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A genome-wide screen in Saccharomyces cerevisiae Reveals Pathways affected By Arsenic Toxicity

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Abstract

We have used *Saccharomyces cerevisiae* to identify toxicologically important proteins and pathways involved in arsenic-induced toxicity and carcinogenicity in humans. We performed a systemic screen of the complete set of 4,733 haploid *S. cerevisiae* single gene deletion mutants to identify those that have decreased or increased growth, relative to wild-type, after exposure to sodium arsenite ($NaAsO_2$). IC_{50} values for all mutants were determined to further validate our results. Ultimately we identified 248 mutants sensitive to arsenite and 5 mutants resistant to arsenite exposure. We analyzed the proteins corresponding to arsenite-sensitive mutants and determined that they belonged to functional categories that include protein binding, phosphate metabolism, vacuolar/lysosomal transport, protein targeting, sorting, and translocation, cell growth/morphogenesis, cell polarity and filament formation. Furthermore, these data were mapped onto a protein interactome to identify arsenite toxicity-modulating networks. These networks are associated with the cytoskeleton, ubiquitination, histone acetylation and the MAPK signaling pathway. Our studies have potential implications for understanding toxicity and carcinogenesis in arsenic-induced human conditions, such as cancer and aging.

Keywords

Arsenite; Toxicity; *Saccharomyces cerevisiae*

Introduction

Arsenic (As) is a ubiquitously present metalloid and a human carcinogen that is associated with skin, bladder, lung, kidney and liver cancer [1;2;3]. It is also implicated in vascular diseases, neurological and neurobehavioral disorders, diabetes and as a teratogen [4;5]. Paradoxically, arsenic trioxide is currently used in the treatment of acute promyelocytic leukemia (APL) [6; 7]. Inorganic arsenic is considered the most hazardous among all the arsenic species present in the environment. Inorganic arsenic exists in the environment in two major forms, arsenite [As (III)] or arsenate [As (V)]. In general, As (III) is more acutely toxic than As (V) [8]. Arsenic is a paradoxical non-mutagenic carcinogen, as there are arsenic-induced cancers observed in

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humans but there has been a lack of acceptable animal models. The mechanisms of arsenic-mediated toxicity and carcinogenesis are poorly understood, but it has been suggested that at least part of its toxicity is due to oxidative stress, which in turn causes protein denaturation, lipid damage and DNA strand breaks [9]. Arsenic activates signal transduction pathways including AP-1, NFκB and MAPK (see review [10]). In addition, arsenic is involved in epigenetic mechanisms, for example, the alteration of epigenetic marks such as H3K4 tri-methylation and H3K9 di-methylation [11].

The availability of a complete set of single gene deletion *Saccharomyces cerevisiae* strains has allowed us to functionally characterize the yeast genes that respond to cellular insults at the systemic level [12;13]. The complete yeast nucleotide sequence contains ~6,300 genes [14;15], but only the 4,733 nonessential yeast mutants can be examined because deletion of the essential genes is lethal. Since there is a high degree of homology among the eukaryotes, *S. cerevisiae* can be used as a model to identify genes that might be important in arsenic-induced carcinogenesis in other eukaryotes, including humans.

Cells have developed adaptive defense systems against environmental stress, such as detoxification, repair, removal of damaged molecules[16]. To better understand how cells respond to As (III) exposure, we screened the *S. cerevisiae* deletion strain set for sensitivity and resistance and identified the genes that have human homologues. In principle, genes whose deletion conferred sensitivity to arsenite would correspond to proteins involved in cellular recovery against arsenite-induced toxicity while genes whose deletion conferred resistance would correspond to proteins that arrest or reduce growth after arsenite exposure. We have analyzed the contribution of proteins that correspond to sensitive and resistant phenotypes in the framework of 12,232 protein-protein and protein-DNA interactions making up the known yeast interactome. Our results using this unbiased whole genomic approach reveal that genes whose deletion confers sensitivity to As (III) exposure correspond to proteins significantly enriched in various cellular functions, including vacuolar transport, cytoskeleton, acetylation and deacetylation processes, osmotic sensing and response, ubiquitination and proteosomal degradation, cell growth, regulation of carbon-compound and carbohydrate metabolism, protein binding, endocytosis, mitotic (M) phase, transport AT Pases, protein targeting, sorting and translocation, puine nucleotide/nucleoside/nucleobase anabolism, vacuole or lysosome function, homeostasis of protons, phosphate metabolism, stress response, budding, cell polarity and filament formation, cytoplasmic and nuclear protein degradation and MAPKKK cascade (Table 2). In contrast to 248 arsenite-toxicity sensitive proteins, only 5 arsenite-toxicity resistant proteins were identified (Mub1, Uth1, Fps1, Upf3, Ask10 and P15B12).

Materials and Methods

Medium, Solution, and strains

All yeast strains were grown in YPD (1% yeast extract, 2% peptone, 2% dextrose, 2% agar for plates) supplemented with 200 μg/ml G418. Sodium arsenite was purchased from sigma (St. Louis, MO). The complete set of 4,733 non-essential haploid *S. cerevisiae* single gene deletion mutants were obtained and described as before [17;18].

High-Throughput screening

High-throughput genomic screening was performed using the complete set of 4,733 mutants, as described before [17;18]. Briefly, 96-well master plates containing individual deletion strains were resuspended with 60 μl bursts of forced air from a Hydra liquid handling apparatus (Robbins Scientific, Sunnyvale, CA), and then 1 μl samples were spotted on YPD agar plates containing 0, 0.75, and 1 mM sodium arsenite. Inoculated plates were incubated for 60 h at 30 °C and the resulting plates were imaged using an AlphaImager (Alpha Innotech Corporation, San Leandro, CA). The mutants were scored as sensitive or resistant compared with the non-treated and the wild type strain (BY4741). The experiments were done in triplicate.

Determination of IC_{50}

5 μl of log-phase yeast culture was transferred into 195 μl YPD medium containing sodium arsenite in 96 well plates. The concentrations of sodium arsenite were 0, 0.375, 0.75, 1, 1.25 and 2.5 mM for sensitive strains and 0, 1.5, 2, 2.5, 3.75 and 5 mM for resistant strains. The cultures were incubated at 30 °C for 20 h, and cell density was determined by measuring the absorbance at 590 nm by Perkin Elmer HTS 7000 Bio Assay Reader. The concentration responsible for half-maximal inhibition of growth (IC_{50}) was calculated using GraphPad Prism 5 program.

Biological function analysis of arsenite toxicity modulating proteins

The deletion mutants that showed arsenic-sensitive phenotypes were categorized based on the biological functions using the program FunSpec (Functional Specification). The categories were downloaded from the *MIPS Database* and the *GO Database*. The p-values, calculated using the hypergeometric distribution, represent the probabilities that the intersection of a given list with any given functional category occurs by chance. Note that many genes are contained in many categories, especially in the MIPS database (which are hierarchical) and that this can create biases.

Interactome mapping analysis of arsenite toxicity modulating proteins

The deletion mutants were analyzed using the Cytoscope software for protein interaction networks as described [19]. *S. cerevisiae* protein–protein interaction information were obtained from the Database of Interacting Proteins [20]. In all we compiled 14,493 interactions between 5,433 proteins. The interactome is an extensive framework that can be used to identify protein networks activated by stress but it is a non saturated structure with regard to molecular interactions. None the less it provides a framework to analyze and associate discrete data points. Protein-protein interaction information was imported into Cytoscape for network visualization and subnetwork filtering. Subnetwork filtering was performed by tab selection of identified arsenite-toxicity modulation proteins and their associated protein-protein interactions. Analysis of the filtered interactome was set to identify sub networks => 4 nodes. It should be noted that interactome filtering does not use statistical validation to assign p-values to sub-networks. Instead, the filtering step identifies all connected As-toxicity modulating proteins in the interactome to provide a global view of how different functional activities are potentially coordinated.

Human homologues to yeast genes

Human homologues to the identified yeast genes were determined by BLAST using the tBLASTn program, which is available online from the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/blast/Blast.cgi) [21]. Note only the top scoring human homologue for each gene was used.

Results and discussion

Screening of single-gene deletion mutants of *S. cerevisiae* for arsenite sensitivity and resistance

We screened a library of 4,733 *S. cerevisiae* gene deletion strains in triplicate to determine which proteins influence resistance or sensitivity after exposure to As (III). Strains from saturated cultures grown in 96-well format were robotically spotted onto agar plates with and without As (III) in the agar. Following 60 h incubation, plates were recorded by digital imaging of colony growth. By visual inspection of the imaged colonies, the strains were scored for sensitivity or resistance. The strains that had a significant decrease in the growth of colonies relative to wild type BY4741 were scored as sensitive, and the strains that displayed increased colony growth relative to wild-type were scored as resistant. Typical colony growth images were shown in Figure 1. In order to identify the possible pathways of arsenic response in humans, only the genes that have human homologues were listed (Table 1).

To identify genes whose deletion renders yeast most sensitive or resistant to arsenite toxicity, we determined the IC_{50} of the indentified mutants as well as the wild type strain. The degree of sensitivity or resistance of each gene was ordered based on the IC_{50} value (Table 1). The IC_{50} of the wild type strain for sodium arsenite is 4.47 mM. While most mutants are sensitive to As (III), a few of them (Mub1, Uth1, Fps1, Upf3, Ask10 and P15B12) are resistant to As (III) when compared to the IC_{50} of the wild type (Table 1).

Biological categories of arsenite-toxicity modulating proteins

Several studies have used *S. cerevisiae* as a tool to identify the molecules and cellular pathways linking arsenic induced toxicity and carcinogenicity. Nucleic acid metabolism, oxidative phosphorylation, protein synthesis and vacuolar acidification were involved in either arsenite sensitivity or resistance as determined by screening single gene knockout strains of *S. cerevisiae* in mitochondrial biogenesis and function [22]. The strains whose deletion confers sensitivity to arsenic trioxide were found to be significantly enriched in the biological processes of osmoregulation, stress-related transcription regulation, cytoskeletal assembly and maintenance, signal transduction, DNA repair, oxidative stress, glutathione synthesis, secretory pathways and vacuole function, and general defense mechanisms [23]. Here we analyzed the effect of arsenite on yeast single-gene deletion mutants. Our studies with sodium arsenite found many genes in common with those of studies done by others using arsenic trioxide, and yet additional genes whose deletion leads to sensitivity or resistance exclusively to arsenite were also identified in this study.

Cytoskeleton and structure proteins—The strain most sensitive to sodium arsenite exposure, with an IC50 of 0.24 mM, lacks Pfd1 (Table 1). Pfd1 is subunit 1 of prefoldin, involved in the biogenesis of actin and of alpha- and gamma-tubulin, which are, in turn, important for cytoskeleton stability. A strain that lacks Gim4, which is prefoldin subunit 2 and a component of the Gim protein complex that promotes formation of functional alpha- and gamma-tubulin [24], was the second most sensitive strain to sodium arsenite exposure in the category of cytoskeleton assembly and maintenance. Thirteen other mutants that were sensitive to As (III), including Hsl7, Bem1, Ste50, Rvs161, Rpn4, Rvs167, Pac10, Sac1, Yke2, Tub3, Cla4, Svl3 and Nip100, correspond to cytoskeleton or structural proteins (Table 2). Cytoskeleton formation is important in establishing cell shape, providing mechanical strength, regulation of cell motility, chromosome separation in mitosis and meiosis, and intracellular transport of vesicles and protein complexes. Microtubules are one of the components of the cytoskeleton and are polymers of α- and β-tubulin dimers. Sodium arsenite directly interacts with the sulfhydryl-containing cysteine residues of tubulin, disrupting tubulin organization and microtubule assembly, and is proposed to induce aneuploidy in arsenite-treated human lymphocytes [25]. Thus, the requirement of Pdf1 and Gim4 in synthesizing tubulins, as well as other proteins that maintain cell structure, should be important in protecting cells from arsenite-induced damage to the cytoskeleton.

Acetylation and deacetylation—Histone acetylation is associated with activation of gene expression and it also seems to be affected by arsenic. We have found that eleven of the *S. cerevisiae* strains sensitive to arsenite lack proteins involved in the acetylation or deacetylation process (Table 2), and these include Sgf29, Mak31, Ada2, Sgf73, Gcn5, Ard1, Hda1, Pho23, Hfi1, Mak3 and Hda3. Ada2, Gcn5 and Sgf29 are part of Spt-Ada-Gcn5 acetyltransferase (SAGA) complex which contains more than 20 subunits [26]. The IC_{50} of Ada2, Gcn5 and Sgf29 deletion mutants are 0.375, 0.5 and 0.53, respectively. SAGA preferentially acetylates multiple lysine residues on the N-terminal tails of histone H3 and H2B [27], including acetylation of K9, K14, K18 and K23 of H3 [28]. The component protein Gcn5 (general control nonderepressible 5) has histone acetyltransferase activity [29] and Ada2 potentiates Gcn5 acetyltransferase activity [30]. SAGA regulates transcription of approximately 10% of the genome, most of which are upregulated in response to environmental stresses, including heat, oxidation, acidity, DNA damage, carbon or nitrogen starvation, and excess unfolded proteins [31].

Osmotic stress response and MAPK pathway—Six of the *S. cerevisiae* strains sensitive to As (III) were missing genes whose corresponding proteins were involved in osmoregulation. These included Ste50, Doa4, PbsS2, Hog1, Nst1 and Ssk2. In yeast, cells respond to osmotic stress through a high-osmolarity glycerol (HOG1) pathway to maintain optimal cell volume and viability [32]. In humans, the mitogen-activated protein kinase (MAPK) super-family consists of three major sets of kinases: the extracellular-receptor kinases (ERKs), the c-Jun N-terminal kinases/stress-activated protein kinases (JNK/SAPK), and the p38 MAPK. Hog1 is homologous to the p38 MAPK [32] and it activates its targets, including several transcription factors, which in turn activate genes devoted to osmoadaptation [33;34; 35]. Osmotic stress activates Hog1 through the MAPKKK Ssk2 and the MAPKK Pbs2. Notably, HOG1 is the second most sensitive mutant with an IC_{50} of 0.31 mM (Table 1). Strains lacking Pbs2 and Ssk2 are also very sensitive to As (III), with IC_{50} of 0.5 mM and 0.55 mM, respectively (Table 1). In mammalian cells, the MAPK p38 pathway is activated by As (III) [36]. Similarly, tolerance of fission yeast *Schizosaccharomyces pombe* to As (III) involves the MAPK Spc1, a homologue of mammalian p38 MAPK [37].

Vacuolar transport—Vacuoles function to compartmentalize materials that may be harmful to cells. Glutathione-conjugated arsenic can be sequestered by Ycf1 in the vacuole, which contributes to cellular tolerance of arsenic [38]. The proteins whose deletions confer sensitivity to As(III) in the category of vacuolar transport are Yps8, Stp22, Fen1, Cup5, Vps25, Vps24, Vps51, Snf7, Srn2, Pep3, Vps36, Vma6, Mvp1, Vps21, Vma4, Vts1, Snf8, Vps16 and Bro1 (Table 2).

Ubiquitination and proteosomal degradation—Removal of damaged molecules is a defense mechanism that maintains cellular and genetic integrity in response to environmental insults. Proteins are generally degraded by the ubiquitin (Ub)-mediated protein degradation pathway. Ub is conjugated to proteins by ubiquitin ligases. This tagging process leads to their recognition by the 26S proteasome, and ubiquitinated proteins are targeted to the 26S proteasome for degradation. Eight of the sensitive mutants lack genes whose corresponding proteins are involved in ubiquitination and deubiquitination, including Doa4, Ubc8, Ubp3, Rtt101, Grr1, Ubi4, Bre5 and Ubp2, and ten of the sensitive mutants lack proteins involved in proteosomal degradation, namely Rpn4, Ubc8, Bst1, Doc1, Pre9, Rpl40A, Rtt101, Grr1, Doa1 and Bro1(Table 2).

In the category of ubiquitination and proteosomal degradation, Grr1 displays a significant sensitivity to As (III) with an IC_{50} of 0.35 mM (Table 1). Similarly, Grr1 null yeast cells exhibit an elongated sausage-shape, and are sensitive to osmotic stress caused by ethylene glycol [39]. Grr1 is an F-box protein and is part of the SCF ubiquitin ligase complexes [40]. SCF consists of four proteins, Skp1, Cdc53/cullin, Rbx1/Roc1 and an F-box protein. The F-box protein functions as a substrate adaptor and mediates substrate specificity. Although it’s known that Grr1 is involved in glucose repression and that it targets the G1 cyclins Cln1 and Cln2 for degradation [39;41;42], the mechanism of As (III) induced-sensitivity of Grr1 mutants is unclear.

Arsenite-resistance modulating proteins

For a complete understanding of the toxicity induced by arsenite, it is important to study the function and regulation of uptake or secretory pathways. As(III) is transported into the cells through the aquaglyceroporin Fps1 [43]. Deletion of Fps1 decreases As (III) influx into the cell and allows glycerol accumulation when cells are treated with As (III). Fps1 deletion mutants are resistant to As (III) toxicity (Table 2). Interestingly, the activity of Fps1 is modulated by Hog1 [44]. Hog1 inactivates Fps1 by phosphorylation on T231 within the N-terminal domain of Fps1 [44].

Another of the most resistant strains lacks the yeast aging gene Uth1. It is a member of the family of yeast genes termed the “*SUN* family”. It is the first indentified gene providing a link between oxidative stress response, aging and mitochondria [45]. It has been shown to interfere with mitochondria biogenesis and it is involved in the autophagic degradation of mitochondria [46;47]. It is also required for Bax-induced cell death in yeast [48]. Since arsenic induces oxidative stress, it’s very likely that Uth1 is important in mediating arsenic-induced toxicity through oxidative stress.

Computational interactome mapping of genomic screening data

The genes whose inactivation led to arsenic sensitivity were analyzed for various cellular interactions. Using the *Cytoscape* software, protein-protein or protein-DNA interactions were analyzed. Toxicity modulating subnetworks consisting of greater than 3 connected nodes, corresponding to sensitive strains, are shown in Figure 2.

Figure 2 illustrates the engagement of various cellular processes aiding the recovery of *S. cerevisiae* from arsenite exposure; the processes embraced by each subnetwork are indicated in Table 2. All of the proteins in each network confer recovery of *S. cerevisiae* from arsenite exposure. Subnetwork (1) contains cytoskeleton/structural maintaining proteins (Pfd1), as well as vacuolar transport proteins (Snf7, Vma6, Vma4). Subnetwork (2) contains a group of proteins involved in ubiquitination (Grr1 and Ubi4). Subnetwork (2) also contains proteins involved in budding, cell polarity and filament formation during endocytosis (Rvs167, Rvs161 and Sla1) as well as a protein of unknown function (YBR284W). Subnetwork (3) contains Ste50, which encodes for a protein that is involved in mating response, invasive/filamentous growth, and osmotolerance. Subnetwork (4) contains components of ADA and SAGA histone acetyltransferase complexes (Ada2, Gcn5 and Sgf29). Histone acetylation is a modification mark of active gene transcription. Histone acetyltransferase complexes may provide resistance by participating in transcriptional activation of genes whose products aid recovery. Subnetwork (5) is dominated by proteins involved in the high osmolarity MAPK signaling pathway, Hog1 (MAPK), Pbs2 (MEK) and Ssk2 (MAPKKK).

Conclusion

Several studies have been done to screen the *S. cerevisiae* gene deletion strains to assess the role of nonessential proteins in modulating toxicity upon exposure to arsenic compounds. Haugen et al. [49] identified two metabolic networks, L-threonine and L-homoserine synthesis/degradation and the sikimate pathway, that are important for sodium arsenite tolerance. Jin et al. [50] have shown that the mutants engaged in *S. cerevisiae* toxicity to sodium arsenite functioning in processes of stress-related transcription regulation, tubulin folding, signal transduction, secretory pathway, and response to stimulus. Dilda et al., [23] identified the sensitive mutant involved in the processes to include the high osmolarity glycerol stress signaling pathway, storage carbohydrate metabolism, DNA repair, oxidative stress defense, ergosterol biosynthesis, actin function, vacuolar acidification, secretory pathway function and NADPH biosynthesis. The focus of our study was to elucidate previously unidentified mechanisms and cellular pathways important for regulating the toxicity of arsenic in human cells, and restrict our studies to those sensitive and resistant strains whose gene deletion product has a human homologue. In this study, we have identified 248 arsenite-sensitive and 5 arsenite-resistant mutants by performing a genome-wide screen of genes in yeast. Functional categorization and interactome mapping suggests that cells develop multiple pathways to defend against arsenic-induced toxicity. In addition to the previously identified genes and pathways that confer sensitivity to arsenic, we have identified pathways of acetylation and deacetylation processes, cell growth/morphogenesis, endocytosis, M phase, protein targeting, sorting and translocation, purine nucleotide/nucleoside/nucleobase anabolism, homoestasis of protons, budding, cell polarity and filatment formation. This knowledge can be utilized to determine and understand the molecular and biological mechanisms by which arsenic induces toxicity. Future studies will determine if the identified genes control the activity of arsenic uptake or efflux, by measuring the concentration of arsenic in the mutant yeast cells after arsenic exposure, and if the human homologue of the yeast protein whose absence renders the cells either more sensitive or resistant to arsenite and therefore may have a direct role in the toxicity of arsenic compounds to human cells.

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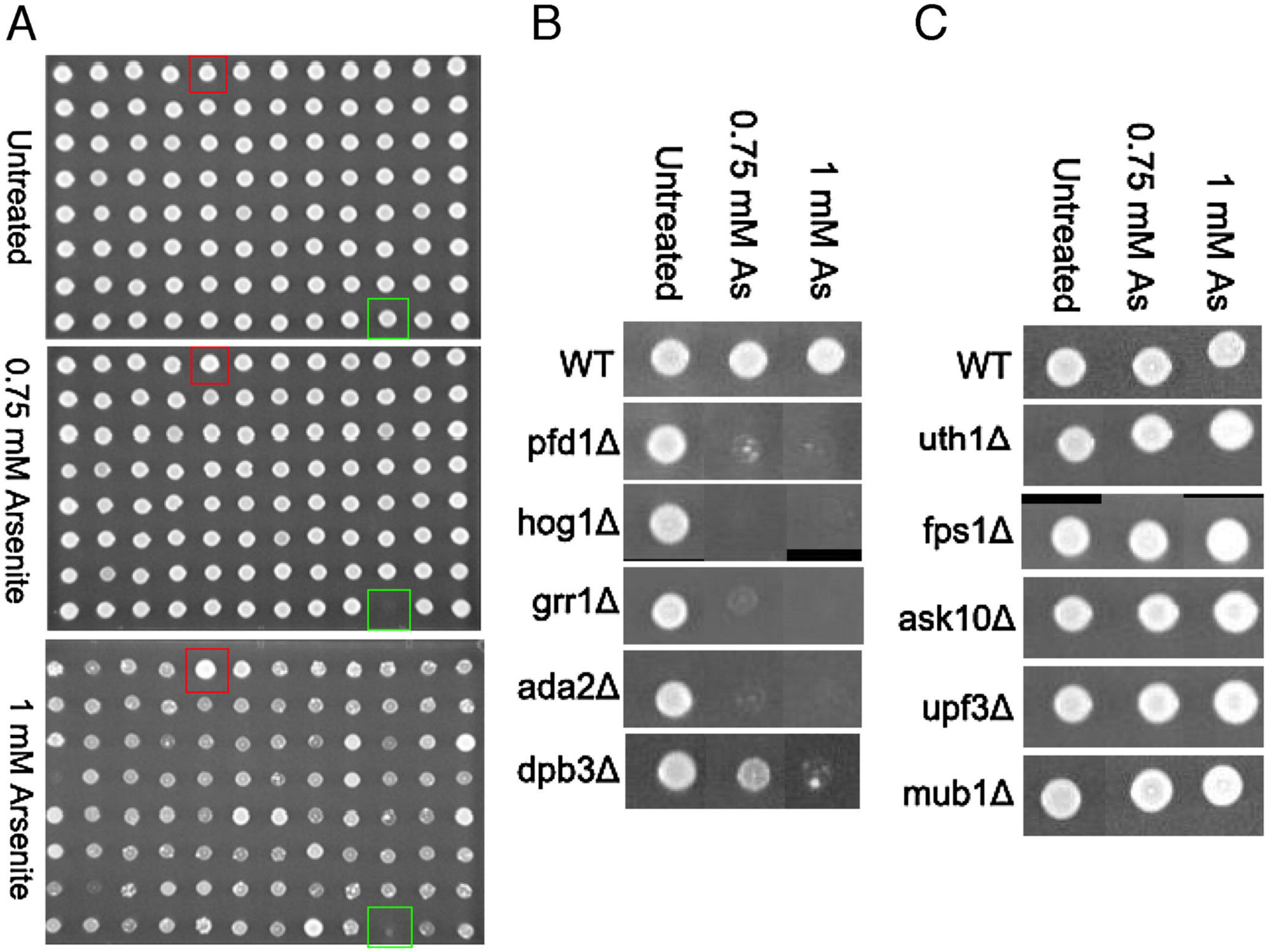

Figure 1.

High-throughput screen of arsenite. (A) 96 gene-deletion mutants were spotted onto agar plates containing 0.75 and 1.25 mM arsenite, incubated at 30 °C for 60 h, and imaged. Red squares denote the arsenite-resistant gene-deletion mutant *fps1*Δ. Green squares denote the arsenite-sensitive gene-deletion mutant *hog1*Δ. (B) Growth of wild type BY4741 (WT), *pfd1Δ, hog1Δ, grr1Δ, ada2Δ and dpb3Δ*. These mutants are the most sensitive gene-deletion mutants as determined by IC_{50}. Images were cropped and recompiled together. (C) Growth of wild type BY4741 (WT), *uth1Δ, fps1Δ, ask10Δ, upf3Δ and mub1Δ*. These mutants are the most resistant gene-deletion mutants as determined by IC_{50}. Images were cropped and recompiled together.

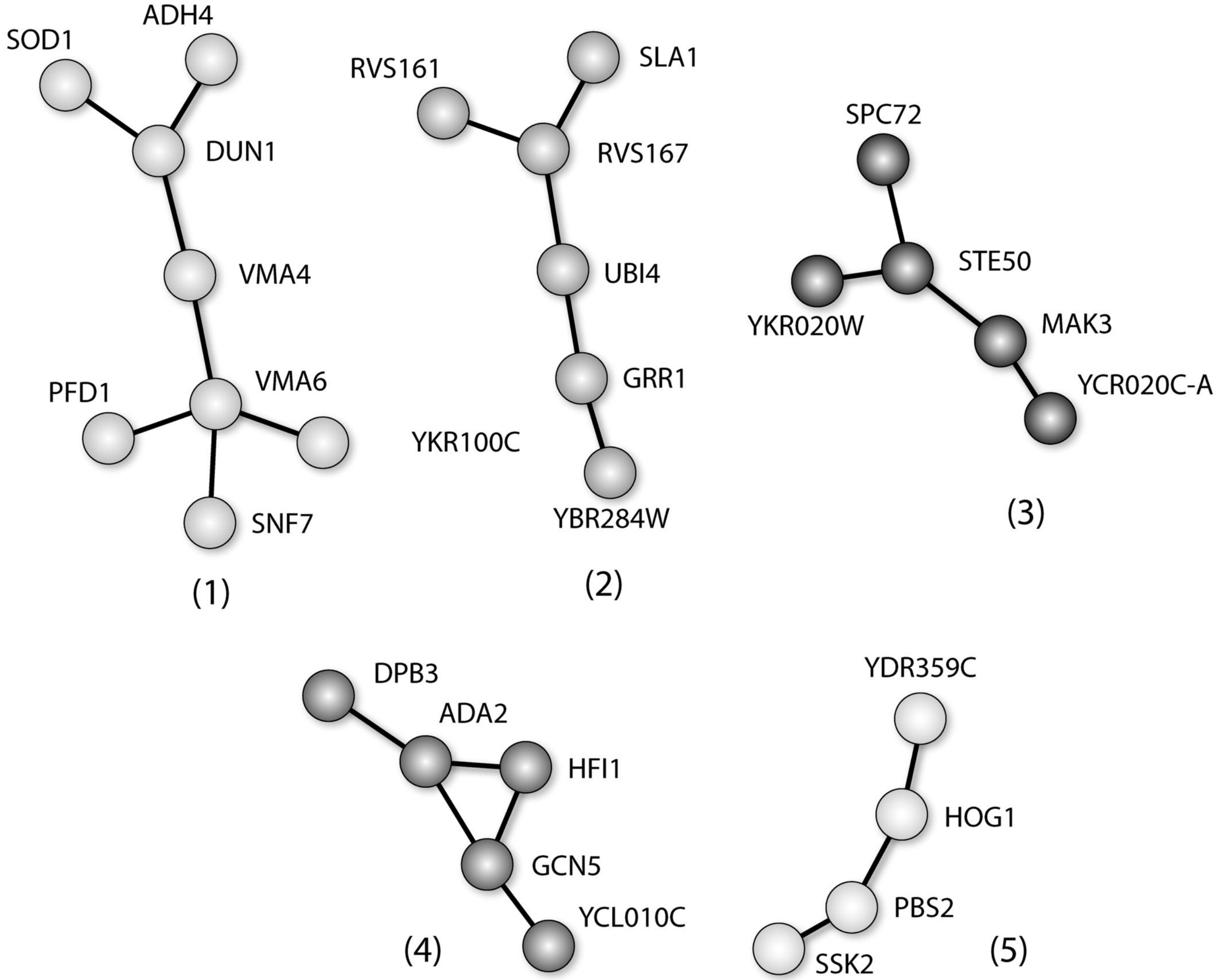

Figure 2.

Cellular interaction analysis of the mutants whose deletion confers sensitivity to arsenite exposure. *Cytoscape* software was used to analyze protein-protein interaction analysis.

Table 1

List of yeast deletion mutants that are sensitive or resistant to arsenite. All the sensitive and resistant mutants identified are presented in this table. The mutants are ordered from the most to the least sensitive. IC_{50} values are indicated in mM sodium arsenite.

	Yeast Protein name	Yeast Function	IC50	Human SwissProt number	Human Function
YJL179W	PFD1	Protein with similarity to bovine prefoldin subunit 1	0.2444	O60925	Prefoldin subunit 1
YLR113W	HOG1	MAP kinase (MAPK) central to the high-osmolarity signal transduction pathway	0.3059	Q16539	Mitogen-activated protein kinase 14
YJR090C	GRR1	F-box protein that targets G1 cyclins and Gic1p and other proteins for degradation by the SCF-Grr1p complex (Skp1p-Cdc53p-Cdc34p-Grr1p); also required for glucose repression and for glucose and cation transport	0.3464	AAH07557	F-box/LRR-repeat protein 20
YDR448W	ADA2	Component of two nucleosomal histone	0.375	O75478	Transcriptional adapter 2-alpha
YBR278W	DPB3	DNA polymerase epsilon third subunit	0.4023	Q9NR33	DNA polymerase epsilon subunit 4
YCR027C	RHB1	Putative Rheb-related GTPase involved in regulating canavanine resistance and arginine uptake; member of the Ras superfamily of G-proteins	0.4121	Q15382	GTP-binding protein Rheb [Precursor]
YPL105C	SYH1	Protein of unknown function that may interact with ribosomes, based on co-purification experiments; authentic, non-tagged protein is detected in highly purified mitochondria in high-throughput studies	0.4152	O75137	PERQ amino acid-rich with GYF domain-containing protein 2
YOL081W	IRA2	GTPase-activating protein for Ras1p and Ras2p	0.4156	P21359	Neurofibromin
YGL084C	GUP1	Plasma membrane protein involved in remodeling GPI anchors; member of the MBOAT family of putative membrane-bound O-acyltransferases; proposed to be involved in glycerol transport	0.4504	Q9NVH9	Protein-cysteine N-palmitoyltransferase HHAT
YNL229C	URE2	Nitrogen catabolite repression transcriptional regulator that acts by inhibition of GLN3 transcription in good nitrogen source; altered form of Ure2p creates [URE3] prion	0.4504	P30711	Glutathione S-transferase theta-1
YEL003W	GIM4	Prefoldin subunit 2, component of the Gim protein complex that promotes formation of functional alpha- and gamma-tubulin	0.4787	Q9UHV9	Prefoldin subunit 2
YBR298C	MAL31	High affinity maltose/H+ symporter (maltose permease), member of the hexose transporter family of the major facilitator superfamily (MFS)	0.4962	P11168	Solute carrier family 2, facilitated glucose transporter member 2
YPL042C	SSN3	Cyclin-dependent serine/threonine protein kinase of the RNA polymerase II holoenzyme complex and Kornberg's mediator (SRB) subcomplex	0.4992	P49336	Cell division protein kinase 8
YGR252W	GCN5	Component of two nucleosomal histone acetyltransferase complexes	0.4996	Q92831	Histone acetyltransferase PCAF
YJL128C	PBS2	MAP kinase kinase (MEK) activated by high osmolarity through the Sln1p-Ypd1p-Ssk1p two-component osmosensor and the Sho1p osmosensor	0.5	P36507	Dual specificity mitogen-activated protein kinase kinase 2
YNL307C	MCK1	Serine/threonine/tyrosine protein kinase, positive regulator of meiosis and spore formation	0.5	AAH27984	Glycogen synthase kinase-3 alpha
YBL051C	PIN4	Protein involved in G2/M phase progression and response to DNA damage, interacts with Rad53p; contains an RNA recognition motif, a nuclear localization signal, and several SQ/TQ cluster domains; hyperphosphorylated in response to DNA damage	0.5056	AAN05429	Cleavage stimulation factor 64 kDa subunit, tau variant
YCL001W-A		Protein of unknown function	0.5102		
YBR133C	HSL7	Negative regulatory protein of the Swe1p protein kinase	0.5163	Q9UKH1	Protein arginine N-methyltransferase 5
YCR009C	RVS161	Protein required for viability after N, C, or S starvation, for internalization step of endocytosis, and for cell fusion during mating; roles in endocytosis and in cell fusion are independent of one another	0.5181	Q9NQY0	Bridging integrator 3
YGL012W	ERG4	Sterol C-24 (28) reductase	0.5262	Q14739	Lamin-B receptor
YCL010C	SGF29	SaGa associated Factor 29kDa; Probable 29kKDa Subunit of SAGA histone acetyltransferase complex	0.527	Q96ES7	SAGA-associated factor 29 homolog
YNR031C	SSK2	Map kinase kinase kinase (MAPKKK) of the high-osmolarity signal transduction pathway	0.552	BAA13204	Mitogen-activated protein kinase kinase kinase 4
YDR028C	REG1	Regulatory subunit for protein phosphatase Glc7p, required for glucose repression	0.5533	Q9NZW4	Dentin sialophosphoprotein [Precursor]
YBL007C	SLA1	Protein involved in assembly of cortical actin cytoskeleton, has three SH3 domains	0.5535	Q9UIQ3	Proto-oncogene tyrosine-protein kinase FGR
YER014C-A	BUD25	Protein involved in bud-site selection; diploid mutants display a random budding pattern instead of the wild-type bipolar pattern	0.5587		
YCR045C		Protein with similarity to protease B (Prb1p) and	0.5638	Q8NBP7	Proprotein convertase

	Yeast Protein name	Yeast Function	IC50	Human SwissProt number	Human Function
		subtilisin family proteases			subtilisin/kexin type 9 [Precursor]
YER155C	BEM2	GTPase-activating (GAP) protein; regulates Rho1p and has a role in bud emergence and cell cycle-related cytoskeletal reorganization	0.5718	AAH38976	Rho GTPase-activating protein 15
YCR026C	NPP1	Nucleotide pyrophosphatase/phosphodiesterase family member; mediates extracellular nucleotide phosphate hydrolysis along with Npp2p and Pho5p; activity and expression enhanced during conditions of phosphate starvation	0.5725	Q9UJA9	Ectonucleotide pyrophosphatase/phosphodiesterase family member 5 [Precursor]
YER110C	KAP123	Karyopherin-beta involved in nuclear import of ribosomal proteins	0.5772	Q8TEX9	Importin-4
YCL063W	VAC17	Protein involved in vacuole inheritance; acts as a vacuole-specific receptor for myosin Myo2p	0.5813	AAH40354	Caldesmon
YBR286W	APE3	Aminopeptidase Y (yscIII, APY), major vacuolar aminopeptidase with preference for basic amino acids and proline	0.582	Q9UQQ1	N-acetylated-alpha-linked acidic dipeptidase-like protein
YDR359C	EAF1	Component of the NuA4 histone acetyltransferase complex; required for initiation of pre-meiotic DNA replication, probably due to its requirement for significant expression of IME1	0.5904	Q96L91	E1A-binding protein p400
YCL032W	STE50	Protein required for feedback control of pheromone-induced signal transduction	0.5926	O43419	Intestinal mucin [Fragment]
YBR281C	DUG2	Probable di- and tri-peptidase; forms a complex with Dug1p and Dug3p to degrade glutathione (GSH) and other peptides containing a gamma-glu-X bond in an alternative pathway to GSH degradation by gamma-glutamyl transpeptidase (Ecm38p)	0.599	Q96KN2	Beta-Ala-His dipeptidase [Precursor]
YCR087C-A	LUG1	Protein of unknown function	0.6023		
YPL165C	SET6	Protein of unknown function; deletion heterozygote is sensitive to compounds that target ergosterol biosynthesis, may be involved in compound availability	0.6043	Q9NRG4	SET and MYND domain-containing protein 2
YDR388W	RVS167	Protein that affects actin distribution and bipolar budding, has an SH3 domain	0.605	Q96HL8	SH3 domain-containing YSC84-like protein 1
YER007W	PAC2	Putative tubulin-specific chaperone, involved in formation of alpha-beta-tubulin heterodimer	0.6177	Q15813	Tubulin-specific chaperone E
YCR036W	RBK1	Ribokinase; member of a family of sugar kinases that includes Pfk2p	0.6283	Q9H477	Ribokinase
YML121W	GTR1	Cytoplasmic GTP binding protein and negative regulator of the Ran/Tc4 GTPase cycle; component of GSE complex, which is required for sorting of Gap1p; involved in phosphate transport and telomeric silencing; similar to human RagA and RagB	0.6322	AAH34726	Ras-related GTP-binding protein B
YCL037C	SRO9	Suppressor of ypt6 null and rho3 mutations	0.6364	Q9NW12	La-related protein 2
YLR079W	SIC1	P40 inhibitor of Cdc28p-Clb protein kinase complex	0.6452	Q8NHA9	Seven transmembrane helix receptor
YHR013C	ARD1	Protein N-acetyltransferase subunit; mating functions are reduced in mutants due to derepression of silent mating type loci	0.6467	P41227	N-terminal acetyltransferase complex ARD1 subunit homolog A
YJL136C	RPS21B	Ribosomal protein S21 (yeast S26; YS25; rat S21), to Rps21Ap	0.6509	Q8WVC2	RPS21 protein
YAL047C	SPC72	Component of spindle pole body that interacts with Stu2p	0.6523		
YCL033C		Putative protein-methionine-R-oxide reductase; involved in response to oxidative stress; similar to mouse Sepx1p and fly SelRp; YCL033C is not an essential gene	0.6639	Q9Y3D2	Methionine-R-sulfoxide reductase B2, mitochondrial [Precursor]
YPL059W	GRX5	Hydroperoxide and superoxide-radical responsive glutathione-dependent oxidoreductase; mitochondrial matrix protein involved in the synthesis/assembly of iron-sulfur centers; monothiol glutaredoxin subfamily member along with Grx3p and Grx4p	0.6678	AAH23528	Glutaredoxin-related protein 5
YDR335W	MSN5	Karyopherin involved in nuclear import and export; to be responsible for nuclear import of replication protein A and for export of several proteins including Swi6p, Far1p, and Pho4p; cargo dissociation involves binding to RanGTP	0.6794	Q9BZV5	Exportin-5
YOR290C	SNF2	Component of SWI-SNF global transcription activator complex, acts to assist gene-specific activators through chromatin remodeling	0.6797	Q9HBD4	SMARCA4 isoform 2 (SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4, isoform CRA_c)
YPL174C	NIP100	Mitotic spindle positioning protein, dynactin complex protein associated with the spindle	0.683	P30622	CAP-Gly domain-containing linker protein 1
YKL006W	RPL14A	Ribosomal protein L14 (mammalian L14), nearly	0.6885	P50914	60S ribosomal protein L14

	Yeast Protein name	Yeast Function	IC50	Human SwissProt number	Human Function
		identical to Rpl14Bp			
YGR078C	PAC10	Protein required in the absence of Cin8p	0.6981	CAA76761	Prefoldin subunit 3
YCL060C		Protein of unknown function	0.7028		
YBR231C	SWC5	Protein of unknown function, component of the SWR1 complex, which exchanges histone variant H2AZ (Htz1p) for chromatin-bound histone H2A	0.7067	Q9UEE9	Craniofacial development protein 1
YEL027W	CUP5	Protein of unknown function	0.7128	P27449	Vacuolar ATP synthase 16 kDa proteolipid subunit
YEL031W	SPF1	Putative Ca2+-transporting ATPases, member of the P-type ATPase superfamily	0.7154	Q9HD20	Probable cation-transporting ATPase 13A1
YPL084W	BRO1	Protein that interacts with components of the PKC1-MAP kinase pathway	0.7197	Q9BX86	Programmed cell death 6-interacting protein
YPL262W	FUM1	Fumarate hydratase; mitochondrial and cytoplasmic fumarase, converts L-malate to fumarate as part of the cycle	0.7284	P07954	Fumarate hydratase, mitochondrial [Precursor]
YOL001W	PHO80	Cyclin that interacts with Pho85p protein kinase, regulates the phosphate pathway through phosphorylation of Pho4p	0.7321	Q9H4N0	Uncharacterized protein C2orf24
YOR360C	PDE2	3',5'-Cyclic-nucleotide phosphodiesterase, high-affinity	0.7328	Q13945	3',5'-cyclic AMP phosphodiesterase [Fragment]
YGL066W	SGF73	Subunit of SAGA histone acetyltransferase complex; in formation of the preinitiation complex assembly at promoters; null mutant displays defects in premeiotic DNA synthesis	0.7364	Q9ULK2	Ataxin-7-like protein 1
YAR002aW		Protein of unknown function	0.7652		
YNL087W	TCB2	Bud-specific protein with a potential role in membrane trafficking; GFP-fusion protein migrates from the cell surface to intracellular vesicles near vacuole; contains 3 calcium and lipid binding domains; mRNA is targeted to the bud	0.7657	Q96LX0	Multiple C2 and transmembrane domain-containing protein 1
YKL213C	DOA1	WD repeat protein required for ubiquitin-mediated protein degradation, forms complex with Cdc48p, plays a role in controlling cellular ubiquitin concentration; also promotes efficient NHEJ in postdiauxic/stationary phase	0.77	Q9UF53	Phospholipase A-2-activating protein
YML124C	TUB3	Tubulin alpha-3 chain, non-essential	0.7732	AAH06468	Tubulin alpha-1A chain
YKL119C	VPH2	Vacuolar H(+)-ATPase (V-ATPase) assembly protein in the endoplasmic reticulum	0.7901	O75336	Liprin-beta-1
YDR393W	SHE9	Protein with similarity to Arabidopsis thaliana CIP1, lethality when overexpressed	0.793	P13533	Myosin-6
YOL012C	HTA3	Histone-related protein that can suppress histone H4 point mutation	0.8078	AAH20936	Histone H2A.Z
YDR069C	DOA4	Ubiquitin-specific protease (ubiquitin C-terminal hydrolase), involved in recycling ubiquitin from protein substrates targeted to the proteasome and the vacuole	0.8121	P40818	Ubiquitin carboxyl-terminal hydrolase
YBR085W	AAC3	ADP/ATP transporter protein, member of the mitochondrial carrier (MCF) family	0.8173	AAH31912	ADP/ATP translocase 3
YBL047C	EDE1	Key endocytic protein involved in a network of interactions with other endocytic proteins, binds membranes in a ubiquitin-dependent manner, may also bind ubiquitinated membrane-associated proteins	0.8291	Q9UBC2	Epidermal growth factor receptor substrate 15-like 1
YER151C	UBP3	Ubiquitin-specific protease, ubiquitin C-terminal hydrolase	0.834	Q9BWG7	Ubiquitin carboxyl-terminal hydrolase 10
YJR073C	OPI3	Phospholipid-N-methyltransferase; carries out second and third methylation steps of the phosphatidylcholine biosynthesis pathway	0.8357	Q9BW86	Phosphatidylethanolamine N-methyltransferase
YCR020C-A	MAK31	Protein required for structural stability of L-A double-stranded RNA- (dsRNA-) containing particles, has similarity to snRNA-associated proteins of the Sm family	0.8388		
YNR010W	CSE2	Component of RNA polymerase II mediator (SRB) subcomplex	0.8433	O75179	Ankyrin repeat domain-containing protein 17
YBR284W		Putative protein of unknown function	0.8464	Q96IA1	AMP deaminase 2
YAL012W	CYS3	Cystathionine gamma-lyase, generates cysteine from cystathionine	0.8467	P32929	Cystathionine gamma-lyase
YPR179C	HDA3	Subunit of a possibly tetrameric trichostatin A-sensitive class II histone deacetylase complex that contains an Hda1p homodimer and an Hda2p-Hda3p heterodimer; required for the activity of the complex; has similarity to Hda2p	0.8494	Q8N7Z2	Golgin subfamily A member 6-like protein 1
YNL201C	PSY2	Putative subunit of an evolutionarily conserved protein phosphatase complex containing the catalytic subunit Pph3p and the regulatory subunit Psy4p; required for cisplatin and oxaliplatin resistance; localizes to nucleus	0.8569	BAC23106	SMEK1
YGR061C	ADE6	5'-phosphoribosylformyl glycinamidine synthetase, has	0.8577	Q9BX02	

	Yeast Protein name	Yeast Function	IC50	Human SwissProt number	Human Function
		glutamine amidotransferase domain and aminator domain			
YNL107W	YAF9	Subunit of both the NuA4 histone H4 acetyltransferase complex and the SWR1 complex, may function to antagonize silencing near telomeres; interacts directly with Swc4p, has homology to human leukemogenic protein AF9, contains a YEATS domain	0.8635	O95619	YEATS domain-containing protein 4
YCL008C	STP22	Protein required for vacuolar targeting of temperature-sensitive plasma membrane proteins such as Ste2p and Can1p	0.872	Q9BUM5	Tumor susceptibility gene 101 protein
YLR025W	SNF7	Protein involved in glucose derepression and in protein sorting in pre-vacuolar endosome	0.8731	Q9H444	Charged multivesicular body protein 4b
YBR200W	BEM1	Protein required for cell polarization and bud formation, contains two SH3 domains	0.8796	Q9Y338	Sorbin and SH3 domain-containing protein 1
YJL080C	SCP160	Protein involved in control of mitotic chromosome transmission, contains 14 KH motifs found in RNA-binding proteins such as Mer1p and mouse hnRNP X	0.8926	AAH01179	Vigilin
YOR124C	UBP2	Ubiquitin-specific protease (ubiquitin C-terminal hydrolase), cleaves at the C-terminus of ubiquitin	0.9048	Q96RU2	Ubiquitin carboxyl-terminal hydrolase 28
YDR293C	SSD1	Protein with a role in maintenance of cellular integrity, interacts with components of the TOR pathway; ssd1 mutant of a clinical S. cerevisiae strain displays elevated virulence	0.9048	Q9Y2L1	Exosome complex exonuclease RRP44
YML014W	TRM9	tRNA methyltransferase, catalyzes esterification of modified uridine nucleotides in tRNA(Arg3) and tRNA(Glu), likely as part of a complex with Trm112p; deletion confers resistance to zymocin	0.9082	Q9P272	Putative methyltransferase KIAA1456
YDL101C	DUN1	Protein kinase required for induction of Rnr3p and DNA repair genes after DNA damage	0.9116	O96017	Serine/threonine-protein kinase Chk2
YDL146W	LDB17	Protein of unknown function	0.912	AAH16052	NCK interacting protein with SH3 domain
YDR358W	GGA1	Golgi-localized protein with homology to gamma-adaptin, interacts with and regulates Arf1p and Arf2p in a GTP-dependent manner in order to facilitate traffic through the late Golgi	0.9303	Q9NZ52	ADP-ribosylation factor-binding protein GGA3
YBR030W	RKM3	Protein with weak similarity to Sin3p	0.9322	Q9H787	SET domain-containing protein 6
YLL039C	UBI4	Ubiquitin, mature protein is cleaved from polyubiquitin (Ubi4p) or from fusions with ribosomal proteins Rps31p, Rpl40Ap, or Rpl40Bp	0.9427	AAH39193	Ubiquitin
YLR417W	VPS36	Protein involved in vacuolar sorting; mutant has a prominent novel pre-vacuolar organelle	0.9471	Q9H8Z5	Vacuolar protein-sorting-associated protein 36
YKR007W	MEH1	Component of the EGO complex, which is involved in the regulation of microautophagy, and of the GSE complex, which is required for proper sorting of amino acid permease Gap1p; loss results in a defect in vacuolar acidification	0.9476	Q9NVC8	Ubiquitin carboxyl-terminal hydrolase 36
YBL064C	PRX1	Mitochondrial peroxiredoxin (1-Cys Prx) with thioredoxin peroxidase activity, has a role in reduction of hydroperoxides; induced during respiratory growth and under conditions of oxidative stress; phosphorylated	0.9489	AAH35857	Peroxiredoxin-6
YLR447C	VMA6	Vacuolar H(+)-ATPase (V-ATPase) 36 kDa subunit (subunit D) of membrane (V0) sector, required for V-ATPase assembly	0.9493	P12953	Vacuolar proton pump subunit d 1
YOR371C	GPB1	Multistep regulator of cAMP-PKA signaling; inhibits PKA downstream of Gpa2p and Cyr1p, thereby increasing cAMP dependency; inhibits Ras activity through direct interactions with Ira1p/2p; regulated by G-alpha protein Gpa2p; homolog of Gpb2p	0.9591	P51610	Host cell factor
YKL134C	10/1/1999	Mitochondrial intermediate peptidase	0.9685	Q96G65	Mitochondrial intermediate peptidase [Precursor]
YDR300C	PRO1	Glutamate 5-kinase, carries out first step in proline biosynthesis pathway	0.9723	P54886	Delta-1-pyrroline-5-carboxylate synthetase
YCR034W	FEN1	Protein involved in the elongation of fatty acids up to 24 carbons	0.9727	Q9NYP7	Elongation of very long chain fatty acids protein 5
YLR200W	YKE2	Protein involved in microtubule biogenesis	1.001	AAH39033	Prefoldin subunit 6
YOR322C	LDB19	Protein of unknown function involved in maintenance of proper telomere length; null mutant shows a reduced affinity for the alcian blue dye suggesting a decreased net negative charge of the cell surface	1.005	Q9UJF2	Ras GTPase-activating protein nGAP
YOL039W	RPP2A	Acidic ribosomal protein P2A (L44; A2; YP2alpha; E. coli L12eIB; human P2alpha), plays a role in the elongation step	1.007	P05387	60S acidic ribosomal protein P2
YPL158C	AIM44	Protein of unknown function; GFP-fusion protein localizes to the bud neck; transcription is regulated by Swi5p; null mutant displays increased frequency of	1.009	Q8NAM5	Putative protein TPRXL

	Yeast Protein name	Yeast Function	IC50	Human SwissProt number	Human Function
		mitochondrial genome loss and reduced growth rate in minimal glycerol media			
YKL041W	VPS24	Protein involved in sorting of proteins in pre-vacuolar endosome	1.012	Q9Y3E7	Charged multivesicular body protein 3
YML057W	CMP2	Calcineurin catalytic (A) subunit, protein serine/threonine phosphatase 2B (PP2B), member of the PPP family of protein phosphatases	1.022	Q8TAW9	Serine/threonine-protein phosphatase 2B catalytic subunit alpha isoform
YLR335W	NUP2	Nuclear pore protein (nucleoporin) with XFXFG motifs; has functional overlap with other proteins of nuclear pore complex	1.026	P49792	E3 SUMO-protein ligase RanBP2
YGR101W	PCP1	Mitochondrial serine protease required for the processing of various mitochondrial proteins and maintenance of mitochondrial DNA and morphology; belongs to the rhomboid-GlpG superfamily of intramembrane peptidases	1.033	Q96CQ4	Presenilins-associated rhomboid-like protein, mitochondrial [Precursor]
YNL021W	HDA1	Component of histone deacetylase A, 75 kDa subunit	1.043	Q9NSW6	Putative uncharacterized protein DKFZp566E044
YOR265W	RBL2	Protein that rescues excess beta-tubulin lethality	1.045	O75347	Tubulin-specific chaperone A
YDL020C	RPN4	Subunit of the regulatory particle of the proteasome	1.046	AAH36038	Zinc finger protein 25
YHR082C	KSP1	Serine/threonine kinase that suppresses prp20 mutant when oveproduced	1.048	Q9P0L2	Serine/threonine-protein kinase MARK1
YJL204C	RCY1	F-box protein involved in recycling plasma membrane proteins internalized by endocytosis; localized to sites of polarized growth	1.056	O00471	Exocyst complex component 5
YHR026W	PPA1	Proteolipid of the vacuolar H(+)-ATPase (V-ATPase)	1.058	Q99437	Vacuolar ATP synthase 21 kDa proteolipid subunit
YKL212W	SAC1	Phosphatidylinositol phosphate (PtdInsP) phosphatase involved in hydrolysis of PtdIns[4]P; transmembrane protein localizes to ER and Golgi; involved in protein trafficking and processing, secretion, and cell wall maintenance	1.06	O94935	Phosphatidylinositide phosphatase SAC1
YGL240W	DOC1	Component of the anaphase-promoting complex (APC); required for Clb2p degradation and for the metaphase-anaphase transition	1.06	Q9Y5R0	Anaphase-promoting complex subunit 10
YKR031C	SPO14	Phospholipase D, catalyzes the hydrolysis of phosphatidylcholine, producing choline and phosphatidic acid; involved in Sec14p-independent secretion; required for meiosis and spore formation; differently regulated in secretion and meiosis	1.061	O14939	Phospholipase D2
YFL025C	BST1	GPI inositol deacylase of the ER that negatively regulates COPII vesicle formation, prevents production of vesicles with defective subunits, required for proper discrimination between resident ER proteins and Golgi-bound cargo molecules	1.066	Q9HA24	GPI inositol-deacylase
YDL223C	HBT1	Substrate of the Hub1p ubiquitin-like protein that localizes to the shmoo tip (mating projection); mutants are defective for mating projection formation, thereby implicating Hbt1p in polarized cell morphogenesis	1.066	Q9NZW4	Dentin sialophosphoprotein, [Precursor]
YNL298W	CLA4	Serine/threonine protein kinase required for cytokinesis	1.068	Q13153	Serine/threonine-protein kinase PAK
YPL002C	SNF8	Protein involved in glucose derepression	1.076	Q96H20	Vacuolar-sorting protein SNF8
YNL215W	IES2	Protein that associates with the INO80 chromatin remodeling complex under low-salt conditions; essential for growth under anaerobic conditions	1.076	Q16081	Nexilin
YMR004W	MVP1	Protein required for sorting proteins to the vacuole, interacts genetically with Vps1p	1.083	Q9Y5X2	Sorting nexin-8
YKR100C	SKG1	Transmembrane protein with a role in cell wall polymer composition; localizes on the inner surface of the plasma membrane at the bud and in the daughter cell	1.085	Q9NW40	Pre-mRNA-splicing factor 38B
YJL189W	RPL39	Ribosomal protein L39	1.09	P02404	60S ribosomal protein L39
YAR015W	ADE1	Phosphoribosylamidoimidazole-succinocarboxamide synthase; (SAICAR synthetase), catalyzes the seventh step in de novo purine biosynthesis pathway	1.097	P22234	Multifunctional protein ADE2
YNL097C	PHO23	Protein involved in expression of PHO5	1.1	Q9NXR8	Inhibitor of growth protein 3
YAL002W	VPS8	Protein involved in vacuolar sorting	1.102	Q8N3P4	Vacuolar protein sorting-associated protein 8 homolog
YML058C-A		Protein of unknown function	1.11		
YJL047C	RTT101	Protein of the cullin family, with similarity to Cdc53p	1.11	AAH09591	Cullin-2 (
YJR145C	RPS4A	Ribosomal protein S4 (yeast S7; YS6; rp5; rat and human S4), identical to Rps4Bp	1.11	P12750	40S ribosomal protein S4, X isoform
YPR030W	CSR2	Nuclear protein with a potential regulatory role in utilization of galactose and nonfermentable carbon sources; overproduction suppresses the lethality at high temperature of a chs5 spa2 double null mutation; potential Cdc28p substrate	1.111	Q9NZW4	Dentin sialophosphoprotein [Precursor]

	Yeast Protein name	**Yeast Function**	**IC50**	**Human SwissProt number**	**Human Function**
YNR051C	BRE5	Ubiquitin protease cofactor, forms deubiquitination complex with Ubp3p that coregulates anterograde and retrograde transport between the endoplasmic reticulum and Golgi compartments; null is sensitive to brefeldin A	1.121	Q9BX49	Proteoglycan-4 [Precursor]
YGR180C	RNR4	Ribonucleotide reductase small subunit	1.123	AAH30154	Ribonucleoside-diphosphate reductase subunit M2
YKL135C	APL2	Beta-adaptin, large subunit of the clathrin-associated protein (AP) complex	1.123	Q96J19	AP-2 complex subunit beta-1
YJL036W	SNX4	Sorting nexin, involved in retrieval of late-Golgi SNAREs from post-Golgi endosomes to the trans-Golgi network and in cytoplasm to vacuole transport; contains a PX phosphoinositide-binding domain; forms complexes with Snx41p and with Atg20p	1.124	O95219	Sorting nexin-4
YOL072W	THP1	Nuclear pore-associated protein, forms a complex with Sac3p that is involved in transcription and in mRNA export from the nucleus; contains a PAM domain implicated in protein-protein binding	1.133	Q9NWH3	PCI domain-containing protein 2
YDL155W	CLB3	G2/M-phase-specific cyclin	1.137	O95067	G2/mitotic-specific cyclin-B2
YJR075W	HOC1	Subunit of the Anp1p-Hoc1p-Mnn11p-Mnn9p mannosyltransferase complex of the Golgi involved in cell wall integrity	1.14	Q9Y6P7	snRNA-activating protein complex subunit 4
YOR201C	PET56	Ribose methyltransferase specific for G2270 in mitochondrial 21S rRNA	1.145	Q13395	Probable methyltransferase TARBP1
YKL143W	LTV1	Protein required for viability at low temperature	1.148	Q96GA3	Protein LTV1 homolog
YJL062W	LAS21	Protein required for addition of a side chain to the glycosylphospatidylinositol (GPI) core structure	1.151	Q8NCC9	GPI ethanolamine phosphate transferase 2
YJR113C	RSM7	Mitochondrial ribosomal protein of the small subunit, has similarity to E. coli S7 ribosomal protein	1.152	P46782	40S ribosomal protein S5
YBR295W	PCA1	P-type copper-transporting ATPase	1.166	P35670	Copper-transporting ATPase 2
YKL197C	PEX1	AAA-peroxin that heterodimerizes with AAA-peroxin Pex6p and participates in the recycling of peroxisomal signal receptor Pex5p from the peroxisomal membrane to the cystosol; induced by oleic acid and upregulated during anaerobiosis	1.176	AAH35575	Peroxisome biogenesis factor 1
YDR099W	BMH2	Homolog of mammalian 14-3-3 protein, has strong similarity to Bmh1p	1.178	AAH39025	
YPL032C	SVL3	Protein involved in vacuolar uptake of endocytosed vital dyes	1.186	Q8NAM5	Putative protein TPRXL
YGR270W	YTA7	Protein that localizes to chromatin and 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; potentially phosphorylated by Cdc28p	1.196	Q8N890	ATPase family AAA domain-containing protein 2
YDL081C	RPP1A	Acidic ribosomal protein P1A (A1; YP1alpha; E. coli L12eIIA; human and rat P1)	1.208	P05386	60S acidic ribosomal protein P1
YLR268W	SEC22	Synaptobrevin (v-SNARE) homolog involved in fusion of ER-to-Golgi transport vesicles; recognized by putative target t-SNARE (Sed5p)	1.209	O75396	Vesicle-trafficking protein SEC22b
YPR051W	MAK3	Protein N-acetyltransferase, acetylates N-terminus of L-A virus GAG protein	1.212	P41227	N-terminal acetyltransferase complex ARD1 subunit homolog A
YGL167C	PMR1	Ca2+-transporting P-type ATPase of Golgi membrane involved in Ca2+ import into Golgi	1.212	P98194	Calcium-transporting ATPase type 2C member 1
YNR006W	VPS27	Protein involved in vacuolar sorting; mutants develop a prominent novel pre-vacuolar organelle	1.213	Q9NR36	Hepatocyte growth factor-regulated tyrosine kinase substrate
YKL009W	MRT4	Protein involved in mRNA turnover	1.214	Q9UKD2	mRNA turnover protein 4 homolog
YPL079W	RPL21B	Ribosomal protein L21 (rat L21), nearly identical to Rpl21Ap	1.229	P46778	60S ribosomal protein L21
YJR102C	VPS25	Component of the ESCRT-II complex, which is involved in ubiquitin-dependent sorting of proteins into the endosome	1.235	Q9BRG1	Vacuolar protein-sorting-associated protein 25
YOR332W	VMA4	Vacuolar H(+)-ATPase (V-ATPase) hydrophilic subunit (subunit E), 27 kDa subunit of V1 sector	1.237	AAH04443	Vacuolar proton pump subunit E 1
YNR071C		Putative protein of unknown function	1.238	Q96C23	Aldose 1-epimerase
YPL247C		Putative protein of unknown function; green fluorescent protein (GFP)-fusion protein localizes to the cytoplasm and nucleus; similar to the petunia WD repeat protein an11; overexpression causes a cell cycle delay or arrest	1.242	O15491	WD repeat-containing protein 68
YMR052C-A		Protein of unknown function	1.242		
YNL091W	NST1	Protein with similarity to Uso1p and human NF2 neurofibromatosis type 2 gene product	1.258	Q8NAM5	Putative protein TPRXL
YKL067W	YNK1	Nucleoside diphosphate kinase, responsible for synthesis of all nucleoside triphosphates except ATP	1.268	P22392	Nucleoside diphosphate kinase B
YBR111C	YSA1	Nucleoside diphosphate-sugar hydrolase of the MutT (nudix) family	1.27	Q9UKK9	ADP-sugar pyrophosphatase

	Yeast Protein name	Yeast Function	IC50	Human SwissProt number	Human Function
YOR089C	VPS21	GTP-binding protein of the rab family required for sorting of vacuolar proteins and involved in late stage of endocytosis	1.272	AAO15677	RAB5A protein
YEL012W	UBC8	Ubiquitin-conjugating enzyme that is able to ubiquitinate histones in vitro	1.276	P37286	Ubiquitin-conjugating enzyme E2 H
YBL090W	MRP21	Mitochondrial ribosomal protein of the small subunit	1.282	P82921	28S ribosomal protein S21, mitochondrial
YGL256W	ADH4	Alcohol dehydrogenase IV	1.283	AAK44223	Hydroxyacid-oxoacid transhydrogenase, mitochondrial precursor
YEL062W	NPR2	Nitrogen permease regulator	1.295	Q9Y249	Tumor suppressor candidate 4
YJL112W	MDV1	Peripheral protein of the cytosolic face of the mitochondrial outer membrane, required for mitochondrial fission; interacts with Fis1p and with the dynamin-related GTPase Dnm1p; contains WD repeats	1.299	Q96LE0	F-box/WD repeat-containing protein 7
YOR295W	UAF30	Subunit of UAF (upstream activation factor), which is an RNA polymerase I specific transcription stimulatory factor composed of Uaf30p, Rrn5p, Rrn9p, Rrn10p, histones H3 and H4; deletion decreases cellular growth rate	1.3	Q96GM5	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily D member 1
YML081C-A	ATP18	Subunit of the mitochondrial F1F0 ATP synthase, which is a large enzyme complex required for ATP synthesis; termed subunit I or subunit j; does not correspond to known ATP synthase subunits in other organisms	1.31		
YML032C	RAD52	Protein required for recombination and repair of X-ray damage, has a late function in meiotic recombination	1.31	P43351	DNA repair protein RAD52 homolog
YMR116C	ASC1	Abundant protein with effects on translational efficiency and cell size, has two WD (WD-40) repeats	1.311	AAH32006	Guanine nucleotide-binding protein subunit beta-2-like 1
YJR104C	SOD1	Copper-zinc superoxide dismutase	1.316	AAL15444	Superoxide dismutase
YJL121C	RPE1	Ribulose-5-phosphate 3-epimerase, interconverts ribulose-5-phosphate and xylulose-5-phosphate	1.317	Q9BSB5	Ribulose-phosphate 3-epimerase
YLR148W	PEP3	Vacuolar peripheral membrane protein involved in vacuolar protein sorting and required for vacuole biogenesis	1.317	Q9P253	Vacuolar protein sorting-associated protein 18 homolog
YOR258W	HNT3	Member of the third branch of the histidine triad (HIT) superfamily of nucleotide-binding proteins; similar to Aprataxin, a Hint related protein that is mutated in individuals with ataxia with oculomotor apraxia	1.322	Q9NXM5	
YMR198W	CIK1	Coiled-coil protein of spindle pole body involved in spindle formation and the congression (nuclear migration) step of karyogamy	1.322	Q13439	Golgin subfamily A member 4
YKR020W	VPS51	Component of the GARP (Golgi-associated retrograde protein) complex, Vps51p-Vps52p-Vps53p-Vps54p, which is required for the recycling of proteins from endosomes to the late Golgi; links the (VFT/GARP) complex to the SNARE Tlg1p	1.324	Q13999	Kinectin
YJL102W	MEF2	Mitochondrial translation elongation factor, promotes GTP-dependent translocation of nascent chain from A-site to P-site of ribosome	1.33	Q8N6D8	G elongation factor, mitochondrial 2
YJL063C	MRPL8	Mitochondrial ribosomal protein of the large subunit (YmL8)	1.338	Q9C066	39S ribosomal protein L17, mitochondrial [Precursor]
YIL148W	RPL40A	Fusion protein comprised of ribosomal protein L40 (C-terminal half) and ubiquitin (N-terminal half) (rat L40), identical to Rpl40Bp	1.338	Q9BX98	60S ribosomal protein L40
YPL045W	VPS16	Vacuolar sorting protein; mutant has pleiotropic defects in vacuolar morphology and vacuolar protein targeting	1.342	Q9H269	Vacuolar protein sorting-associated protein 16 homolog
YKL160W	ELF1	Transcription elongation factor that contains a conserved zinc finger domain; implicated in the maintenance of proper chromatin structure in actively transcribed regions; deletion inhibits Brome mosaic virus (BMV) gene expression	1.343	Q96II4	Transcription elongation factor 1 homolog
YPR024W	YME1	Mitochondrial zinc-dependent protease of the AAA family of ATPases	1.357	AAH23507	ATP-dependent metalloprotease YME1L1
YGL136C	MRM2	Mitochondrial 2' O-ribose methyltransferase, required for methylation of U(2791) in 21S rRNA; MRM2 deletion confers thermosensitive respiration and loss of mitochondrial DNA; has similarity to Spb1p and Trm7p, and to E. coli FtsJ/RrmJ	1.357	Q9UI43	Putative ribosomal RNA methyltransferase 2
YKR055W	RHO4	Non-essential small GTPase of the Rho/Rac subfamily of Ras-like proteins, likely to be involved in the establishment of cell polarity	1.36	P06749	Transforming protein RhoA precursor
YGR092W	DBF2	Serine/threonine protein kinase related to Dbf20p, required for events in anaphase/telophase	1.36	Q9Y2H1	Serine/threonine-protein kinase 38-like

	Yeast Protein name	Yeast Function	IC50	Human SwissProt number	Human Function
YNL022C		Protein of unknown function	1.377	Q9NW70	Putative methyltransferase NSUN5
YMR145C	NDE1	Mitochondrial external NADH dehydrogenase, a type II NAD(P)H:quinone oxidoreductase that catalyzes the oxidation of cytosolic NADH; Nde1p and Nde2p provide cytosolic NADH to the mitochondrial respiratory chain	1.378	AAH23601	Apoptosis-inducing factor 2
YKL211C	TRP3	Bifunctional enzyme exhibiting both indole-3-glycerol-phosphate synthase and anthranilate synthase activities, forms multifunctional hetero-oligomeric anthranilate synthase:indole-3-glycerol phosphate synthase enzyme complex with Trp2p	1.379	AAH12178	GMP synthase
YML016C	PPZ1	Protein serine/threonine phosphatase required for normal osmoregulation, member of the PPP family of protein phosphatases and related to PP1 phosphatases	1.383	P36873	Serine/threonine-protein phosphatase PP1-gamma catalytic subunit
YKR099W	BAS1	Transcription factor; involved in regulation of basal and induced activity of histidine and adenine biosynthesis genes	1.388	Q9Y6P7	snRNA-activating protein complex subunit 4
YAL043C-A		Protein of unknown function	1.395		
YDL065C	PEX19	Farnesylated protein required for peroxisome biogenesis (peroxin)	1.395	Q9HAT7	Ninein
YOR027W	STI1	Stress-induced protein required for optimal growth at high and low temperature, has tetratricopeptide (TPR) repeats	1.397	P31948	Stress-induced-phosphoprotein 1
YPL254W	HFI1	Component of the ADA complex, interacts functionally with histone H2Ai	1.398	Q96FJ7	Protein ADRM1
YAL042W	ERV46	Protein localized to COPII-coated vesicles, forms a complex with Erv41p; involved in the membrane fusion stage of transport	1.403	Q9Y282	Endoplasmic reticulum-Golgi intermediate compartment protein 3
YOR359W	VTS1	Post-transcriptional gene regulator, RNA-binding protein containing a SAM domain; shows genetic interactions with Vti1p, which is a v-SNARE involved in cis-Golgi membrane traffic	1.406	Q9UPU9	Sterile alpha motif domain-containing protein 4A
YLR119W	SRN2	Suppressor of rna1-1 mutant	1.407	Q96KQ3	Apoptosis-stimulating of p53 protein 2
YML026C	RPS18B	Ribosomal protein S18 (E. coli S13; rat S18), identical to Rps18Ap	1.413	P25232	40S ribosomal protein S18
YFL001W	DEG1	Pseudouridine synthase that catalyzes the formation of pseudouridine-38 and -39 in cytoplasmic and mitochondrial tRNAs	1.415	Q96NB4	tRNA pseudouridine synthase 3
YOR123C	LEO1	Protein of unknown function, extremely hydrophilic	1.42	Q8WVC0	RNA polymerase-associated protein LEO1
YKL197C	PEX1	Peroxisomal biogenesis protein (peroxin); member of the AAA family of ATPases	1.424	AAH35575	Peroxisome biogenesis factor 1
YML033W		Protein of unknown function	1.424		
YNL299W	TRF5	Protein functionally similar to DNA topoisomerase I	1.424	Q9Y6C1	DNA polymerase sigma
YGL227W	VID30	Protein involved in proteasome-dependent catabolite degradation of fructose-1,6-bisphosphatase (FBPase); binds FBPase; shifts the balance of nitrogen metabolism toward glutamate production; localizes to the nucleus and the cytoplasm	1.44	Q9P264	Ran-binding protein 10
YLR068W	FYV7	Essential protein required for maturation of 18S rRNA; required for survival upon exposure to K1 killer toxin	1.453	Q05682	Caldesmon
YMR039C	SUB1	Transcriptional coactivator; may be involved in the release of TFIIB from the transcription complex during RNA polymerase II transcription initiation	1.464	Q96L29	Activated RNA polymerase II transcriptional coactivator p15
YMR234W	RNH1	Ribonuclease H, endonuclease that degrades RNA in RNA-DNA hybrids	1.47	O60930	Ribonuclease H1
YOL051W	GAL11	Component of RNA polymerase II holoenzyme and Kornberg's mediator complex with positive and negative effects on transcription of individual genes	1.479	Q8NAM5	Putative protein TPRXL
YDR017C	KCS1	Potential transcription factor of the basic leucine zipper (bZIP) type, suppressor of temperature-sensitive growth and hyperrecombination in pkc1-4	1.482	Q96PC2	Inositol hexaphosphate kinase 3
YNR052C	POP2	Component of the CCR4 complex required for glucose derepression	1.482	AAH17366	CCR4-NOT transcription complex subunit 8
YMR060C	TOM37	Component of mitochondrial outer membrane receptor complex, needed only at high temperature, has tetratricopeptide (TPR) repeats	1.494	Q13505	Metaxin-1
YDR001C	NTH1	Neutral trehalase	1.494	O43280	Trehalase [Precursor]
YNL329C	PEX6	Peroxisomal biogenesis protein (peroxin) of the AAA family of ATPases	1.497	Q8WYQ2	Peroxisome assembly factor 2
YJL172W	CPS1	Gly-X carboxypeptidase yscS, involved in nitrogen metabolism	1.507	Q96DM4	Probable carboxypeptidase PM20D1 [Precursor]
YHR004C	NEM1	Protein required for nuclear morphology	1.51	Q96GQ9	Serine/threonine-protein phosphatase dullard

	Yeast Protein name	Yeast Function	IC50	Human SwissProt number	Human Function
YJL029C	VPS53	Component of the GARP (Golgi-associated retrograde protein) complex, Vps51p-Vps52p-Vps53p-Vps54p, which is required for the recycling of proteins from endosomes to the late Golgi; required for vacuolar protein sorting	1.554	Q9BY02	Vacuolar protein sorting-associated protein 53 homolog
YMR219W	ESC1	Protein of unknown function	1.586	Q9NZW4	Dentin sialophosphoprotein [Precursor]
YDR162C	NBP2	Nap1p-binding protein, has an SH3 domain	1.612	Q9P234	Putative E3 ubiquitin-protein ligase SH3RF1
YGR135W	PRE9	Proteasome subunit alpha3_sc	1.619	Q8TBD1	Proteasome subunit alpha type-4
YNR032W	PPG1	Protein serine/threonine phosphatase involved in glycogen accumulation, member of the PPP family of protein phosphatases and related to PP2A phosphatases	1.718	P33172	Serine/threonine-protein phosphatase 4 catalytic subunit
YHR066W	SSF1	Protein with a potential role in mating	1.731		
YGR085C	RPL11B	Ribosomal protein L11 (yeast L16; YL22; rp39B; E. coli L5; rat L11), nearly identical to Rpl11Ap	1.736	Q9Y674	60S ribosomal protein L11
YNL248C	RPA49	RNA polymerase I third largest subunit	1.753	Q96L20	DNA-directed RNA polymerase I subunit RPA49
YNL302C	RPS19B	Ribosomal protein S19 (rp55; YS16B; rat S19), nearly identical to Rps19Ap	1.757	Q8WVX7	Ribosomal protein S19 [Fragment]
YGL228W	SHE10	Protein that causes lethality when overexpressed	1.808	O60437	Periplakin
YDL096C	OPI6	Protein of unknown function	1.921		
YLR061W	RPL22A	Ribosomal protein L22, similar to Rpl22Bp	1.932	P35268	60S ribosomal protein L22
YDR227W	SIR4	Coiled-coil protein involved in maintenance of silencing of HMR, HML, and telomeres	1.936	BAA74868	Neurofilament heavy polypeptide
YHR178W	STB5	Protein with similarity to transcription factors	1.996	Q8NAM5	Putative protein TPRXL
YKL191W	DPH2	Protein required, along with Dph1p, Kti11p, Jjj3p, and Dph5p, for synthesis of diphthamide, which is a modified histidine residue of translation elongation factor 2 (Eft1p or Eft2p); may act in a complex with Dph1p and Kti11p	2	Q9BQC3	Diphthamide biosynthesis protein 2
YLR388W	RPS29A	Ribosomal protein S29 (yeast S36; YS29; rat S29), similar to Rps29Bp	2.098	AAH35313	40S ribosomal protein S29
YGL203C	KEX1	Carboxypeptidase specific for terminal arg or lys, involved in processing precursors of alpha-factor and K1 and K2 killer toxins	2.115	Q9BR08	Lysosomal protective protein [Precursor]
YCR031C	RPS14A	Ribosomal protein S14A (rp59, E. coli S11, rat and human S14) involved in crytopleurine resistance, nearly identical to Rps14Bp	2.199	P06366	40S ribosomal protein S14
YKL190W	CNB1	Calcineurin regulatory (B) subunit	2.274	AAH27913	Calcineurin subunit B type 1
YNL246W	VPS75	NAP family histone chaperone; binds to histones and Rtt109p, stimulating histone acetyltransferase activity; possesses nucleosome assembly activity in vitro; proposed role in vacuolar protein sorting and in double-strand break repair	2.5	Q9UJ03	
YLR024C	UBR2	Cytoplasmic ubiquitin-protein ligase (E3); required for ubiquitylation of Rpn4p; mediates formation of a Mub1p-Ubr2p-Rad6p complex	2.5	AAL32101	E3 ubiquitin-protein ligase UBR2
YMR304W	UBP15	Putative ubiquitin-specific protease, ubiquitin C-terminal hydrolase	2.5	Q93009	Ubiquitin carboxyl-terminal hydrolase 7
YAL023C	PMT2	Mannosyltransferase; (dolichyl phosphate-D-mannose	2.932	Q9P1W0	Protein O-mannosyl-transferase 2
YML106W	URA5	Orotate phosphoribosyltransferase 1; fifth step in pyrimidine biosynthesis pathway	3.233	BAB93468	Uridine 5'-monophosphate synthase
YOL008W	COQ10	Coenzyme Q (ubiquinone) binding protein, functions in the delivery of Q_6 to its proper location for electron transport during respiration; START domain protein with homologs in bacteria and eukaryotes	3.487	Q9BUP4	Protein COQ10 A, mitochondrial [Precursor]
YOR039W	CKB2	Casein kinase II Protein kinase CK2), regulatory (beta-prime) subunit	3.597	AAH35349	
YOR084W	LPX1	Oleic acid-inducible, peroxisomal matrix localized lipase; transcriptionally activated by Yrm1p along with genes involved in multidrug resistance; peroxisomal import is dependent on the PTS1 receptor, Pex5p and on self-interaction	3.599	Q9NVT5	Protein phosphatase methylesterase 1
YMR214W	SCJ1	Homolog of E. coli DnaJ, functions in the endoplasmic reticulum by interaction with Kar2p	3.943	O60884	DnaJ homolog subfamily A member 2
YMR100W	MUB1	Zinc finger protein, involved in the regulation of bud site selection	4.642	CAC16691	Zinc finger MYND domain-containing protein 19
YKR042W	UTH1	Mitochondrial outer membrane and cell wall localized SUN family member required for mitochondrial autophagy; involved in the oxidative stress response, life span during starvation, mitochondrial biogenesis, and cell death	above 5	BAB79693	Receptor activator of nuclear factor kappa B ligand 3
YLL043W	FPS1	Glycerol channel protein, member of the major intrinsic	above 5	O43315	Aquaporin-9

	Yeast Protein name	Yeast Function	IC50	Human SwissProt number	Human Function
		protein (MIP) family of transmembrane channel proteins			
YGR072W	UPF3	Protein involved with Nam7p and Nmd2p in decay of mRNA containing nonsense codons	above 5	Q9H1J0	Regulator of nonsense transcripts 3B
YGR097W	ASK10	Potential transcription factor involved in Skn7p-mediated two-component regulatory system	above 5	O75404	Pre-mRNA-processing factor 40 homolog A

Table 2

Categories of yeast deletion mutants sensitive to arsenite. The deletion mutants that showed arsenic-sensitive phenotype were categorized based on the biological functions using FunSpec. The category was ordered by *p* value. Some of these mutants are present in more than one category as they have several functions.

Functional Category	**p-value**	**In category from cluster**	**Arsenite Toxitciy Modulating**	**Total in Category**
vacuolar/lysosomal transport[20.09.13]	3.31E-08	VPS8 STP22 FEN1 CUP5 VPS25 VPS24 VPS51 SNF7 SRN2 PEP3 VPS36 VMA6 MVP1 VPS21 VMA4 VTS1 SNF8 VPS16 BRO1	19	153
cytoskeleton/structural proteins[42.04]	4.14E-07	HSL7 BEM1 STE50 RES161 RPN4 RVS167 GIM4 PAC10 PFD1 SAC1 YKE2 TUB3 CLA4 SVL3 NIP100	15	113
modification by acetylation, deacetylation [14.07.04]	2.47E-06	SGF29 MAK31 ADA2 SGF73 GCN5 ARD1 HDA1 PHO23 HFI1 MAK3 HDA3	11	69
cell growth / morphogenesis [40.01]	1.66E-05	SLA1 HSL7 STE50 RVS161 FEN1 RPN4 HBT1 REG1 BMH2 SSD1 RVS167 HOC1 GRR1 CLA4 STI1 SVL3 NIP100	17	189
regulation of C-compound and carbohydrate metabolism [01.05.25]	4.11E-05	REG1 PBS2 GRR1 VPS25 SNF7 HOG1 VPS36 PSY2 POP2 GAL11 SNF2 SNF8 SSN3	13	126
protein binding [16.01]	6.77E-05	SLA1 PIN4 BEM1 STP22 RVS161 BMH2 MSN5 RVS167 GIM4 UBC8 PAC2 PAC10 RTT101 PBS2 PFD1 GRR1 VPS51 UBI4 SIC1 PFP3 YKE2 THP1 STI1 RBL2 NIP100	25	391
endocytosis [20.09.18.09.01]	0.0001976	SLA1 EDE1 RVS161 DOA4 RVS167 CUP5 VPS21 SVL3	8	59
osmosensing and response [34.11.03.13]	0.0003469	STE50 DOA4 PBS2 HOG1 NST1 SSK2	6	35
M phase [10.03.01.01.11]	0.0004621	SPC72 DOC1 TUB3 CIK1 MCK1 CSE2 NIP100	7	51
trapnsport ATPases [20.03.22]	0.0005872	PCA1 CUP5 SPF1 PMR1 PPA1 VMA6 VMA4	7	53
protein targeting, sorting and translocation [14.04]	0.000737	VPS8 STP22 PEX19 MSN5 CUP5 KAP123 VPS25 VPS24 VPS51 SNF7 SRN2 PEP3 VPS36 MVP1 VPS21 VTS1 SNF8 VPS16	18	281
purine nucleotide/nucleoside/nucleobase anabolism [01.03.01.03]	0.00107	ADE1 YSA1 ADE6 YNK1 BAS1	5	29
vacuole or lysosome [42.25]	0.001227	VAC17 KCS1 DOA4 CUP5 PEP3 VPS16	6	44
modification by ubiquitination deubiquitination [14.07.05]	0.001451	DOA4 UBC8 UBP3 RTT101 GRR1 UBI4 BRE5 UBP2	8	79
homeostasis of protons [34.01.01.3]	0.001743	CUP5 PPA1 VPH2 MEH1 VMA6 VMA4	6	47
proteasomal degradation (ubiquitin/proteasomal pathway) [14.13.01.01]	0.0028	RPN4 UBC8 BST1 DOC1 PRE9 RPL40A RTT101 GRR1 DOA1 BRO1	10	128
vacuolar protein degradation [14.13.04.02]	0.002932	APE3 VID30 MEH1	3	11
phosphate metabolism [01.04]	0.00345	YSA1 NPP1 RBK1 DUN1 KCS1 REG1 PRO1 DBF2 YTA4 KSP1 PBS2 YNK1 PEX1 SAC1 HOG1 PPZ1 CLA4 MCK1 PEX6 SSK2 SSN3	21	401
stress response [32.01]	0.005175	NTH1 KCS1 SSD1 PBS2 GRR1 UBI4 TRM9 PPZ1 MCK1 SSK2 BRO1	11	162
osmotic and salt stress response [32.01.03]	0.005561	STE50 REV161 RVS167 HOG1 NST1 GRX5	6	59
budding, cell polarity and filament [43.01.03.05]	0.005666	SLA1 HSL7 BEM1 STE50 RVS161 FEN1 RPN4 BMH2 SSD1 RVS167 BEM2 HOC1 GRR1 CLA4 THR1 SVL3 NIP100	17	312
cytoplasmic and nuclear protein degradation [14.13.01]	0.006041	DOA4 UBP3 YTA7 CPS1 UBI4 UBP2	6	60
MAPKKK cascade [30.01.05.01.03]	0.006082	STE50 PBS2 HOG1 SSK2	4	27