepatocerebral mtDNA depletion syndromes (MDDS), and complements yeast null mutant.	+
<i>WHI2</i>	Protein required for full activation of the general stress response; required with binding partner Psr1, possibly through Msn2 dephosphorylation; regulates growth during the diauxic shift.	+
<i>WHI5</i>	Repressor of G1 transcription; binds to SCB binding factor (SBF) at SCB target promoters in early G1.	+

Signal transduction

Gene	Function	Susceptibility level
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<i>GPB2</i>	Multistep regulator of cAMP-PKA signaling; inhibits PKA downstream of Gpa2 and Cyr1, thereby increasing cAMP dependency; inhibits Ras activity through direct interactions with Ira1/2.	+
<i>IRS4</i>	EH domain-containing protein; involved in regulating phosphatidylinositol 4,5-bisphosphate levels and autophagy; Irs4 and Tax4 bind and activate the PtdIns phosphatase Inp51; Irs4 and Tax4 are involved in localizing Atg17 to the PAS; <i>IRS4</i> has a paralog.	++
<i>NBP2</i>	Protein involved in the HOG (high osmolarity glycerol) pathway; negatively regulates Hog1 by recruitment of phosphatase Ptc1 the Pbs2-Hog1 complex; interacts with Bck1 and down regulates the cell wall integrity pathway; found in the nucleus and cytoplasm, contains an SH3 domain and a Ptc1 binding domain (PBM).	++
<i>PDE2</i>	High-affinity cyclic AMP phosphodiesterase; component of the cAMP-dependent protein kinase signaling system, protects the cell from extracellular cAMP	+
<i>RAS2</i>	GTP-binding protein; regulates nitrogen starvation response, sporulation, and filamentous growth; farnesylation and palmitoylation required for activity and localization to plasma membrane; homolog of mammalian Ras proto-oncogenes; <i>RAS2</i> has a paralog, <i>RAS1</i> , that arose from the whole genome duplication.	+++
<i>REI1</i>	Cytoplasmic pre-60S factor; required for the correct recycling of shuttling factors Alb1, Arx1 and Tif6 at the end of the ribosomal large subunit biogenesis; involved in bud growth in the mitotic signaling network.	++
<i>SIP1</i>	Alternate beta-subunit of the Snf1 kinase complex; may confer substrate specificity; vacuolar protein containing KIS (Kinase-Interacting Sequence) and ASC (Association with Snf1 kinase Complex) domains involved in protein interaction	+
<i>SNF1</i>	AMP-activated S/T protein kinase; forms a complex with Snf4 and members of the Sip1/Sip2/Gal83 family; required for transcription of glucose-repressed genes, thermotolerance, sporulation, and peroxisome biogenesis; regulates nucleocytoplasmic shuttling of Hxk2; regulates filamentous growth and acts as a non-canonical GEF, activating Arf3 during invasive growth; SUMOylation by Mms21 inhibits its function and targets Snf1 for destruction via the Slx5-Slx8 Ub ligase.	++
<i>STE50</i>	Adaptor protein for various signaling pathways; involved in mating response, invasive/filamentous growth, osmotolerance.	+
<i>TUS1</i>	Guanine nucleotide exchange factor (GEF) that modulates Rho1 activity; involved in the cell integrity signaling pathway; interacts with Rgl1; localization of Tus1 to the bud neck is regulated by Rgl1; multicopy suppressor of <i>tor2</i> mutation and <i>ypk1 ypk2</i> double mutation; potential Cdc28 substrate.	++

Transcription factors

Gene	Function	Susceptibility level
<i>CBF1</i>	Basic helix-loop-helix (bHLH) protein; forms homodimer to bind E-box consensus sequence CACGTG present at <i>MET</i> gene promoters and centromere DNA element I (CDEI); affects nucleosome positioning at this motif; associates with other transcription factors such as Met4 and Isw1 to mediate transcriptional activation or repression; associates with kinetochore proteins, required for chromosome segregation; protein abundance increases in response to DNA replication stress.	++
<i>HAP5</i>	Subunit of the Hap2/3/4/5 CCAAT-binding complex; complex is heme-activated and glucose repressed; complex is a transcriptional activator and global regulator of respiratory gene expression.	+
<i>MGA2</i>	ER membrane protein involved in regulation of <i>OLE1</i> transcription; inactive ER form dimerizes and one subunit is then activated by ubiquitin/proteasome-dependent processing followed by nuclear targeting; <i>MGA2</i> has a paralog, <i>SPT23</i> , that arose from the whole genome duplication.	++
<i>OAF1</i>	Oleate-activated transcription factor; subunit of a heterodimeric complex with Pip2, which binds to oleate-response elements (ORE) in the promoter of genes involved in beta-oxidation of fatty acids, peroxisome organization and biogenesis, activating transcription in the presence of oleate.	+
<i>RPN4</i>	Transcription factor that stimulates expression of proteasome genes; Rpn4 levels are in turn regulated by the 26S proteasome in a negative feedback control mechanism; RPN4 is transcriptionally regulated by various stress responses; relative distribution to the nucleus increases upon DNA replication stress.	+++
<i>RSF2</i>	Zinc-finger protein; involved in transcriptional control of both nuclear and mitochondrial genes, many of which specify products required for glycerol-based growth, respiration.	+
<i>SFL1</i>	Transcriptional repressor and activator; involved in repression of flocculation-related genes, and activation of stress responsive genes; has direct role in <i>INO1</i> transcriptional memory; negatively regulated by cAMP-dependent protein kinase A subunit Tpk2; premature stop codon (C1430T, Q477-stop) in SK1 background is linked to the aggressively invasive phenotype of SK1 relative to BY4741 (S288C).	++
<i>SFP1</i>	Regulates transcription of ribosomal protein and biogenesis genes; regulates response to nutrients and stress, G2/M transitions during mitotic cell cycle and DNA-damage response and modulates cell size; regulated by TORC1 and Mrs6; sequence of zinc finger, ChIP localization data, and protein-binding microarray (PBM) data, and computational analyses suggest it binds DNA directly at highly active RP genes and indirectly through Rap1 at others; can form the [ISP+] prion.	+++

<i>STP1</i>	Transcription factor; contains a N-terminal regulatory motif (RI) that acts as a cytoplasmic retention determinant and as an Asi dependent degron in the nucleus; undergoes proteolytic processing by SPS (Ssy1-Ptr3-Ssy5)-sensor component Ssy5 in response to extracellular amino acids; activates transcription of amino acid permease genes and may have a role in tRNA processing.	+
<i>SWI6</i>	Transcription cofactor; forms complexes with Swi4 and Mbp1 to regulate transcription at the G1/S transition; involved in meiotic gene expression; also binds Stb1 to regulate transcription at START; cell wall stress induces phosphorylation by Mpk1, which regulates Swi6 localization; required for the unfolded protein response, independently of its known transcriptional coactivators.	++
<i>TUP1</i>	General repressor of transcription; forms complex with Cyc8, involved in the establishment of repressive chromatin structure through interactions with histones H3 and H4.	+
<i>UME6</i>	Rpd3L histone deacetylase complex subunit; key transcriptional regulator of early meiotic genes; involved in chromatin remodeling and transcriptional repression via DNA looping; binds <i>URS1</i> upstream regulatory sequence, represses transcription by recruiting conserved histone deacetylase Rpd3 (through co-repressor Sin3) and chromatin-remodeling factor Isw2; couples metabolic responses to nutritional cues with initiation and progression of meiosis.	+++
<i>UPC2</i>	Sterol regulatory element binding protein; induces sterol biosynthetic genes, upon sterol depletion; acts as a sterol sensor, binding ergosterol in sterol rich conditions.	+
<i>URE2</i>	Nitrogen catabolite repression transcriptional regulator; inhibits <i>GLN3</i> transcription in good nitrogen source; role in sequestering Gln3 and Gat1 to the cytoplasm; has glutathione peroxidase activity and can mutate to acquire GST activity; self-assembly under limited nitrogen conditions creates [<i>URE3</i>] prion and releases catabolite repression.	+

Transporters

Gene	Function	Susceptibility level
<i>DAL5</i>	Allantoate permease; ureidosuccinate permease; also transports dipeptides, though with lower affinity than for allantoate and ureidosuccinate; expression is constitutive but sensitive to nitrogen catabolite repression.	+
<i>FPS1</i>	Aquaglyceroporin, plasma membrane channel; involved in efflux of glycerol and xylitol, and in uptake of acetic acid, arsenite, and antimonite; key factor in maintaining redox balance by mediating passive diffusion of glycerol; phosphorylated by Hog1 MAPK under acetate stress; deletion improves xylose fermentation; regulated by Rgc1 and Ask10, which are regulated by Hog1p phosphorylation under osmotic stress; phosphorylation by Ypk1 required to maintain an open state.	+++
<i>MME1</i>	Transporter of the mitochondrial inner membrane that exports magnesium; involved in mitochondrial Mg ²⁺ homeostasis; has similarity to human mitochondrial ATP-Mg/Pi carriers.	++
<i>NHA1</i>	Na ⁺ /H ⁺ antiporter; involved in sodium and potassium efflux through the plasma membrane; required for alkali cation tolerance at acidic pH.	+

<i>OPT2</i>	Oligopeptide transporter; localized to peroxisomes and affects glutathione redox homeostasis; also localizes to the plasma membrane (PM) and to the late Golgi, and has a role in maintenance of lipid asymmetry between the inner and outer leaflets of the PM; member of the OPT family, with potential orthologs in <i>S. pombe</i> and <i>C. albicans</i> ; also plays a role in formation of mature vacuoles and in polarized cell growth.	+
<i>SPF1</i>	P-type ATPase, ion transporter of the ER membrane; required to maintain normal lipid composition of intracellular compartments and proper targeting of mitochondrial outer membrane tail-anchored proteins; involved in ER function and Ca ²⁺ homeostasis; required for regulating Hmg2 degradation; confers sensitivity to a killer toxin (SMKT) produced by <i>Pichia farinosa</i> KK1.	+++
<i>TPN1</i>	Plasma membrane pyridoxine (vitamin B6) transporter; member of the purine-cytosine permease subfamily within the major facilitator superfamily; proton symporter with similarity to Fcy21, Fcy2, and Fcy22.	++
<i>TPO1</i>	Polyamine transporter of the major facilitator superfamily; member of the 12-spanner drug:H ⁺ antiporter <i>DHA1</i> family; recognizes spermine, putrescine, and spermidine; catalyzes uptake of polyamines at alkaline pH and excretion at acidic pH; during oxidative stress exports spermine, spermidine from the cell, which controls timing of expression of stress-responsive genes; phosphorylation enhances activity and sorting to the plasma membrane.	+
<i>YIA6</i>	Mitochondrial NAD ⁺ transporter; involved in the transport of NAD ⁺ into the mitochondria (see also <i>YEA6</i>); member of the mitochondrial carrier subfamily; disputed role as a pyruvate transporter; has putative mouse and human orthologs; <i>YIA6</i> has a paralog, <i>YEA6</i> , that arose from the whole genome duplication.	++

Unknown function

Gene	Function	Susceptibility level
<i>AIM4</i>	Protein proposed to be associated with the nuclear pore complex; null mutant is viable, displays elevated frequency of mitochondrial genome loss and is sensitive to freeze-thaw stress.	+
<i>API2</i>	Putative protein of unknown function; conserved among <i>S. cerevisiae</i> strains; not conserved in closely related <i>Saccharomyces</i> species; 26% of ORF overlaps the dubious ORF YDR524C-A	+
<i>BIL1</i>	Protein that binds Bud6 and has a role in actin cable assembly; involved in the Bnr1p-dependent pathway of cable assembly; localizes to bud tip and bud neck.	++
<i>BUD26</i>	Dubious open reading frame; unlikely to encode a functional protein, based on available experimental and comparative sequence data; not conserved in closely related <i>Saccharomyces</i> species; 1% of ORF overlaps the verified gene SNU56.	+
<i>HGH1</i>	Nonessential protein of unknown function.	++
<i>IRC13</i>	Putative protein of unknown function; conserved across <i>S. cerevisiae</i> strains.	+
<i>JIP4</i>	Protein of unknown function; previously annotated as two separate ORFs, YDR474C and YDR475C, which were merged as a result of corrections to the systematic reference sequence.	+

<i>MRP8</i>	Protein of unknown function; undergoes sumoylation; transcription induced under cell wall stress; protein levels are reduced under anaerobic conditions.	+
<i>OPI10</i>	Protein with a possible role in phospholipid biosynthesis; null mutant displays an inositol-excreting phenotype that is suppressed by exogenous choline; protein abundance increases in response to DNA replication stress.	++
<i>OPI7</i>	Dubious open reading frame; unlikely to encode a functional protein.	+
<i>OPI9</i>	Dubious open reading frame; unlikely to encode a functional protein.	+++
<i>PAL1</i>	Protein of unknown function thought to be involved in endocytosis.	+
<i>RGL1</i>	Regulator of Rho1p signaling, cofactor of Tus1; required for the localization of Tus1 during all phases of cytokinesis; green fluorescent protein (GFP)-fusion protein localizes to the bud neck and cytoplasm; null mutant is viable and exhibits growth defect on a non-fermentable (respiratory) carbon source.	++
<i>RMD8</i>	Cytosolic protein required for sporulation.	+
<i>RRG1</i>	Protein of unknown function; required for vacuolar acidification and mitochondrial genome maintenance; the authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies.	+
<i>SRP40</i>	Nucleolar serine-rich protein; role in preribosome assembly or transport; may function as a chaperone of small nucleolar ribonucleoprotein particles (snoRNPs).	+
<i>TPH3</i>	Putative protein of unknown function; GFP-fusion protein localizes to the cytoplasm; contains two adjacent PH-like domains; conserved in closely related <i>Saccharomyces</i> species.	+
<i>TVP15</i>	Integral membrane protein; localized to late Golgi vesicles along with the v-SNARE Tlg2.	+
<i>YAR029W</i>	Member of <i>DUP240</i> gene family but contains no transmembrane domains; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm in a punctate pattern.	+
<i>YBL071C-B</i>	Putative protein of unknown function.	++
<i>YBL094C</i>	Dubious open reading frame; unlikely to encode a functional protein.	+
<i>YBL100C</i>	Dubious open reading frame; unlikely to encode a functional protein.	+++
<i>YCL007C</i>	Dubious open reading frame; unlikely to encode a functional protein.	+++
<i>YCL026C</i>	Deleted ORF; does not encode a protein.	+
<i>YDR008C</i>	Dubious open reading frame; unlikely to encode a functional protein.	+++
<i>YDR203W</i>	Dubious open reading frame; unlikely to encode a functional protein.	+
<i>YDR442W</i>	Dubious open reading frame; unlikely to encode a functional protein.	+++
<i>YDR524C-B</i>	Putative protein of unknown function.	++
<i>YDR524W-C</i>	Putative protein of unknown function.	++
<i>YGL024W</i>	Dubious open reading frame; unlikely to encode a functional protein.	+

YGL218W	Dubious open reading frame; unlikely to encode a functional protein.	++
YGR079W	Putative protein of unknown function.	+
YHR175W-A	Putative protein of unknown function.	++
YIL028W	Dubious open reading frame; unlikely to encode a functional protein.	++
YIL029C	Putative protein of unknown function.	++
YIL077C	Putative protein of unknown function.	+
YIL092W	Putative protein of unknown function.	+
YIL141W	Dubious open reading frame; unlikely to encode a functional protein.	+
YJR011C	Putative protein of unknown function.	+++
YJR114W	Dubious open reading frame; unlikely to encode a functional protein.	++
YKL118W	Dubious open reading frame; unlikely to encode a functional protein.	++
YKR004C-A	Merged open reading frame; does not encode a discrete protein; YKR004C-A was originally annotated as an independent ORF.	+
YLR202C	Dubious open reading frame; unlikely to encode a functional protein.	++
YLR235C	Dubious open reading frame; unlikely to encode a functional protein.	++
YLR264C-A	Putative protein of unknown function.	+
YLR297W	Protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the vacuole.	+
YLR358C	Protein of unknown function.	+++
YLR407W	Putative protein of unknown function.	++
YMR001C-A	Putative protein of unknown function.	+
YNL190W	Hydrophilin essential in desiccation-rehydration process; cell wall protein; contains a putative GPI-attachment site.	++
YNL193W	Putative protein of unknown function.	+
YNL194C	Integral membrane protein; required for sporulation and plasma membrane sphingolipid content; similar to <i>SUR7</i> ; GFP-fusion protein is induced in response to the DNA-damaging agent MMS; GFP-fusion protein is more abundant at MCCs (membrane compartment occupied by Can1) in the presence of glycerol and oleate; <i>YNL194C</i> has a paralog, <i>FMP45</i> , that arose from the whole genome duplication.	+
YOL050C	Dubious open reading frame; unlikely to encode a functional protein.	+
YOL107W	Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and colocalizes in a punctate pattern with the early Golgi/COPI vesicles; <i>YOL107W</i> is not an essential protein.	++
YOR082C	Dubious open reading frame; unlikely to encode a functional protein.	+
YOR139C	Dubious open reading frame; unlikely to encode a functional protein.	++
YPL205C	Hypothetical protein; deletion of locus affects telomere length.	+