MD 627 994 Seminar in Medical Microbiology

Department of Microbiology, Faculty of Medicine, Khon Kaen University

Title: Contribution of mutations in ERG11 to Azole resistance in *Candida albicans*

Student: Mr. Tran Tuan Khoi Student ID: 657070021-9

Advisor: Assist. Prof. Kittipan Samerpitak

Date: July 02nd, 2024

Abstract

Candida albicans is a significant yeast responsible for various infections in humans known as candidiasis, ranging from minor oral and vaginal infections to severe systemic infections. Invasive candidiasis is particularly dangerous, with high rates of illness and mortality. Azoles are the primary antifungal drugs used for treatment, targeting the enzyme lanosterol 14-α-demethylase encoded by the ERG11 gene. However, resistance to antifungals, especially azoles, has increased in recent decades. Understanding the mechanisms and mutations causing this resistance is crucial for developing better treatments and diagnostics.

Urbanek et al[1]. used PCR and Sanger sequencing to study single nucleotide polymorphisms (SNPs) and point mutations in the ERG11 of *C. albicans* strains grown with glucose and lactate, with and without fluconazole (FLC). They identified 45 amino acid mutations, suspecting 15 might reduce FLC susceptibility, though no specific mutation was definitively linked to increased resistance.

Dovo et al[2]. collected *Candida* strains from vaginal swabs, testing antifungal susceptibility with the Kirby-Bauer disk diffusion method. They used conventional PCR to identify the mutant ERG11 gene in azole-resistant *C. albicans* isolates. Among 262 clinical strains, 157 were *C. albicans*, with the 92 resistance *C. albicans* to fluconazole. The mutated ERG11 gene was found in 9 of azole-resistant *C. albicans* strains, all showing co-resistance to azoles.

Majid et al[3]. investigated the expression of drug-resistance genes ERG11 and TAC1 in 50 *C. albicans* isolates from women with vulvovaginal candidiasis. Using the broth microdilution method, they found a 62% resistance rate to fluconazole. They measured gene expression changes with RT-PCR, finding significant differences between fluconazole-resistant and susceptible groups, and concluded that drug resistance in *C. albicans* is complex and influenced by multiple factors and mechanisms.

Overall, understanding the mechanisms behind antifungal drug resistance is essential and remains challenging.

References

1. Urbanek, A.K.; Łapi´nska, Z.; Derkacz, D.; Krasowska, A. The Role of ERG11 Point Mutations in the Resistance of *Candida albicans* to Fluconazole in the Presence of Lactate. **Pathogens 2022**, 11, 1289.
2. Dovo, E.E., Zohoncon, T.M., Tovo, S.F. et al. First detection of mutated ERG11 gene in vulvovaginal *Candida albicans* isolates at Ouagadougou/Burkina Faso. **BMC Infect Dis 22**, 678 (2022).
3. Zare-Bidaki, M., Maleki, A., Ghanbarzadeh, N. et al. Expression pattern of drug-resistance genes ERG11 and TAC1 in *Candida albicans* Clinical isolates. **Mol Biol Rep 49**, 11625–11633 (2022).