Supplemental Table 1.

| **Rank** | **Gene** | **Locus** | **Defect vs WT** | **Retested** | **Retested sensitive** | **Description** |
| --- | --- | --- | --- | --- | --- | --- |
| 1 | YPK1 | YKL126W | 6.61 | - |  | 76.5 kDa Serine/threonine protein kinase with similarity to protein kinase C, is 90% identical to Ypk2p |
| 2 | AFT1 | YGL071W | 5.07 | + | + | Involved in iron homeostasis and affects cell size regulation. Activates the expression of its target genes in response to low-iron conditions. |
| 3 | YDR269C | YDR269C | 4.27 | + | + | Dubious ORF; deletion prevents expression of CCC2. |
| 4 | FET3 | YMR058W | 4.24 | + | + | Ferro-O2-oxidoreductase required for high-affinity iron uptake and involved in mediating resistance to copper ion toxicity, belongs to class of integral membrane multicopper oxidases |
| 5 | PHO86 | YJL117W | 4.18 | - |  | Protein specifically required for packaging of the high-affinity phosphate transporter Pho84p into COPII coated vesicles for transport to the plasma membrane; transcription and localization are regulated by phosphate levels |
| 6 | SAC1 | YKL212W | 4.16 | + | + | Inactivation of Sac1p leads to specific increase in cellular levels of phosphatidylinositol 4-phosphate, accompanied by changes in vacuole morphology and accumulation of lipid droplets. |
| 7 | SIP3 | YNL257C | 4.12 | + | - | Protein that activates transcription through interaction with DNA-bound Snf1p, C-terminal region has a putative leucine zipper motif; potential Cdc28p substrate |
| 8 | YMR031W-A | YMR031W-A | 4.09 | + | - |  |
| 9 | GEF1 | YJR040W | 4.08 | + | + | Chloride channel localized to late- or post-Golgi vesicles, involved in iron metabolism; highly homologous to voltage-gated chloride channels in vertebrates |
| 10 | VPS52 | YDR484W | 4.06 | + | - | May interact with actin as a component or controller of the assembly or stability of the actin cytoskeleton |
| 11 | TFP1 | YDL185W | 4.02 | + | - | Encodes a protein with three regions (ABC) that is spliced to yield the extein AC & the intein B; AC is a 69K vacuolar (H+)-ATPase & B is a 50K site-specific endonuclease named VDE (PI-SceI) that is homologous to HO |
| 12 | YHR155W | YHR155W | 3.97 | + | + |  |
| 13 | CCC2 | YDR270W | 3.69 | + | + | copper-transporting P-type ATPase with similarity to human Menkes and Wilsons genes |
| 14 | PGD1 | YGL025C | 3.52 | + | - | Probable transcription factor, polyglutamine domain protein |
| 15 | VPS36 | YLR417W | 3.46 | + | - | Defective in vacuolar protein sorting |
| 16 | CTR1 | YPR124W | 3.44 | + | +/- | High-affinity copper transporter of the plasma membrane, mediates nearly all copper uptake under low copper conditions; transcriptionally induced at low copper levels and degraded at high copper levels |
| 17 | ERG3 | YLR056W | 3.42 | + | + | C-5 sterol desaturase, catalyzes the introduction of a C-5(6) double bond into episterol, a precursor in ergosterol biosynthesis; mutants are viable, but cannot grow on non-fermentable carbon sources |
| 18 | ATX1 | YNL259C | 3.34 | + | + | Cytosolic copper metallochaperone that transports copper to the secretory vesicle copper transporter Ccc2p for eventual insertion into Fet3p, which is a multicopper oxidase required for high-affinity iron uptake |
| 19 | VMA21 | YGR105W | 3.27 | + | + | Protein involved in vacuolar H-ATPase assembly or function. Required for the biogenesis of a functional vacuolar ATPase (V-ATPase), but not part of the final enzyme complex. |
| 20 | MAC1 | YMR021C | 3.23 | + | + | Copper-sensing transcription factor involved in regulation of genes required for high affinity copper transport. |
| 21 | VMA13 | YPR036W | 3.19 | + | + | vacuolar ATPase V1 domain subunit H (54 kDa) |
| 22 | HTZ1 | YOL012C | 3.17 | + | - | 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 |
| 23 | LEM3 | YNL323W | 3.05 | + | + | Membrane protein of the plasma membrane and ER, involved in translocation of phospholipids and alkylphosphocholine drugs across the plasma membrane |
| 24 | VMA3 | YEL027W | 3.01 | + | + | Proteolipid subunit of the vacuolar H(+)-ATPase V0 sector (subunit c; dicyclohexylcarbodiimide binding subunit); required for vacuolar acidification and important for copper and iron metal ion homeostasis |
| 25 | COG6 | YNL041C | 3.01 | + | + | Component of the conserved oligomeric Golgi complex; interacts with Cog2p |
| 26 | YCL046W | YCL046W | 2.98 | + | + |  |
| 27 | GAL11 | YOL051W | 2.97 | + | + | Component of the Mediator complex; interacts with RNA polymerase II and the general transcription factors to form the RNA polymerase II holoenzyme; affects transcription by acting as target of activators and repressors |
| 28 | VMA5 | YKL080W | 2.90 | - |  | 42 kDa subunit of V1 sector |
| 29 | ERV14 | YGL054C | 2.88 | + | + | Protein localized to COPII-coated vesicles, involved in vesicle formation and incorporation of specific secretory cargo; required for the delivery of bud-site selection protein Axl2p to cell surface; related to Drosophila cornichon |
| 30 | FTR1 | YER145C | 2.87 | + | + | High affinity iron permease involved in the transport of iron across the plasma membrane; forms complex with Fet3p; expression is regulated by iron |
| 31 | ERG4 | YGL012W | 2.82 | + | - | C-24(28) sterol reductase, catalyzes the final step in ergosterol biosynthesis; mutants are viable, but lack ergosterol |
| 32 | RIC1 | YLR039C | 2.78 | - |  | Ric1p binds to Rgp1p, on the Golgi, and the complex catalyzes nucleotide exchange on Ypt6p. |
| 33 | VPS61 | YDR136C | 2.76 | - |  | Dubious open reading frame, unlikely to encode a protein; not conserved in closely related Saccharomyces species; 4% of ORF overlaps the verified gene RGP1; deletion causes a vacuolar protein sorting defect |
| 34 | YDR455C | YDR455C | 2.75 | - |  | Dubious ORF; deletion likely compromises expression of Nhx1. |
| 35 | VMA7 | YGR020C | 2.75 | - |  | vacuolar H-ATPase 14 kDa subunit (subunit F) of the catalytic (V1) sector |
| 36 | RAV1 | YJR033C | 2.63 | - |  | Regulator of (H+)-ATPase in vacuolar membrane |
| 37 | RAV2 | YDR202C | 2.58 | - |  | Regulator of (H+)-ATPase in Vacuolar membrane |
| 38 | YDR271C | YDR271C | 2.57 | - |  | Dubious ORF; deletion results in CCC2 trunkation. |
| 39 | SPT3 | YDR392W | 2.55 | - |  | Subunit of the SAGA and SAGA-like transcriptional regulatory complexes, interacts with Spt15p to activate transcription of some RNA polymerase II-dependent genes, also functions to inhibit trancription at some promoters |
| 40 | VMA22 | YHR060W | 2.54 | - |  | Required for V-ATPase activity. Required for the biogenesis of a functional vacuolar ATPase (V-ATPase), but not part of the final enzyme complex. |
| 41 | VPS63 | YLR261C | 2.50 | - |  | Dubious open reading frame, unlikely to encode a protein; not conserved in closely related Saccharomyces species; 98% of ORF overlaps the verified gene YPT6; deletion causes a vacuolar protein sorting defect |
| 42 | TLG2 | YOL018C | 2.49 | - |  | member of the syntaxin family of t-SNAREs |