

TAC1 (https://www.gephebase.org/search-criteria?/and+GeneGephebase=^TAC1^#gephebase-summary-title)	Gephebase Gene	GP00001095	GepheID
Published	Entry Status	Martin	Main curator

	Trait Category
Physiology (#https://www.gephebase.org/search-criteria?/and+TraitCategory=~Physiology #gephebase-summary-title)	Trait
Xenobiotic resistance (drug) (#https://www.gephebase.org/search-criteria?/and+Trait=~Xenobiotic resistance (drug) #gephebase-summary-title)	Trait State in Taxon A
Candida albicans- drug sensitive	Trait State in Taxon B
Candida albicans- drug resistant	Ancestral State
Taxon A	Taxonomic Status
Intraspecific (#https://www.gephebase.org/search-criteria?/and+TaxonomicStatus=~Intraspecific #gephebase-summary-title)	

GENOTYPIC CHANGE

	Generic Gene Name	UniProtKB <i>Candida albicans</i>
TAC1	A7IZW4 (http://www.uniprot.org/uniprot/A7IZW4)	
	Synonyms	GenebankID or UniProtKB
TAC1-13; TAC1-19; TAC1-23	EU054337 (https://www.ncbi.nlm.nih.gov/nuccore/EU054337)	
	String	
-		
	Sequence Similarities	
-		
	GO - Molecular Function	
GO:0008270 : zinc ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0008270)		
GO:0003677 : DNA binding (https://www.ebi.ac.uk/QuickGO/term/GO:0003677)		
GO:0000981 : DNA-binding transcription factor activity, RNA polymerase II-specific (https://www.ebi.ac.uk/QuickGO/term/GO:0000981)		

GO:0006351 : transcription, DNA-templated
(<https://www.ebi.ac.uk/QuickGO/term/GO:0006351>)

GO:0005634 : nucleus (<https://www.ebi.ac.uk/QuickGO/term/GO:0005634>)

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

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

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

Nonsynonymous

A736V

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

Presumptive Null

Molecular Type

Aberration Type

SNP Coding Change

Molecular Details of the Mutation

Experimental Evidence

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

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 (ERG11 = CYP51A1) (<https://www.gephebase.org/search-criteria?/or+Taxon ID=~5476~/and+Trait=Xenobiotic resistance/and+groupHaplotypes=true#gephebase-summary-title>)

Related Haplotypes

6 (<https://www.gephebase.org/search-criteria?/or+Gene Gephebase=~TAC1~/and+Taxon ID=~5476~/or+Gene Gephebase=~TAC1~/and+Taxon ID=~5476~#gephebase-summary-title>)

EXTERNAL LINKS

COMMENTS