

**Supplementary Table 1A. Genes induced in *S. pombe* copper starvation (100  $\mu$ M BCS)**

Gene Name	Max Cu-	Max Cu+	Max Fe-	Annotation
<b>Metal ion transport</b>				
<i>ctr4</i> <sup>a</sup>	24.4*	1.0	-1.2	copper transporter
<i>ctr5</i> <sup>a</sup>	6.5	-1.2	4.3	copper transporter
<i>ctr6</i> <sup>a</sup>	1.9	-1.1	1.5	copper transporter
<i>str1</i> <sup>a</sup>	1.6	1.8	1.6	siderochrome-iron transporter
<i>frp1</i> <sup>a</sup>	1.8	18.1	16.9	Ferric reductase
<b>Other transport</b>				
SPBC887.17 <sup>a</sup>	1.5	-1.4	1.0	uracil permease
<b>Peroxisomal proteins</b>				
<i>pex7</i> <sup>a</sup>	2.3	-1.1	1.6	peroxisomal targeting signal receptor
SPAC3G6.05 <sup>a</sup>	2.3	1.3	2.4	Mvp17/PMP22 family, localisation peroxisomal membrane
<b>Others</b>				
SPAC458.03 <sup>a</sup>	1.5	-1.1	-1.1	leucine-rich repeat protein involved in telomere maintenance
SPAPB18E9.02	1.6	1.2	-1.1	serine/threonine protein kinase
SPBPB2B2.05 <sup>a</sup>	2.2	1.1	1.5	GMP synthase

\* Value obtained by quantitative real-time PCR

<sup>a</sup> Contains putative Cufp1p binding site in the promotor region

**Supplementary Table 1B. Genes repressed in *S. pombe* copper starvation (100  $\mu$ M BCS)**

Gene Name	Max Cu-	Max Cu+	Max Fe-	Annotation
<b>Flavoproteins</b>				
<i>obr1</i>	-1.7	1.6	1.2	flavodoxin
SPAC869.02c	-1.9	1.3	-1.4	flavoprotein
<b>Oxidoreductases and dehydrogenase</b>				
SPAC26H5.09c	-1.3	1.1	-1.1	oxidoreductase
SPAC750.01	-1.6	1.9	-1.2	pseudogene, oxidoreductase
SPBC23G7.10c	-1.6	2.7	1.3	NADH-dependent flavin oxidoreductase
<b>Antioxidants</b>				
<i>gst2</i>	-1.5	3.0	-1.6	glutathione S-transferase
<i>sod1</i>	-2.2	1.7	-1.6	Cu, Zn-superoxide dismutase

**Supplementary Table 2A. Genes induced in *S. pombe* iron starvation (300  $\mu$ M Ferrozine)**

Gene Name	Max Cu-	Max Cu+	Max Fe-	Annotation
<b>Metal ion transport</b>				
<i>ctr5</i>	6.5	-1.2	4.3	copper transporter
<i>frp1</i> <sup>a</sup>	1.8	18.1	16.9	ferric-chelate reductase activity
<i>fip1</i> <sup>a</sup>	1.8	2.9	2.4	iron permease
<i>fio1</i> <sup>a</sup>	-1.1	NA	2.6	iron transport multicopper oxidase
<i>str3</i> <sup>a</sup>	1.2	4.1	6.8	siderochrome-iron transporter Str3
<i>str1</i> <sup>a</sup>	1.6	1.8	1.6	siderochrome-iron transporter Str1
SPBC947.05c <sup>a</sup>	1.1	-1.1	4.3	ferric-chelate reductase activity
SPAC8C9.12c	-1.6	1.8	2	mitochondrial carrier, putatively involved in iron transport
<b>Other transport</b>				
<i>vht1</i>	1.9	-2.1	1.9	vitamin H transporter
<i>vps53</i> <sup>a</sup>	-1.0	2.0	2.0	involved in intracellular protein transport
<b>Iron-sulfur cluster assembly</b>				
<i>isu1</i> <sup>a</sup>	1.2	1.4	1.6	iron-sulfur cluster assembly scaffold protein
<b>Peptide biosynthesis</b>				
<i>sib1</i> <sup>a</sup>	1.4	2.1	2.2	ferrichrome synthetase
<i>sib2</i> <sup>a</sup>	1.3	3.2	3.2	ornithine N5 monooxygenase, involved in iron homeostasis
<b>Others</b>				
SPAC1F8.02c <sup>a</sup>	-1.3	NA	15.5	GPI-anchored glycoprotein
<i>ppr1</i> <sup>a</sup>	1.5	-2.1	2.6	L-azetidine-2-carboxylic acid acetyltransferase
SPAC22F8.05	-1.3	2.6	1.6	alpha, alpha-trehalose-phosphate synthase
<i>tps1</i>	-1.2	2.4	1.9	alpha, alpha-trehalose-phosphate synthase [UDP-forming]
<i>rds1</i> <sup>a</sup>	-1.8	3.1	1.9	involved in response to stress
<i>ish1</i> <sup>a</sup>	-2	2.2	1.8	LEA domain protein
<i>srx1</i> <sup>a</sup>	-5.3	1.4	1.6	Sulphiredoxin
SPAC3G6.05	2.3	1.3	2.4	Mvp17/PMP22 family
SPAC56E4.03 <sup>a</sup>	1.2	1.6	1.7	aromatic aminotransferase
SPBC1271.07c	-1.4	2.0	1.8	N-acetyltransferase
<i>sid4</i> <sup>a</sup>	NA	NA	1.6	SIN component
SPBC27B12.03c <sup>a</sup>	1.4	1.7	2.1	lathosterol oxidase, uses iron as cofactor
<i>cfh4</i>	-1.2	1.1	1.5	Chs Four Homologue, cell wall chitin biosynthesis
SPCC70.08c	1.7	2.8	3.1	SAM dependent methyltransferase
<b>Unknown</b>				
SPAC23H3.15c <sup>a</sup>	-3.6	6.6	1.7	
SPAC29A4.17c	-1.2	NA	1.6	
SPBC1271.08c <sup>a</sup>	-1.1	1.8	2.4	
SPBC21C3.19	-2.7	2.7	2.7	
SPAC15E1.02c <sup>a</sup>	-1.6	1.2	1.6	

<sup>a</sup> Contains putative Fep1p binding site in the promotor region

**Supplementary Table 2B. Genes repressed in *S. pombe* iron starvation (300  $\mu$ M Ferrozine)**

<b>Gene Name</b>	<b>Max Cu-</b>	<b>Max Cu+</b>	<b>Max Fe-</b>	<b>Annotation</b>
<b>Metal metabolism</b>				
<i>fep1</i>	1.6	NA	-1.9	iron-sensing transcriptional regulator
<i>hem3</i>	2.0	NA	-2.0	hydroxymethylbilane synthase
<b>Localized to the mitochondrion</b>				
<i>cyc1</i>	1.6	1.1	-2.9	cytochrome c
<i>sdh3</i>	1.6	-1.3	-2.2	succinate dehydrogenase
<i>sdh2</i>	1.9	-1.3	-2.9	succinate dehydrogenase
SPAC20G8.04c	1.6	1.6	-1.8	electron transfer flavoprotein-ubiquinone oxidoreductase
SPAP14E8.05c	1.2	1.1	-2.2	conserved eukaryotic protein
<i>tim18</i>	1.7	NA	-2.9	membrane anchor subunit
<b>Transporters</b>				
<i>bsu1</i>	-1.1	NA	-3.0	MFS efflux transporter
SPAC869.05c	-1.3	4.1	-2.0	sulfate transporter
SPBC13A2.04c	-2.1	-7.1	-2.3	PTR family peptide transporter
<b>Iron/sulfur cluster proteins</b>				
<i>leu2</i>	1.4	-1.3	-1.6	3-isopropylmalate dehydratase
SPAC24C9.06c	1.8	1.7	-1.6	aconitate hydratase
<b>Thiamine biosynthesis</b>				
SPBP8B7.18c	1.3	-1.3	-1.9	TENA/THI domain
<i>nmt1</i>	-1.2	-1.5	-2.3	repressed by thiamine
<b>Others</b>				
<i>pho4</i>	-1.2	-1.2	-1.8	acid phosphatase activity
<i>rpl4302</i>	1.2	NA	-1.6	60S ribosomal protein L37a
SPCC162.03	1.1	-1.1	-1.5	short chain dehydrogenase
<i>gln1</i>	1.4	-1.9	-2.1	glutamate-ammonia ligase, glutamine biosynthesis
<b>Unknown</b>				
SPAC17G8.08c	1.5	-1.3	-1.9	
SPBC1289.14	NA	NA	-2.5	
SPBC29A3.21	1.5	NA	-2.4	
SPBC530.07c	1.2	-1.2	-2.0	
SPAC694.04c	1.2	-1.3	-1.6	

**Supplementary Table 3A. Genes induced in *S. pombe* copper excess (2.0  $\mu$ M CuSO<sub>4</sub>)**

Gene Name	Max Cu-	Max Cu+	Max Fe-	Annotation
<b>Antioxidants</b>				
SPAC688.04c <sup>a</sup>	-1.3	1.9	1.4	glutathione S-transferase
SPCC965.07c <sup>a</sup>	-1.5	3.0	-1.6	glutathione S-transferase
<i>pmp20<sup>f</sup></i>	1.2	1.7	1.2	peroxiredoxin, AhpC/TSA family
<i>sod1<sup>a</sup></i>	-2.2	1.7	-1.6	Cu, Zn superoxide dismutase
<i>trx2<sup>a</sup></i>	1.3	1.9	1.2	thioredoxin I
<i>zym1<sup>a</sup></i>	-1.9	1.8	1.4	zinc metallothionein
<b>Carbohydrate metabolism</b>				
SPBC32F12.10	1.4	1.8	1.3	phosphoglucomutase involved in glucose 1-phosphate and 6-phosphate utilization
SPCC663.09c	1.1	1.7	1.1	short chain dehydrogenase
<i>tps1<sup>a</sup></i>	-1.2	2.4	1.9	alpha, alpha-trehalose-phosphate synthase
<i>zwf1<sup>a, b</sup></i>	1.3	2.4	1.3	glucose-6-phosphate 1-dehydrogenase involved in pentose-phosphate pathway
<b>Lipid biosynthesis</b>				
SPAC26F1.04c <sup>a</sup>	-1.4	2.4	1.3	zinc binding dehydrogenase
SPBC27B12.03c	1.4	1.7	2.1	lathosterol oxidase, sterol desaturase
<b>Iron uptake</b>				
<i>fip1</i>	1.8	2.9	2.4	iron permease
<i>irp1</i>	1.8	18.1	16.9	ferric-chelate reductase activity, involved in iron ion transport
<i>str3</i>	1.2	4.1	6.8	membrane transporter involved in iron-siderochrome transport
<b>Peptide biosynthesis</b>				
<i>sib1</i>	1.4	2.1	2.2	ferrichrome synthetase
<i>sib2<sup>a</sup></i>	1.3	3.2	3.2	ornithine N5 monooxygenase, involved in iron homeostasis
<b>Protein folding / chaperone</b>				
SPBC1711.08 <sup>b</sup>	1.2	1.9	1.4	chaperone activator, target Hsp90p
SPBC4F6.16c <sup>a, b</sup>	-1.2	1.8	1.3	disulfide oxidoreductase, FAD dependent, involved in protein disulfide bond formation
<i>hsp16<sup>a, b</sup></i>	-1.3	23.3	1.5	heat shock protein 16
<i>hsp9<sup>a, b</sup></i>	-1.7	3.3	1.5	heat shock protein 9
<i>isp6<sup>a, b</sup></i>	1.3	2.1	1.4	serine protease, involved in sexual differentiation
<i>psi<sup>a, b</sup></i>	1.3	3.8	1.6	Psi protein, heat shock protein
<i>Hsp70<sup>b</sup></i>	1.4	1.9	1.4	heat shock protein 70 family
<i>sti1<sup>a, b</sup></i>	1.3	2.5	1.3	chaperone activator
<i>swo1: hsp90<sup>b</sup></i>	1.5	2.0	1.4	heat shock protein, hsp90 family
<i>ubi4</i>	1.2	2.6	-1.1	ubiquitin, involved in meiosis
<i>ubx3<sup>a, b</sup></i>	1.1	1.9	1.2	UBX domain protein
<i>wos2</i>	1.4	2.5	1.4	chaperone activator, interacts with Hsp90p
<b>Signaling and transcriptional regulation</b>				
<i>ish1<sup>a</sup></i>	-2	2.2	1.8	LEA domain protein, regulated by Atf1p, MAPK pathway
<i>srk1<sup>a</sup></i>	-1.9	2.3	1.4	MAPK-activated protein kinase, Sty1 SAPK cascade
<b>Stress response</b>				
<i>cdc48<sup>b</sup></i>	1.4	1.8	1.2	AAA family ATPase
<i>cuf5<sup>a</sup></i>	NA	NA	NA	MFS multidrug efflux transporter
<i>rds1<sup>a</sup></i>	-1.8	3.1	1.9	adenine-repressible; regulated by glucose, ammonium, phosphate, CO <sub>2</sub> and temp.
<i>slt1<sup>a</sup></i>	-1.2	5.9	1.6	involved in response to drug and caffeine
<b>Other</b>				
<i>cgs1<sup>a</sup></i>	-1.4	1.7	1.3	cAMP-dependent protein kinase, negative regulator of meiosis
SPBC12C2.03c	-1.3	1.7	1.1	FAD binding oxidoreductase
SPAC19G12.09	1.8	2.8	1.4	oxidoreductase, aldo/keto reductase
SPBC215.11c <sup>a</sup>	1.6	2.0	1.2	aldo/keto reductase
SPCC285.01c <sup>b</sup>	1.3	2.3	1.2	quinone oxidoreductase
SPBC23G7.10c <sup>a</sup>	-1.6	2.7	1.3	NADH-dependent flavin oxidoreductase
SPBC725.10 <sup>a</sup>	-1.4	3.0	1.3	similar to peripheral-type benzodiazepine receptor
SPAC977.14c	-1.5	1.9	-1.2	aldo/keto reductase
<i>Plp<sup>a</sup></i>	1.5	2.5	1.3	pyridoxal reductase, aldo/keto reductase family 8
<i>vip1<sup>a</sup></i>	-1.2	2.2	1.3	protein with RNA recognition motif
<i>wis2</i>	1.4	2.0	1.4	cyclophilin, involved in mitosis regulation
SPBC359.05 <sup>b</sup>	1.4	2.0	1.7	ABC transporter, MDR subfamily, unknown specificity

**Sulphur amino acid biosynthesis**

SPAC869.05c	-1.3	4.1	-2.0	sulfate transporter activity, involved in sulfate transport
SPBPB10D8.01	1.3	2.4	-2.1	membrane transporter, unknown specificity
SPBP16F5.08c	1.2	2.7	-1.2	flavin dependent monooxygenase, involved in disulphide bond formation
<i>pof1</i>	1.2	2.3	-1.1	F-box protein
SPCC1739.06c	-1.6	2.8	-1.1	uroporphyrin methyltransferase
SPAPB24D3.08c <sup>ab</sup>	1.6	1.7	1.1	NADP-dependent oxidoreductase

**Unknown function**

SPBC11C11.06c <sup>a</sup>	-1.6	1.7	1.6
SPBC16E9.16c <sup>a</sup>	-2.5	3.9	1.5
SPBC17D11.03c	-1.1	1.9	-1.1
SPCC191.01 <sup>a</sup>	-1.4	3.2	1.5
SPBC21B10.08c	1.2	2.2	1.3
SPBC21C3.19 <sup>a</sup>	-2.7	2.7	2.7
SPAC22F3.11c	1.2	1.7	-1.1
SPAC25H1.01c <sup>a</sup>	-3.6	6.6	1.7
SPBC3B9.01 <sup>b</sup>	1.4	5.0	1.6
SPCC576.04 <sup>a</sup>	-1.4	1.9	1.4
SPCC63.14 <sup>a</sup>	1.2	2.1	1.3
SPBC660.06 <sup>a</sup>	1.3	2.9	1.4
SPBC725.03 <sup>a</sup>	-2.2	1.8	NA
SPAC750.01 <sup>a</sup>	-1.5	1.9	-1.2
SPACUNK4.15 <sup>a</sup>	1.3	1.8	1.4
SPBP35G2.02	-1.2	1.6	1.2

a) Core Environmental Stress Response Genes

b) Genes with orthologs in *S. cerevisiae* that show similar expression changes when *S. cerevisiae ace1-Δ* mutants are exposed to 8 μM CuSO<sub>4</sub>

**Supplementary Table 3B. Genes repressed in *S.pombe* copper excess (2.0 μM CuSO<sub>4</sub>)**

Gene Name	Max Cu-	Max Cu+	Max Fe-	Annotation
<b>Aminoacid metabolism and transport</b>				
SPAC1039.01	-1.4	-2.2	-1.5	amino acid permease family
SPAC1039.08	-1.1	-3.0	-1.3	serine acetyltransferase, involved in cysteine metabolism
SPBC359.03c	1.1	-1.5	-1.2	amino acid permease family
SPAP7G5.06	-1.4	-2.6	-1.5	amino acid permease family
<b>Ribosomal proteins</b>				
<i>rpl44: rpl28<sup>a</sup></i>	1.3	-1.6	-1.3	60S ribosomal protein L28/L44
<i>rps20<sup>a</sup></i>	1.2	-1.5	-1.5	40S ribosomal protein S20
<b>Transporters</b>				
SPAC11D3.18c	1.7	-6.5	-1.8	membrane transporter, unknown specificity
SPAC1399.02	1.5	-1.6	-1.4	membrane transporter, unknown specificity
SPAC212.10	1.1	-2.0	-1.2	pseudo-malic acid transport protein
SPBC8E4.01c <sup>b</sup>	1.3	-1.8	1.3	inorganic phosphate transporter
<i>ght6: meu12</i>	1.4	-1.5	-1.1	hexose transporter
<i>isp4</i>	-1.4	-2.0	-1.1	OPT oligopeptide transporter
<i>ptr2</i>	-2.1	-7.1	-2.3	PTR family peptide transporter, translocates di-/tripeptides
<b>Others</b>				
SPAC1039.02	1.3	-2.0	-1.3	calcineurin-like phosphoesterase
SPAC11D3.15	1.4	-4.0	-1.5	oxoprolinase
SPCC1223.09	-1.1	-2.6	-1.3	Uricase
SPCC132.04c	1.9	-1.6	2.6	glutamate dehydrogenase NAD-specific, involved in nitrogen & glutamate metabolism
SPCC222.11	1.1	-1.7	-1.2	coproporphyrinogen III oxidase
<i>gln1<sup>a</sup></i>	1.4	-1.9	-2.1	glutamate-ammonia ligase, involved in glutamate and nitrogen metabolism
<i>mei2</i>	1.3	-1.9	-1.6	RNA-binding protein, involved in meiosis
SPBPB2B2.06c	1.2	-1.9	1.3	calcineurin-like phosphoesterase
SPBPB7E8.01	-2.1	-1.7	1.5	glycoprotein
<i>prl3</i>	1.9	-2.0	-1.2	non-coding RNA
<b>Unknown function</b>				
SPAC5H10.01	1.9	-18	-1.5	

a) Core Environmental Stress Response Genes

b) Genes with orthologs in *S. cerevisiae* that show similar expression changes when *S. cerevisiae ace1-Δ* mutants are exposed to 8 μM CuSO<sub>4</sub>

**Supplementary Table 4A. Genes induced in copper excess in *S. cerevisiae ace1-Δ* mutants (8.0 μM CuSO<sub>4</sub>)**

Gene Name	Max Cu+	Annotation
<b>protein catabolism</b>		
<i>MDJ1</i>	3.5	Protein involved in mitochondrial biogenesis and protein folding during heat shock
<i>YDJ1</i>	3.6	Protein involved in protein import into mitochondria and ER, homolog of <i>E. coli</i> DnaJ
<i>PRE3</i>	2.0	Proteasome subunit beta1_sc involved in activity of the proteasome
<i>LAP4<sup>a</sup></i>	2.0	Aminopeptidase I (yscI, API) of the vacuole
<i>RPN2</i>	1.9	Non-ATPase component of 26S proteasome complex
<i>PRE2</i>	2.0	Proteasome subunit beta5_sc (protease yscE subunit Pre2/Prg1)
<i>RPN7</i>	2.0	Non-ATPase of the 26S proteasome complex
<i>RPT5</i>	2.4	ATPase component of 26S proteasome complex
<i>RPT4</i>	1.8	Component of the 19S regulatory cap complex of the 26S proteasome complex
<i>PRE10</i>	2.2	Proteasome subunit alpha7_sc (YC1 - protease yscE subunit 1)
<i>PRE8</i>	1.6	Proteasome subunit alpha2_sc (protease yscE subunit Y7)
<i>PRE5</i>	2.0	Proteasome subunit alpha6_sc
<i>UBX4</i>	1.8	Protein containing a UBX domain, which are found in ubiquitin regulatory proteins
<i>DSK2</i>	2.2	Protein involved in ubiquitin-dependent protein degradation and proteasome
<i>RPN6</i>	2.0	Non-ATPase subunit of the 26S proteasome complex
<i>CDC48<sup>b</sup></i>	2.1	component of the ubiquitin/proteasomal-dependent ER-associated degradation system
<i>RPT2</i>	1.8	ATPase component of the 26S proteasome complex
<i>RPN9</i>	1.9	Non-ATPase subunit of the 26S proteasome complex
<i>RPT3</i>	2.0	ATPase component of the 26S proteasome complex
<i>PRE6</i>	2.2	Proteasome subunit alpha4_sc
<i>UBC4</i>	2.0	Ubiquitin-conjugating (E2) enzyme
<i>PIM1</i>	2.0	Serine protease required for intramitochondrial proteolysis
<i>SHP1<sup>b</sup></i>	2.0	Potential regulatory subunit for Glc7p
<i>PRD1</i>	2.3	Proteinase yscD (saccharolysin), contains the zinc metalloendoprotease motif HEXXH
<i>RPN4</i>	2.7	Subunit of the regulatory particle of the proteasome
<i>NPL4</i>	2.3	Nuclear pore protein required for ubiquitin-dependent degradation of ER substrates
<i>UMP1</i>	2.1	Proteasome maturation factor, a chaperone involved in proteasome assembly
<i>RPT6</i>	1.8	ATPase component of 26S proteasome complex
<i>SCL1</i>	1.8	Proteasome subunit alpha1_sc (YC7alpha/Y8, protease yscE subunit 7)
<i>RPN10</i>	1.9	Non-ATPase component of the 26S proteasome complex
<i>ECM29</i>	3.0	Protein possibly involved in cell wall structure or biosynthesis
<i>PUP3</i>	1.8	Proteasome subunit beta3_sc
<i>PRE1</i>	2.2	Proteasome subunit beta4_sc (C11 - protease yscE subunit 11)
<i>PRB1<sup>a,b</sup></i>	2.4	Protease B (yscB/PrB/cerevisin), serine protease of the subtilisin family
<i>PRE4</i>	1.8	Proteasome subunit beta7_sc
<i>RPN12</i>	2.1	Non-ATPase component of 26S proteasome complex
<i>RPN11</i>	2.0	Protein of the 19S regulatory particle of the proteasome
<i>RPN3</i>	1.9	Non-ATPase component of 26S proteasome complex
<b>response to stress</b>		
<i>HSP42</i>	6.1	Heat shock protein with similarity to Hsp26p, involved in restoration of the cytoskeleton
<i>HSP78<sup>a</sup></i>	4.7	Mitochondrial heat shock protein of the ClpB family of ATP-dependent proteases
<i>HSC82<sup>b</sup></i>	4.5	Chaperonin homologous to <i>E. coli</i> HtpG and mammalian HSP90
<i>SSA4</i>	11.7	Protein chaperone of the HSP70 family
<i>AHA1<sup>b</sup></i>	3.8	Protein of unknown function
<i>YAP1</i>	2.0	Possible redox sensor involved in oxidative stress response
<i>TSL1</i>	2.0	Regulatory component of the trehalose-6-phosphate synthase/phosphatase complex
<i>KAR2</i>	6.2	Heat shock protein of the ER lumen
<i>HSP104<sup>a</sup></i>	5.1	Heat shock protein
<i>YJL144W</i>	3.5	Protein of unknown function
<i>HCH1</i>	3.7	Protein of unknown function
<i>UBC5</i>	2.4	Ubiquitin-conjugating enzyme
<i>SSA3</i>	1.8	Chaperone of the HSP70 family
<i>HSP26<sup>a,b</sup></i>	7.1	Heat shock protein of 26 kDa
<i>YHB1</i>	2.5	Flavohemoglobin involved in protection from nitrosative stress
<i>TRX2<sup>b</sup></i>	2.0	Thioredoxin II
<i>HSP82</i>	5.8	Heat-inducible chaperonin homologous to <i>E. coli</i> HtpG and mammalian HSP90
<i>GRE3</i>	1.9	Aldo/keto reductase with NADPH specificity, induced by osmotic stress
<i>HSP12<sup>a,b</sup></i>	2.6	Heat shock protein of 12 kDa, induced by heat, osmotic stress, and oxidative stress
<i>MAG1<sup>a</sup></i>	2.9	DNA-3-methyladenine glycosylase, repair of alkylation-damaged DNA
<i>STI1<sup>b</sup></i>	5.3	Stress-induced protein required for optimal growth at high and low temperature
<i>SSA2</i>	7.3	Cytoplasmic protein chaperone of the HSP70 family
<i>HSP10</i>	3.0	Mitochondrial chaperonin that cooperates with Hsp60p, counterpart of <i>E. coli</i> GroES
<i>SSE1</i>	4.5	Heat shock protein of the HSP70 family

<i>SSE2</i>	1.8	Heat shock protein of the HSP70 family
<i>SSE2</i>	1.8	Heat shock protein of the HSP70 family
<b>Transport</b>		
<i>BTN2</i>	17.9	Protein with a role in cellular pH homeostasis
<i>SSA1<sup>b</sup></i>	6.9	Cytoplasmic chaperone and heat shock protein of the HSP70 family
<i>GSF2</i>	1.6	Protein involved in glucose repression
<i>HSP60</i>	2.5	Mitochondrial chaperonin that cooperates with Hsp10p, homolog of <i>E. coli</i> GroEL
<i>YKT6</i>	1.8	Synaptobrevin (v-SNARE) homolog essential for endoplasmic reticulum-Golgi transport
<i>MIA40</i>	1.9	Mitochondrial protein that may play a role in cell cycle progression
<i>VPS65</i>	2.0	Class F vacuolar sorting protein involved in Prc1p vacuolar trafficking pathway
<i>SSC1</i>	2.4	Mitochondrial protein that acts as an import motor with Tim44p and as a chaperonin
<i>YCF1<sup>b</sup></i>	2.1	Vacuolar glutathione S-conjugate transporter; ATP-binding cassette (ABC) superfamily
<i>ATG8<sup>b</sup></i>	2.0	Protein required for delivery of autophagic vesicles to the vacuole
<i>GTS1</i>	1.6	Putative zinc-finger transcription factor of the Gcs1p/Glo3p/Sps18p family
<i>ERV29</i>	1.9	Component of COPII-coated vesicles, required for vesicular transport
<b>Organelle organization and biogenesis</b>		
<i>SED1</i>	1.9	Abundant cell surface glycoprotein
<i>TCP1</i>	1.6	Component of chaperonin-containing T-complex (TCP ring complex, TRiC)
<i>PNC1<sup>a</sup></i>	1.8	Pyrazinamidase and nicotinamidase
<i>YHR138C<sup>a</sup></i>	2.1	Protein possibly involved in vacuolar fusion
<b>Protein modification</b>		
<i>BET4</i>	1.9	Geranylgeranyltransferase Type II alpha subunit, complexes with Bet2p
<i>UBA1</i>	2.1	Ubiquitin-activating (E1) enzyme
<i>STE24</i>	1.6	Prenyl-dependent protease involved both in the first N-terminal proteolytic step
<i>ERO1<sup>b</sup></i>	3.2	Protein required for protein disulfide bond formation in the endoplasmic reticulum
<i>RTS3</i>	2.8	Protein of unknown function
<i>YPI1<sup>a</sup></i>	1.8	Protein of unknown function, may physically interact with Glc7p and Ppz1p
<b>Protein biosynthesis</b>		
<i>MEF2</i>	1.8	Putative mitochondrial translation elongation factor G
<i>DBP1</i>	1.9	ATP-dependent RNA helicase of the DEAD box family
<i>SIS1<sup>b</sup></i>	4.0	Protein required for initiation of translation; DnaJ family of protein chaperones
<i>MRPL11</i>	1.8	Mitochondrial ribosomal protein of the large subunit (YmL11)
<i>FES1<sup>b</sup></i>	3.2	Protein involved in resistance to H <sub>2</sub> O <sub>2</sub>
<b>Transcription</b>		
<i>MBF1</i>	3.0	Transcriptional coactivator of Gcn4p
<i>PDR1</i>	1.7	Zinc-finger transcription factor; regulator of genes involved in multiple drug resistance
<i>YOD1<sup>a</sup></i>	1.9	Protein of unknown function, has a single C <sub>2</sub> H <sub>2</sub> -type zinc finger
<b>Others / Unknown</b>		
<i>EDC2</i>	1.8	Protein involved in mRNA decapping
<i>YOL155C</i>	2.7	Protein with similarity to <i>S. cerevisiae</i> glucan 1,4-alpha-glucosidase
<i>ISU2</i>	2.6	Protein with similarity to iron-sulfur cluster nitrogen fixation proteins
<i>GCV2</i>	1.8	Glycine decarboxylase pyridoxal phosphate containing P subunit
<i>ARO9</i>	2.6	Aromatic amino acid aminotransferase II
<i>FRM2</i>	13.5	Protein involved in the integration of lipid signaling pathways with cellular homeostasis
<i>CPR6</i>	5.0	Cyclophilin (peptidylprolyl cis-trans isomerase or PPIase)
<i>GSH1</i>	1.7	gamma-Glutamylcysteine synthetase
<i>GTT2</i>	3.4	Glutathione transferase
<i>HEM3</i>	1.7	Porphobilinogen deaminase (pre-uroporphyrinogen synthase)
<i>PDI1</i>	2.0	Protein disulfide isomerase and oxidoreductase
<i>YFL006W</i>	1.8	Protein of unknown function
<i>YFR024C</i>	1.7	Protein with possible role in the regulation of actin cytoskeletal organization
<i>YLR108C</i>	2.7	Protein containing a K <sup>+</sup> channel tetramerization domain
<i>REH1</i>	1.9	Protein possibly involved in proteasome function
<i>YLR247C</i>	1.9	Protein containing an SNF2 related N-terminal domain
<i>RBF9</i>	3.8	Protein with high similarity to <i>S. cerevisiae</i> Stf2p
<i>YIL169C</i>	2.3	Protein of unknown function
<i>DRE2</i>	2.5	Protein of unknown function
<i>YKR011C</i>	2.5	Protein of unknown function
<i>SGT2</i>	3.2	Protein of unknown function
<i>OYE3<sup>a</sup></i>	2.1	NADPH dehydrogenase (old yellow enzyme), isoform 3
<i>YMR034C</i>	2.1	Protein of unknown function
<i>YPR158W</i>	4.0	Protein of unknown function
<i>YML131W<sup>b</sup></i>	2.3	Putative NAD-dependent oxidoreductase
<i>YMR155W</i>	1.8	Protein of unknown function

YNL155W	2.9	Protein predicted to have structural similarity to disulfide oxidoreductases
YNL134C	2.1	Member of the zinc-containing alcohol dehydrogenase family
YOR052C <sup>a</sup>	2.4	Protein containing an AN1-like zinc finger domain
APJ1	2.5	Protein induced by cell stress
YDL206W	1.7	Putative membrane transporter of the Ca <sup>2+</sup> :cation antiporter (CaCA) family
YDR154C	1.9	Protein of unknown function
HSP31	2.5	Member of the DJ-1 or Pfpl family, has high similarity to <i>S. cerevisiae</i> Ypl280p
YBR099C	3.1	Protein that might affect sensitivity to UV radiation
YCR061W	1.9	Protein that may be involved in response to heat and high salinity
YAR068W	1.9	Protein of unknown function
YHR214W-A	2.1	Protein of unknown function
FMP52	2.1	Protein of unknown function
YEL045C	1.7	Protein of unknown function
ZTA1 <sup>b</sup>	1.7	Zeta-crystallin homolog
CPR1	1.8	Cyclophilin (peptidylprolyl cis-trans isomerase or PPIase) of the cytosol
ZWF1 <sup>b</sup>	1.8	Glucose-6-phosphate dehydrogenase
ZPR1	2.1	Zinc finger protein required for normal cell proliferation

a) Core Environmental Stress Response Genes

b) Genes with orthologs in *S. pombe* that show similar expression changes when *S. pombe* is exposed to 2  $\mu$ M CuSO<sub>4</sub>

**Supplementary Table 4B. Genes repressed in copper excess in *S. cerevisiae* *ace1-Δ* mutants (8.0  $\mu$ M CuSO<sub>4</sub>)**

Gene Name	Max Cu+	Annotation
<b>Transport</b>		
TPO2	-2.2	Polyamine transport protein; multidrug-resistance 12-spanner (DHA12) family
CTR1	-2.3	Copper transport protein required for high-affinity uptake of copper
PIC2	-2.8	Member of the mitochondrial carrier (MCF) family of membrane transporters
PHO84 <sup>a,b</sup>	-2.7	High-affinity inorganic phosphate/H <sup>+</sup> symporter
HXT4	-2.0	Moderate- to low-affinity hexose transporter
TPO4	-1.8	Polyamine transport protein; multidrug-resistance 12-spanner (DHA12)
PDR5	-5.5	Drug-efflux pump involved in resistance to multiple drugs
OPT2	-3.1	Oligopeptide transporter
DIC1	-1.8	Mitochondrial dicarboxylate transport protein
AQY1	-2.1	Aquaporin water channel protein
FET4	-2.3	Low-affinity Fe(II) transport protein
MTH1	-1.9	Repressor of hexose transport genes
OAC1	-1.6	Mitochondrial oxaloacetate transporter
<b>Amino acid and derivative metabolism</b>		
MET12	-1.9	Methylenetetrahydrofolate reductase (MTHFR), involved in methionine biosynthesis
ECM17	-1.6	Sulfite reductase (ferredoxin)
CAR2	-1.9	Ornithine aminotransferase (ornithine oxo-acid aminotransferase)
SAM2	-2.1	S-adenosylmethionine synthetase 2
MET6	-2.4	Homocysteine methyltransferase; methionine synthase, cobalamin-independent
SER3	-2.7	3-phosphoglycerate dehydrogenase, catalyzes the first step in synthesis of serine
LYS4	-1.8	Homoaconitate hydratase (homoaconitase), third step in lysine biosynthesis pathway
ILV3 <sup>b</sup>	-2.1	Dihydroxyacid dehydratase (DAD), third step in valine and isoleucine biosynthesis
LEU1	-2.3	3-Isopropylmalate dehydratase, second step in leucine biosynthesis pathway
BAT1	-1.7	Mitochondrial branched-chain amino acid transaminase
<b>Carbohydrate metabolism</b>		
GSY1	-2.3	UDP-glucose-starch glucosyltransferase (glycogen synthetase) isoform 1
HAP4	-2.2	Transcription factor with acidic activation domain
MDH2	-1.8	Malate dehydrogenase, cytosolic, probably functions in the glyoxylate cycle
KNH1	-1.8	Putative secreted protein with similarity to Kre9p
SDH2	-1.8	Succinate dehydrogenase (ubiquinone) iron-sulfur protein subunit
<b>response to stress</b>		
HSP30	-5.7	Heat shock protein located in the plasma membrane
GRE1	-1.7	Protein induced by osmotic stress
CCP1	-1.7	Cytochrome-c peroxidase, involved in destruction of toxic radicals in the cell
<b>lipid metabolism</b>		
SCS7	-2.1	Ceramide hydroxylase
SUR2	-1.7	Hydroxylase involved in sphingolipid metabolism
ATF2	-1.7	Sterol O-acetyltransferase



<b>transcription</b>		
<i>ACE1</i>	-12.8	Copper-dependent transcription factor
<i>CUP9</i>	-2	Homeodomain protein involved in copper homeostasis
<b>Others / Unknown</b>		
<i>LDB7</i>	-1.7	Protein of unknown function
<i>SPI1</i>	-2.4	Protein induced in stationary phase, has similarity to Sed1p
<i>YER067W</i>	-3.1	Protein of unknown function
<i>YIR043C</i>	-1.8	Member of the duplication (DUP) family
<i>STP4</i>	-3.3	Protein with strong similarity to Stp1p
<i>YPR157W</i>	-2.8	Protein with high similarity to <i>S. cerevisiae</i> Vps62p
<i>YPL014W</i>	-2.0	Protein of unknown function
<i>FMP48</i>	-2.0	Serine/threonine protein kinase of unknown function
<i>ICY1</i>	-2.0	Protein of unknown function
<i>DLD2</i>	-2.8	D-lactate dehydrogenase, mitochondrial
<i>PHM6</i>	-2.8	Protein predicted to have a role in phosphate metabolism
<i>YOR225W</i>	-1.9	Protein of unknown function
<i>YER053C-A<sup>a</sup></i>	-2.7	Protein possibly involved in tolerance of high salt, osmotic stress, and low temperature
<i>ERR1</i>	-2.5	Enolase-related subtelomeric sequence, identical to Err2p
<i>YLR099W-A</i>	-1.8	Protein of unknown function
<i>YLR346C</i>	-1.8	Protein of unknown function
<i>GAS3</i>	-2.9	Protein with similarity to Gas1p
<i>YEL073C</i>	-2.2	Protein of unknown function
<i>CPR5</i>	-2.8	Cyclophilin (peptidylprolyl cis-trans isomerase or PPIase) of the endoplasmic reticulum
<i>YAR028W</i>	-1.7	Protein with strong similarity to subtelomericly-encoded proteins
<i>YAL061W</i>	-1.7	Member of the zinc-containing alcohol dehydrogenase family
<i>YBR187W</i>	-1.7	Protein of unknown function, contains six potential transmembrane segments
<i>YJL217W</i>	-2.5	Protein of unknown function
<i>YJL200C</i>	-1.9	Protein with similarity to aconitase, has potential mitochondrial transit peptide
<i>YGL117W</i>	-2.2	Protein of unknown function
<i>YHR140W</i>	-2.0	Cytoplasmic protein of unknown function
<i>FMP12</i>	-1.8	Member of the gamma-butyrobetaine hydroxylase family
<i>TIP41</i>	-4.3	Negative regulator of TOR signaling pathway
<i>MRPL44</i>	-2.2	Mitochondrial ribosomal protein of the large subunit (YmR44)
<i>YFR055W</i>	-1.8	Protein with similarity to <i>E. coli</i> cystathionine beta-lyase
<i>RIB4</i>	-4.9	Riboflavin biosynthesis pathway enzyme
<i>REC8</i>	-2.4	Protein required for meiosis and sporulation
<i>RNR2</i>	-2.2	Component of ribonucleotide reductase (ribonucleoside-diphosphate reductase)
<i>SPL2</i>	-3.1	Putative inhibitor of Pho80p-Pho85p cyclin-dependent protein kinase
<i>URA1</i>	-2.4	Dihydroorotate dehydrogenase, fourth step in pyrimidine biosynthesis pathway
<i>AAH1<sup>a</sup></i>	-1.7	Adenine deaminase (adenine aminohydrolase)
<i>PDH1</i>	-1.8	Protein possibly involved in propionate utilization
<i>ADH5</i>	-2.4	Alcohol dehydrogenase, zinc-dependent, also called formaldehyde dehydrogenase
<i>IMD2</i>	-2.7	Inosine-5'-monophosphate dehydrogenase

a) Core Environmental Stress Response Genes

b) Genes with orthologs in *S. pombe* that show similar expression changes when *S. pombe* is exposed to 2  $\mu$ M CuSO<sub>4</sub>