

INFECTIOUS DISEASES (BACTERIAL, FUNGAL, VIRAL, PARASITIC, INFESTATIONS)

THE AFFECTS OF MUTATION AND/OR OVEREXPRESSION OF ERG3 AND EFG1 GENES ON THE AZOLES SUSCEPTIBILITIES OF CANDIDA ALBICANS

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Background: Transcription factor EFG1 can enhance the virulence of *Candida albicans*, yet it is not clear whether it will regulate the drug resistance and ERG3 gene of *Candida albicans*.

Objective: Investigate whether mutation and/or overexpression of ERG3 and EFG1 genes are involved in drug resistance to azoles in *Candida albicans*.

Materials and Methods: Totally 50 clinical isolates of *Candida albicans* are included in this study. Antimicrobial susceptibility tests, including fluconazole (FCA), itraconazole (ITR), and voriconazole (VRC), are performed by broth microdilution method. Mutations in the ERG3 and EFG1 genes sequence are detected. The mRNA levels of ERG3 and EFG1 were measured by RT-PCR. The correlation of the expression levels of ERG3 with EFG1 genes in susceptible isolates and resistant isolates is analyzed by Pearson's correlation analysis.

Results: Among 50 *Candida albicans* isolates, 44.00%, 56.00% and 50.00% isolates are resistant to FCA, ITR, and VRC, respectively. Sequencing results reveal that only 2 silent mutations were found in ERG3 genes of cross-resistant isolates, while 6 amino acid substitutions, including 5 azoles-susceptible isolates and 1 ITR-resistant isolates, are frequently found in EFG1 genes. The mRNA levels of ERG3 genes are significantly elevated in susceptible compared with *Candida albicans* resistant isolates, and EFG1 genes are significantly elevated in resistant compared with susceptible *Candida albicans* isolates. Furthermore, the mRNA level of ERG3 is negatively correlated with EFG1 in *Candida albicans* isolates.

Conclusions: The resistance to azoles may be associated with the mutations in ERG3 but not be made sure EFG1 genes in *Candida albicans* isolates. In addition, overexpressed ERG3 genes are found in susceptible *Candida albicans* isolates, and overexpressed EFG1 genes are found in resistant *Candida albicans* isolates. The mRNA levels of ERG3 genes



may be negatively correlated to EFG1 genes in resistant *Candida albicans* isolates.

