GEPHE SUMMARY

Gephebase Gene
TAC1

GephelD
GP00001094

Entry Status
Published

Main curator
Martin

PHENOTYPIC CHANGE

Trait Category
Physiology

Trait
Xenobiotic resistance (drug)

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

Taxon A

Latin Name
Candida albicans

Common Name
-

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; NCAIM Y.00971; NCYC 597; NCYC:597; NRRL Y-12983; NRRL:Y:12983; PYCC 3436; PYCC:3436; UAMH 8765; UAMH:8765; Candida albican

Rank
species

Lineage
cellular organisms; Eukaryota; Opisthokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Debaryomycetaceae; Candida/Lodderomyces clade; Candida

Parent
Candida () - (Rank: genus)

NCBI Taxonomy ID
5476

is Taxon A an Infraspecies?
No

Taxon B

Latin Name
Candida albicans

Common Name
-

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; NCAIM Y.00971; NCYC 597; NCYC:597; NRRL Y-12983; NRRL:Y:12983; PYCC 3436; PYCC:3436; UAMH 8765; UAMH:8765; Candida albican

Rank
species

Lineage
cellular organisms; Eukaryota; Opisthokonta; Fungi; Dikarya; Ascomycota; saccharomyceta; Saccharomycotina; Saccharomycetes; Saccharomycetales; Debaryomycetaceae; Candida/Lodderomyces clade; Candida

Parent
Candida () - (Rank: genus)

NCBI Taxonomy ID
5476

is Taxon B an Infraspecies?
No

GENOTYPIC CHANGE

Generic Gene Name
TAC1

Synonyms
TAC1-13; TAC1-19; TAC1-23

String
-

Sequence Similarities
-

GO - Molecular Function
GO:0008270 : zinc ion binding
GO:0003677 : DNA binding
GO:0000981 : DNA-binding transcription factor activity, RNA polymerase II-specific

GO - Biological Process
GO:0006351 : transcription, DNA-templated

UniProtKB Candida albicans
A7IZW4

GenebankID or UniProtKB
EU054337

GO - Cellular Component
GO:0005634 : nucleus

Presumptive Null
No

Molecular Type
Coding

Aberration Type
SNP

SNP Coding Change
Nonsynonymous

Molecular Details of the Mutation
G980E

Experimental Evidence
Association Mapping

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

Main Reference
Genotypic evolution of azole resistance mechanisms in sequential Candida albicans isolates. (2007)

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)
Related Haplotypes
6

EXTERNAL LINKS

COMMENTS