## GEPHE SUMMARY

Gephebase Gene
Vacuolar transporter chaperone 4 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Vacuolar transporter chaperone 4^#gephebase-summary-title)

GepheID
GP00001294

Entry Status
Published

Main curator
Arnoult

## PHENOTYPIC CHANGE

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
Saccharomyces cerevisiae

Trait State in Taxon B
Saccharomyces cerevisiae - 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)

### Taxon A

Latin Name
Saccharomyces cerevisiae (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Saccharomyces cerevisiae^#gephebase-summary-title)

Common Name
baker's yeast

Synonyms
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

Rank
species

Lineage
cellular organisms; Eukaryota; Opisthokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Saccharomycetaceae; Saccharomyces

Parent
Saccharomyces () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 4930 )

NCBI Taxonomy ID
4932 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 4932 )

is Taxon A an Infraspecies?
No

### Taxon B

Latin Name
Saccharomyces cerevisiae (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Saccharomyces cerevisiae^#gephebase-summary-title)

Common Name
baker's yeast

Synonyms
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

Rank
species

Lineage
cellular organisms; Eukaryota; Opisthokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Saccharomycetaceae; Saccharomyces

Parent
Saccharomyces () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 4930 )

NCBI Taxonomy ID
4932 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 4932 )

is Taxon B an Infraspecies?
No

## GENOTYPIC CHANGE

Generic Gene Name
VTC4

Synonyms
PHM3; YJL012C-A; YJL012C; J1345

String
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

UniProtKB Saccharomyces cerevisiae (strain ATCC 204508 / S288c)
P47075 (http://www.uniprot.org/uniprot/P47075)

GenebankID or UniProtKB
853441 (https://www.ncbi.nlm.nih.gov/nuccore/853441)

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

Molecular Type

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

Aberration Type

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

SNP Coding Change

Nonsense

Molecular Details of the Mutation

C>A (Glu > Stop) @ position 226

Experimental Evidence

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

| | 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 CBM5 ; putative null