

GEPHE SUMMARY

	Gephebase Gene	GepheID
ERG11 = CYP51A1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^ERG11 = CYP51A1^#gephebase-summary-title)	GP00000285	
Published	Entry Status	Main curator

PHENOTYPIC CHANGE

	Trait Category		
Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)	Trait		
Xenobiotic resistance (https://www.gephebase.org/search-criteria?/and+Trait=Xenobiotic resistance^#gephebase-summary-title)	Trait State in Taxon A		
Candida albicans- drug sensitive	Trait State in Taxon B		
Candida albicans- drug resistant	Ancestral State		
Data not curated	Taxonomic Status		
Intraspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intraspecific^#gephebase-summary-title)			
	Taxon A	Taxon B	
	Latin Name	Latin Name	
Candida albicans (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Candida albicans^#gephebase-summary-title)	Candida albicans (https://www.gephebase.org/search-criteria?/and+Taxon+and+Synonyms=Candida albicans^#gephebase-summary-title)		
	Common Name	Common Name	
-	Synonyms	Synonyms	
Candida stellatoidea; Candida stellatoidea type I; ATCC 11006; ATCC 18804; ATCC 20308; ATCC:11006; ATCC:18804; ATCC:20308; BCC 5390; BCC:5390; BCRC 20512; BCRC:20512; CBS 562; CBS:562; CCRC 20512; CCRC:20512; CECT 1002; CECT:1002; IFO 1385; IFO:1385; JCM 1537; JCM 1542; JCM:1537; JCM:1542; KCTC 7270; KCTC:7270; MUCL 29800; MUCL:29800; NBIMCC 72; NBIMCC:72; NBRC 1385; NBRC:1385; NC AIM Y.00971; NCYC 597; NCYC:597; NRRL Y-12983; NRRL:Y:12983; PYCC 3436; PYCC:3436; UAMH 8765; UAMH:8765; Candida albican	Candida stellatoidea; Candida stellatoidea type I; ATCC 11006; ATCC 18804; ATCC 20308; ATCC:11006; ATCC:18804; ATCC:20308; BCC 5390; BCC:5390; BCRC 20512; BCRC:20512; CBS 562; CBS:562; CCRC 20512; CCRC:20512; CECT 1002; CECT:1002; IFO 1385; IFO:1385; JCM 1537; JCM 1542; JCM:1537; JCM:1542; KCTC 7270; KCTC:7270; MUCL 29800; MUCL:29800; NBIMCC 72; NBIMCC:72; NBRC 1385; NBRC:1385; NC AIM Y.00971; NCYC 597; NCYC:597; NRRL Y-12983; NRRL:Y:12983; PYCC 3436; PYCC:3436; UAMH 8765; UAMH:8765; Candida albican		
	Rank	Rank	
species	Lineage	Lineage	
cellular organisms; Eukaryota; Opistokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Debaryomycetaceae; Candida/Lodderomyces clade; Candida		cellular organisms; Eukaryota; Opistokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Debaryomycetaceae; Candida/Lodderomyces clade; Candida	
	Parent	Parent	
Candida () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=1535326)	Candida () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=1535326)		
	NCBI Taxonomy ID	NCBI Taxonomy ID	
5476 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5476)	5476 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5476)		
	is Taxon A an Infraspecies?	is Taxon B an Infraspecies?	
No	No	No	

GENOTYPIC CHANGE

	Generic Gene Name		
ERG11		UniProtKB Candida albicans (strain SC5314 / ATCC MYA-2876) P10613 (http://www.uniprot.org/uniprot/P10613)	
	Synonyms		
CYP51; ERG16; CAALFM_C500660CA; CaO19.922		GenebankID or UniProtKB FJ403378 (https://www.ncbi.nlm.nih.gov/nuccore/FJ403378)	
	String		
-	Sequence Similarities		
Belongs to the cytochrome P450 family.			
	GO - Molecular Function		
GO:0020037 : heme binding (https://www.ebi.ac.uk/QuickGO/term/GO:0020037) GO:0005506 : iron ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005506) GO:0008144 : drug binding (https://www.ebi.ac.uk/QuickGO/term/GO:0008144) GO:0008398 : sterol 14-demethylase activity			

GO:0055114 : oxidation-reduction process

(<https://www.ebi.ac.uk/QuickGO/term/GO:0055114>)

GO:0036187 : cell growth mode switching, budding to filamentous

(<https://www.ebi.ac.uk/QuickGO/term/GO:0036187>)

GO:0035690 : cellular response to drug

(<https://www.ebi.ac.uk/QuickGO/term/GO:0035690>)

GO:0006696 : ergosterol biosynthetic process

(<https://www.ebi.ac.uk/QuickGO/term/GO:0006696>)

GO:0001766 : membrane raft polarization

(<https://www.ebi.ac.uk/QuickGO/term/GO:0001766>)

GO:0016126 : sterol biosynthetic process

(<https://www.ebi.ac.uk/QuickGO/term/GO:0016126>)

GO:0016125 : sterol metabolic process

(<https://www.ebi.ac.uk/QuickGO/term/GO:0016125>)

GO - Cellular Component

GO:0016021 : integral component of membrane

(<https://www.ebi.ac.uk/QuickGO/term/GO:0016021>)

GO:0005886 : plasma membrane (<https://www.ebi.ac.uk/QuickGO/term/GO:0005886>)

GO:0016020 : membrane (<https://www.ebi.ac.uk/QuickGO/term/GO:0016020>)

GO:0005783 : endoplasmic reticulum

(<https://www.ebi.ac.uk/QuickGO/term/GO:0005783>)

Presumptive Null

No (<https://www.gephebase.org/search-criteria?/and+Presumptive+Null=^No^#gephebase-summary-title>)

Molecular Type

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

Aberration Type

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

Indel Size

unknown

Molecular Details of the Mutation

Copy number Variant

Experimental Evidence

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

Main Reference

Genotypic evolution of azole resistance mechanisms in sequential *Candida albicans* isolates. (2007) (<https://pubmed.ncbi.nlm.nih.gov/17693596>)

Authors

Coste A; Selmecki A; Forche A; Diogo D; Bougnoux ME; d'Enfert C; Berman J; Sanglard D

Abstract

TAC1 (for transcriptional activator of CDR genes) is critical for the upregulation of the ABC transporters CDR1 and CDR2, which mediate azole resistance in *Candida albicans*. While a wild-type TAC1 allele drives high expression of CDR1/2 in response to inducers, we showed previously that TAC1 can be hyperactive by a gain-of-function (GOF) point mutation responsible for constitutive high expression of CDR1/2. High azole resistance levels are achieved when *C. albicans* carries hyperactive alleles only as a consequence of loss of heterozygosity (LOH) at the TAC1 locus on chromosome 5 (Chr 5), which is linked to the mating-type-like (MTL) locus. Both are located on the Chr 5 left arm along with ERG11 (target of azoles). In this work, five groups of related isolates containing azole-susceptible and -resistant strains were analyzed for the TAC1 and ERG11 alleles and for Chr 5 alterations. While recovered ERG11 alleles contained known mutations, 17 new TAC1 alleles were isolated, including 7 hyperactive alleles with five separate new GOF mutations. Single-nucleotide-polymorphism analysis of Chr 5 revealed that azole-resistant strains acquired TAC1 hyperactive alleles and, in most cases, ERG11 mutant alleles by LOH events not systematically including the MTL locus. TAC1 LOH resulted from mitotic recombination of the left arm of Chr 5, gene conversion within the TAC1 locus, or the loss and reduplication of the entire Chr 5. In one case, two independent TAC1 hyperactive alleles were acquired. Comparative genome hybridization and karyotype analysis revealed the presence of isochromosome 5L [i(5L)] in two azole-resistant strains. i(5L) leads to increased copy numbers of azole resistance genes present on the left arm of Chr 5, among them TAC1 and ERG11. Our work shows that azole resistance was due not only to the presence of specific mutations in azole resistance genes (at least ERG11 and TAC1) but also to their increase in copy number by LOH and to the addition of extra Chr 5 copies. With the combination of these different modifications, sophisticated genotypes were obtained. The development of azole resistance in *C. albicans* is therefore a powerful instrument for generating genetic diversity.

Additional References

RELATED GEPHE

Related Genes

1 (TAC1) (<https://www.gephebase.org/search-criteria?/or+Taxon+ID=^5476^/and+Trait=Xenobiotic+resistance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

4 (<https://www.gephebase.org/search-criteria?/or+Gene+Gephebase=^ERG11+=CYP51A1^/and+Taxon+ID=^5476^/or+Gene+Gephebase=^ERG11+=CYP51A1^/and+Taxon+ID=^5476^#gephebase-summary-title>)

EXTERNAL LINKS

COMMENTS

