GEPHE SUMMARY

Gephebase Gene
ERG11 = CYP51A1

GephelD
GP00000282

Entry Status
Published

Main curator
Martin

PHENOTYPIC CHANGE

Trait Category
Physiology

Trait
Xenobiotic resistance

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
ERG11

Synonyms
CYP51; ERG16; CAALFM_C500660CA; CaO19.922

String
-

Sequence Similarities
Belongs to the cytochrome P450 family.

GO - Molecular Function
GO:0020037 : heme binding
GO:0005506 : iron ion binding
GO:0008144 : drug binding
GO:0008398 : sterol 14-demethylase activity

GO - Biological Process

UniProtKB Candida albicans (strain SC5314 / ATCC MYA-2876)
P10613

GenebankID or UniProtKB
EU819548

GO:0055114 : oxidation-reduction process
GO:0036187 : cell growth mode switching, budding to filamentous
GO:0035690 : cellular response to drug
GO:0006696 : ergosterol biosynthetic process
GO:0001766 : membrane raft polarization
GO:0016126 : sterol biosynthetic process
GO:0016125 : sterol metabolic process

GO - Cellular Component
GO:0016021 : integral component of membrane
GO:0005886 : plasma membrane
GO:0016020 : membrane
GO:0005783 : endoplasmic reticulum

Presumptive Null
No

Molecular Type
Coding

Aberration Type
SNP

SNP Coding Change
Nonsynonymous

Molecular Details of the Mutation
S405F

Experimental Evidence
Candidate Gene

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

Main Reference
Amino acid substitutions in the cytochrome P-450 lanosterol 14alpha-demethylase (CYP51A1) from azole-resistant Candida albicans clinical isolates contribute to resistance to azole antifungal agents. (1998)

Authors
Sanglard D; Ischer F; Koymans L; Bille J

Abstract
The cytochrome P-450 lanosterol 14alpha-demethylase (CYP51A1) of yeasts is involved in an important step in the biosynthesis of ergosterol. Since CYP51A1 is the target of azole antifungal agents, this enzyme is potentially prone to alterations leading to resistance to these agents. Among them, a decrease in the affinity of CYP51A1 for these agents is possible. We showed in a group of Candida albicans isolates from AIDS patients that multidrug efflux transporters were playing an important role in the resistance of C. albicans to azole antifungal agents, but without excluding the involvement of other factors (D. Sanglard, K. Kuchler, F. Ischer, J.-L. Pagani, M. Monod, and J. Bille, Antimicrob. Agents Chemother. 39:2378-2386, 1995). We therefore analyzed in closer detail changes in the affinity of CYP51A1 for azole antifungal agents. A strategy consisting of functional expression in Saccharomyces cerevisiae of the C. albicans CYP51A1 genes of sequential clinical isolates from patients was designed. This selection, which was coupled with a test of susceptibility to the azole derivatives fluconazole, ketoconazole, and itraconazole, enabled the detection of mutations in different cloned CYP51A1 genes, whose products are potentially affected in their affinity for azole derivatives. This selection enabled the detection of five different mutations in the cloned CYP51A1 genes which correlated with the occurrence of azole resistance in clinical C. albicans isolates. These mutations were as follows: replacement of the glycine at position 129 with alanine (G129A), Y132H, S405F, G464S, and R467K. While the S405F mutation was found as a single amino acid substitution in a CYP51A1 gene from an azole-resistant yeast, other mutations were found simultaneously in individual CYP51A1 genes, i.e., R467K with G464S, S405F with Y132H, G129A with G464S, and R467K with G464S and Y132H. Site-directed mutagenesis of a wild-type CYP51A1 gene was performed to estimate the effect of each of these mutations on resistance to azole derivatives. Each single mutation, with the exception of G129A, had a measurable effect on the affinity of the target enzyme for specific azole derivatives. We speculate that these specific mutations could combine with the effect of multidrug efflux transporters in the clinical isolates and contribute to different patterns and stepwise increases in resistance to azole derivatives.

Additional References

RELATED GEPHE

Related Genes
1 (TAC1)
Related Haplotypes
4

EXTERNAL LINKS

COMMENTS