

	Gephebase Gene	GepheID
Vacuolar transporter chaperone 4 (https://www.gephebase.org/search-criteria?/and+Gene+Gephebase+Vacuolar+transporter+chaperone+4+*#gephebase-summary-title)	GP00001299	Main curator
Published	Entry Status Arnoult	

	Trait Category
Physiology (https://www.gephebase.org/search-criteria?/and+Trait+Category=~Physiology~#gephebase-summary-title)	Trait
Metal tolerance (copper) (https://www.gephebase.org/search-criteria?/and+Trait=~Metal+tolerance+(copper)~#gephebase-summary-title)	Trait State in Taxon A
<i>Saccharomyces cerevisiae</i>	Trait State in Taxon B
<i>Saccharomyces cerevisiae</i> - after 14 days of growth in high Copper environment. 34 lines	Ancestral State
Taxon A	Taxonomic Status
Experimental Evolution (https://www.gephebase.org/search-criteria?/and+Taxonomic+Status=~Experimental+Evolution~#gephebase-summary-title)	

GENOTYPIC CHANGE

VTC4	Generic Gene Name	UniProtKB <i>Saccharomyces cerevisiae</i> (strain ATCC 204508 / S288c) P47075 (http://www.uniprot.org/uniprot/P47075)
PHM3; YJL012C-A; YJL012C; J1345	Synonyms	GenebankID or UniProtKB 853441 (https://www.ncbi.nlm.nih.gov/nuccore/853441)
4932.YJL012C (http://string-db.org/newstring.cgi/show_network_section.pl?identifier=4932.YJL012C)	String	
Belongs to the VTC4 family.	Sequence Similarities	
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 - Molecular Function	
	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

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

SNP Coding Change

Nonsense

Molecular Details of the Mutation

C>A (Glu > Stop) @ position 1153

Experimental Evidence

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

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	-	-	-

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 (<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#gephebase-summary-title>)

EXTERNAL LINKS

COMMENTS

in line CBM13 ; putative null