

	Gephebase Gene	GepheID
Vacuolar transporter chaperone 4 (#gepibase-summary-title)	GP00001295	
	Entry Status	Main curator
Published	Arnoult	

Trait Category		Trait		Trait State in Taxon A		Trait State in Taxon B		Ancestral State		Taxonomic Status	
Physiology (#https://www.gephebase.org/search-criteria?/and+Trait+Category=~Physiology)		Metal tolerance (copper) (https://www.gephebase.org/search-criteria?/and+Trait=~Metal tolerance (copper))		Saccharomyces cerevisiae		Saccharomyces cerevisiae - after 14 days of growth in high Copper environment. 34 lines		Taxon A		Experimental Evolution (#https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=~Experimental Evolution)	
Taxon A		Taxon B		Taxon A		Taxon B		Taxon A		Taxon B	
Saccharomyces cerevisiae		Saccharomyces cerevisiae		Saccharomyces cerevisiae		Saccharomyces cerevisiae		Saccharomyces cerevisiae		Saccharomyces cerevisiae	
(https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces+cerevisiae">#https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces cerevisiae)		(https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces+cerevisiae">#https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces cerevisiae)		(https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces+cerevisiae">#https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces cerevisiae)		(https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces+cerevisiae">#https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces cerevisiae)		(https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces+cerevisiae">#https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces cerevisiae)		(https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces+cerevisiae">#https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=~Saccharomyces cerevisiae)	
baker's yeast		baker's yeast		baker's yeast		baker's yeast		baker's yeast		baker's yeast	
Saccharomyces capensis; Saccharomyces italicus; Saccharomyces oviformis; Saccharomyces uvarum var. melibiosus; baker's yeast; S. cerevisiae; brewer's yeast; ATCC 18824; ATCC:18824; CBS:1171; CBS:1171; NRRL Y-12632; NRRL:Y:12632; Saccaromyces cerevisiae; Saccharomyce cerevisiae; Saccharomyes cerevisiae; Sccharomyces cerevisiae		Saccharomyces capensis; Saccharomyces italicus; Saccharomyces oviformis; Saccharomyces uvarum var. melibiosus; baker's yeast; S. cerevisiae; brewer's yeast; ATCC 18824; ATCC:18824; CBS:1171; CBS:1171; NRRL Y-12632; NRRL:Y:12632; Saccaromyces cerevisiae; Saccharomyce cerevisiae; Saccharomyes cerevisiae; Sccharomyces cerevisiae		Saccharomyces capensis; Saccharomyces italicus; Saccharomyces oviformis; Saccharomyces uvarum var. melibiosus; baker's yeast; S. cerevisiae; brewer's yeast; ATCC 18824; ATCC:18824; CBS:1171; CBS:1171; NRRL Y-12632; NRRL:Y:12632; Saccaromyces cerevisiae; Saccharomyce cerevisiae; Saccharomyes cerevisiae; Sccharomyces cerevisiae		Saccharomyces capensis; Saccharomyces italicus; Saccharomyces oviformis; Saccharomyces uvarum var. melibiosus; baker's yeast; S. cerevisiae; brewer's yeast; ATCC 18824; ATCC:18824; CBS:1171; CBS:1171; NRRL Y-12632; NRRL:Y:12632; Saccaromyces cerevisiae; Saccharomyce cerevisiae; Saccharomyes cerevisiae; Sccharomyces cerevisiae		Saccharomyces capensis; Saccharomyces italicus; Saccharomyces oviformis; Saccharomyces uvarum var. melibiosus; baker's yeast; S. cerevisiae; brewer's yeast; ATCC 18824; ATCC:18824; CBS:1171; CBS:1171; NRRL Y-12632; NRRL:Y:12632; Saccaromyces cerevisiae; Saccharomyce cerevisiae; Saccharomyes cerevisiae; Sccharomyces cerevisiae		Saccharomyces capensis; Saccharomyces italicus; Saccharomyces oviformis; Saccharomyces uvarum var. melibiosus; baker's yeast; S. cerevisiae; brewer's yeast; ATCC 18824; ATCC:18824; CBS:1171; CBS:1171; NRRL Y-12632; NRRL:Y:12632; Saccaromyces cerevisiae; Saccharomyce cerevisiae; Saccharomyes cerevisiae; Sccharomyces cerevisiae	
species		species		species		species		species		species	
cellular organisms; Eukaryota; Opisthokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Saccharomycetaceae; Saccharomyces		cellular organisms; Eukaryota; Opisthokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Saccharomycetaceae; Saccharomyces		cellular organisms; Eukaryota; Opisthokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Saccharomycetaceae; Saccharomyces		cellular organisms; Eukaryota; Opisthokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Saccharomycetaceae; Saccharomyces		cellular organisms; Eukaryota; Opisthokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Saccharomycetaceae; Saccharomyces		cellular organisms; Eukaryota; Opisthokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Saccharomycetaceae; Saccharomyces	
Saccharomyces () - (Rank: genus)		Saccharomyces () - (Rank: genus)		Saccharomyces () - (Rank: genus)		Saccharomyces () - (Rank: genus)		Saccharomyces () - (Rank: genus)		Saccharomyces () - (Rank: genus)	
(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 4932)		(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 4932)		(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 4932)		(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 4932)		(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 4932)		(https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 4932)	
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is Taxon A an Intraspecies?		is Taxon B an Intraspecies?		is Taxon A an Intraspecies?		is Taxon B an Intraspecies?		is Taxon A an Intraspecies?		is Taxon B an Intraspecies?	
No		No		No		No		No		No	

VTG4	Generic Gene Name	UniProtKB <i>Saccharomyces cerevisiae</i> (strain ATCC 204508 / S288c)
	Synonyms	P47075 (http://www.uniprot.org/uniprot/P47075)
PHM3; YJL012C-A; YJL012C; J1345	String	853441 (https://www.ncbi.nlm.nih.gov/nucore/853441)
4932.YJL012C (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=4932.YJL012C)	Sequence Similarities	
Belongs to the VTC4 family.		
GO - Molecular Function		
GO:0005516 : calmodulin binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005516)		
GO:0000822 : inositol hexakisphosphate binding (https://www.ebi.ac.uk/QuickGO/term/GO:0000822)		
GO:0008976 : polyphosphate kinase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0008976)		
GO - Biological Process		

GO:0048016 : inositol phosphate-mediated signaling
(<https://www.ebi.ac.uk/QuickGO/term/GO:0048016>)
GO:0006797 : polyphosphate metabolic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006797>)
GO:0006799 : polyphosphate biosynthetic process
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006799>)
GO:0016237 : lysosomal microautophagy
(<https://www.ebi.ac.uk/QuickGO/term/GO:0016237>)
GO:0007034 : vacuolar transport (<https://www.ebi.ac.uk/QuickGO/term/GO:0007034>)
GO:0042144 : vacuole fusion, non-autophagic
(<https://www.ebi.ac.uk/QuickGO/term/GO:0042144>)

GO - Cellular Component

GO:0016021 : integral component of membrane
(<https://www.ebi.ac.uk/QuickGO/term/GO:0016021>)
GO:0005783 : endoplasmic reticulum
(<https://www.ebi.ac.uk/QuickGO/term/GO:0005783>)
GO:0000329 : fungal-type vacuole membrane
(<https://www.ebi.ac.uk/QuickGO/term/GO:0000329>)
GO:0031310 : intrinsic component of vacuolar membrane
(<https://www.ebi.ac.uk/QuickGO/term/GO:0031310>)
GO:0033254 : vacuolar transporter chaperone complex
(<https://www.ebi.ac.uk/QuickGO/term/GO:0033254>)

Presumptive Null

Yes ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Presumptive Null=~Yes))

Molecular Type

Coding ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Molecular Type=~Coding))

Aberration Type

Indel ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Aberration Type=~Indel))

Indel Size

-

Molecular Details of the Mutation

Phe > Ser+frameshift @ position 380

Experimental Evidence

Association Mapping ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/and+Experimental Evidence=~Association Mapping))

Main Reference

Too much of a good thing: the unique and repeated paths toward copper adaptation. (2015) (<https://pubmed.ncbi.nlm.nih.gov/25519894>)

Authors

Gerstein AC; Ono J; Lo DS; Campbell ML; Kuzmin A; Otto SP

Abstract

Copper is a micronutrient essential for growth due to its role as a cofactor in enzymes involved in respiration, defense against oxidative damage, and iron uptake. Yet too much of a good thing can be lethal, and yeast cells typically do not have tolerance to copper levels much beyond the concentration in their ancestral environment. Here, we report a short-term evolutionary study of *Saccharomyces cerevisiae* exposed to levels of copper sulfate that are inhibitory to the initial strain. We isolated and identified adaptive mutations soon after they arose, reducing the number of neutral mutations, to determine the first genetic steps that yeast take when adapting to copper. We analyzed 34 such strains through whole-genome sequencing and by assaying fitness within different environments; we also isolated a subset of mutations through tetrad analysis of four lines. We identified a multilayered evolutionary response. In total, 57 single base-pair mutations were identified across the 34 lines. In addition, gene amplification of the copper metallothionein protein, CUP1-1, was rampant, as was chromosomal aneuploidy. Four other genes received multiple, independent mutations in different lines (the vacuolar transporter genes VTC1 and VTC4; the plasma membrane H⁺-ATPase PMA1; and MAM3, a protein required for normal mitochondrial morphology). Analyses indicated that mutations in all four genes, as well as CUP1-1 copy number, contributed significantly to explaining variation in copper tolerance. Our study thus finds that evolution takes both common and less trodden pathways toward evolving tolerance to an essential, but highly toxic, micronutrient.

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Additional References

RELATED GEPHE

Related Genes

5 (MAM3, metallothionein CUP1, Plasma membrane ATPase 1, PMR1, Vacuolar transporter chaperone 1) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=~4932#/and+Trait=Metal tolerance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

6 ([#gephebase-summary-title](https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~Vacuolar transporter chaperone 4#/and+Taxon ID=~4932#/or+Gene Gephebase=~Vacuolar transporter chaperone 4#/and+Taxon ID=~4932))

EXTERNAL LINKS

COMMENTS

in line CBM11 : putative null

