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The combined action of *ERG11* gene overexpression and its mutations in the development of *Candida albicans* resistance to triazolic antifungals

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Abstract

Introduction. Modern medicine is faced with the resistance of *Candida* spp. to antimycotics, due to changes in the expression and structure of the *ERG11* gene, the molecular target of triazoles. These mechanisms often operate simultaneously, but the interaction between them remains poorly understood.

The aim of this study is to investigate the interaction between *ERG11* gene overexpression and mutation in the development of triazole resistance in *C. albicans*.

Materials and methods. Eleven *C. albicans* strains from the G.N. Gabrichevsky Moscow Research Institute of Epidemiology culture collection were analyzed. Each strain was characterized by its *ERG11* gene expression level, the presence of *ERG11* mutations, and its susceptibility to the triazoles posaconazole, voriconazole, itraconazole and fluconazole.

Results. The *C. albicans* strains (*n* – number of tested strains) were categorized into four groups: Group 1 (*n* = 2, *ERG11* overexpression only), Group 2 (*n* = 3, ERG11 mutations only), Group 3 (*n* = 4, both *ERG11* overexpression and mutation) and Group 4 (*n* = 2, neither *ERG11* overexpression nor mutation). The minimum inhibitory concentration (MIC) of Triazoles in Group 1 was 15.76-fold higher than in Group 2, 4.97-fold higher than in Group 3, and 2.51-fold lower than in Group 4 ($p < 0.05$ for all comparisons). The MIC of triazoles in Group 2 was 3.17-fold lower than in Group 3 and 40.00-fold lower than in Group 4 ($p < 0.001$). The MIC of triazoles in Group 3 was 12.5-fold lower than in Group 4 ($p < 0.001$). Population-level variation in triazoles MIC was more strongly influenced by the isolated effect of *ERG11* mutations (45.94%) than by the isolated effect of *ERG11* overexpression (5.27-fold less).

Conclusion. Triazole resistance in *C. albicans* is influenced by the combined actions of *ERG11* overexpression and mutation. *ERG11* overexpression appears to contribute more to the absolute level of resistance, while *ERG11* mutations have a greater impact on the diversity of resistance levels within the *C. albicans* population.

Keywords: *Candida albicans, antimycotics, resistance, ERG11 gene, overexpression, mutations*

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ORIGINAL RESEARCHES

Оригинальное исследование
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Сочетанное действие гиперэкспрессии и мутаций гена *ERG11* при формировании резистентности *Candida albicans* к триазоловым противогрибковым препаратам

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Аннотация

Введение. Современная медицина сталкивается с резистентностью *Candida* spp. к антимикотикам, обусловленной изменением экспрессии и структуры гена *ERG11* — молекулярной мишени триазолов. Эти механизмы часто действуют одновременно, однако взаимодействие между ними остаётся недостаточно изученным.

Цель работы — изучение роли гиперэкспрессии гена *ERG11* и его мутаций в формировании резистентности грибов *C. albicans* к триазолам.

Материалы и методы. Исследование выполнено на 11 штаммах грибов *C. albicans* из коллекции МНИИЭМ им. Г.Н. Габричевского. Штаммы были охарактеризованы по уровню экспрессии гена *ERG11* и наличию в нем мутаций, а также чувствительности к триазолам: позаконазолу, вориконазолу, итраконазолу и флуконазолу.

Результаты. Штаммы *C. albicans* подразделили на 4 группы: 1-я группа — только с повышенной экспрессией гена *ERG11*; 2-я — только с мутациями в данном гене; 3-я — одновременно оба вида генетических изменений; 4-я — без данных генетических изменений. Установлено, что минимальная подавляющая концентрация (МПК) триазолов в 1-й группе была в 15,76 раза выше, чем во 2-й, в 4,97 раза выше, чем в 3-й, и в 2,51 раза ниже, чем в 4-й (везде $p < 0,05$). Во 2-й группе МПК триазолов была в 3,17 раза ниже, чем в 3-й, и в 40 раз ниже ($p < 0,001$), чем в 4-й. МПК триазолов в 3-й группе по сравнению с 4-й группой была в 12,5 раза ниже ($p < 0,001$). Популяционное варьирование МПК триазолов в большей степени зависит от изолированного действия мутаций гена *ERG11* (45,94%), что в 5,27 раза превосходит эффект изолированной гиперэкспрессии гена.

Заключение. Устойчивость *C. albicans* к триазолам обеспечивается кооперативным действием гиперэкспрессии и мутаций гена *ERG11*: наибольшую резистентность обеспечивает гиперэкспрессия, популяционное разнообразие — мутации.

Ключевые слова: *Candida albicans, антимикотики, резистентность, ген ERG11, гиперэкспрессия, мутации*

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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Introduction

Microbial resistance to chemotherapeutic drugs is a longstanding challenge in modern medicine. While numerous mechanisms of antibiotic resistance are well-characterized, including those genetically encoded that increase antibiotic target production or alter target structure, the interplay of these mechanisms remains poorly understood [1–3]. These resistance mechanisms can operate independently or concurrently within a microbial cell, and the consequences of their combined effects require further investigation.

We investigated this issue using *Candida* species as a model, given their well-documented resistance to antimicrobial drugs. One resistance mechanism involves increased expression of genes encoding drug targets, notably *ERG11*, which encodes lanosterol 14α-demethylase. This enzyme is crucial for ergosterol biosynthesis, a key component of the fungal cell wall. *ERG11* overexpression leads to increased ergosterol production, rendering *Candida* species insensitive to therapeutic azole concentrations [4].

However, recent studies have identified non-synonymous *ERG11* mutations that modulate its effects, impacting Candida's triazole susceptibility both positively and negatively [5–9]. Our data [10] show that certain *ERG11* mutations mitigated the effects of overexpression, reducing the Minimal Inhibitory Concentration (MIC) of triazole drugs in mutant Candida albicans strains by up to 100-fold. Complete reversal of resistance, however, was not observed. It is important to note that *ERG11* overexpression and mutations appear to manifest relatively independently across different *Candida* spp. [5, 7–9, 11–15].

Both *ERG11* overexpression and mutation clearly contribute to the population-level diversity in azole sensitivity observed in Candida species. However, the precise nature and outcome of the interaction between these mechanisms remain unclear. Investigating this interaction is crucial for understanding the survival strategies employed by *Candida* spp. under conditions of widespread drug exposure and may reveal promising avenues for combating the growing problem of antimicrobial resistance.

Therefore, **the aim** of this study was to investigate the interaction between *ERG11* overexpression and mutation in the development of triazole resistance in *C. albicans*.

Materials and methods

The study was conducted on 11 *C. albicans* strains from the collection of the G.N. Gabrichevsky Moscow Research Institute of Epidemiology and Microbiology (Rospotrebnadzor), which were initially resistant to the effects of fluconazole and voriconazole.

Strain identification was performed using biochemical assays and real-time multiplex polymerase chain reaction (qPCR), along with *ERG11* expression level analysis and mutation screening. A detailed description of the methodology is provided in another study [10].

According to the available characterization, 7 of the studied strains were carriers of 5 variants of non-synonymous mutations in the *ERG11* gene (*E266D*, *G464S*, *I471L*, *D116E*, and *V488I*), while 6 strains showed *ERG11* overexpression.

Based on these genetic characteristics, *C. albicans* strains were divided into 4 groups: Group 1 (n=2)—strains with only *ERG11* overexpression; Group 2 (n = 3) — strains with only *ERG11* mutations; Group 3 (n = 4) — strains with simultaneous expression of both types of genetic alterations; Group 4 (n = 2) — strains without either of the genetic alterations.

The sensitivity of the studied *C. albicans* strains to four representatives of triazole antifungals (posaconazole, voriconazole, itraconazole, fluconazole) was investigated in accordance with the recommendations of the Interregional Association for Clinical Microbiology and Antimicrobial Chemotherapy (IACMAC) for determining the sensitivity of microorganisms to antimicrobial agents, based on CLSI M44 and M60 standards for fungi and the standards and criteria of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for microdilution methods and bacterial cultures[1].

The minimum inhibitory concentrations (MIC, mg/mL) were determined by the serial microdilution method using the Sensititre YeastOne plates (Trek diagnostic system). For this, the inoculum was prepared similarly to the disk diffusion method, after which it was introduced into a modified RPMI-1640 medium and distributed into 96-well plates for serial microdilutions with previously added triazole antifungals [11]. The results were recorded visually, comparing the growth in the well with the positive control well according to EUCAST criteria [12].

To ensure the comparability of the research results, the data for individual *C. albicans* strains for each triazole antifungal were weighted by the average MIC value for the given drug. Subsequently, the obtained relative values were analyzed.

Statistical analyses were conducted using Microsoft Excel, SciPy and Matplotlib. The significance of the differences was assessed using the Mann–Whitney U-test. The contribution of factors to the population variability of the trait was assessed using single-factor and two-factor ANOVA. The critical error level for testing statistical hypotheses was set at $p < 0.05$.

Results

The MIC of triazole antifungals with various genetic modifications in *C. albicans* is presented in **Table 1**.

[1] IACMAC Recommendations "Determination of the sensitivity of microorganisms to antimicrobial drugs (2021)». URL: https://www.antibiotic.ru/minzdrav/category/clinical-recommendations

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Table 1. MIC of triazole antifungals in various genetic modifications in the *ERG11* gene of *C. albicans* ($X \pm m$)

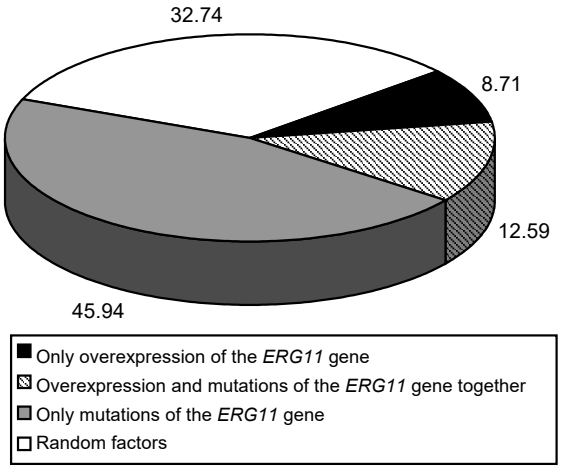
Strain group	*n*	Posaconazole	Voriconazole	Itraconazole	Fluconazole
1	2	1.361 ± 1.351	1.184 ± 1.045	1.363 ± 1.353	1.579 ± 1.483
2	3	0.008 ± 0.002	0.139 ± 0.000	0.008 ± 0.002	0.191 ± 0.000
3	4	0.028 ± 0.019	0.383 ± 0.244	0.026 ± 0.020	0.669 ± 0.317
4	2	4.068 ± 1.357	3.343 ± 1.115	4.075 ± 1.359	2.296 ± 0.765

Statistical analysis revealed no significant differences between the individual drugs for each variant of genetic alterations, indicating a uniform directional effect across all triazoles. Due to this fact, the results of the MIC study were pooled into a single group of triazoles. The defining characteristics of each group are presented in **Table 2**.

Comparative analysis of the obtained results showed that the MIC of triazoles in Group 1 was 15.76 times higher ($p < 0.05$) than in Group 2, 4.97 times higher ($p < 0.05$) than in Group 3, and 2.51 times lower ($p < 0.05$) than in Group 4. In Group 2, the MIC of triazoles was 3.17 times lower than in Group 3, and 40 times lower ($p < 0.001$) than in Group 4. The MIC of triazoles in Group 3 was 12.5 times lower ($p < 0.001$) compared to Group 4.

The assessment of the impact of various genetic alterations on the degree of variation in the MIC of triazoles in the studied *C. albicans* population was conducted using analysis of variance (ANOVA). The single-factor model showed that the combined effect of *ERG11* overexpression and mutation amounts to 58.58% ($p < 0.001$) of the total variance.

A two-factor ANOVA was performed to quantify the relative impact of these genetic alterations (**Figure**). The isolated effect of *ERG11* mutations accounted for almost half (45.94%) of the genetic variance, which is more than 5.27 times greater than the contribution of the isolated effect of *ERG11* overexpression and 3.65 times greater than the combined effect of mutations and overexpression. Taken together, the combined effect of all genetic alterations accounts for 67.26%, which is consistent with the findings of the single-factor ANOVA model.



Two-factor model of the influence of genetic alterations in the *ERG11* gene on the variation of triazole MIC in the *C. albicans* population, %.

Table 2. MIC of triazole antifungals in the studied groups

Strain group	*n*	$X \pm m$	Me [Q_1; Q_3]
1	8	1.371 ± 0.501	1.184 [0.010; 2.470]
2	12	0.087 ± 0.024	0.075 [0.007; 0.139]
3	16	0.276 ± 0.113	0.112 [0.006; 0.152]
4	8	3.445 ± 0.522	2.889 [1.879; 3.759]

Discussion

This study confirms that both *ERG11* overexpression and *ERG11* mutations contribute to triazole resistance in *C. albicans* strains initially resistant to fluconazole and voriconazole. It is further demonstrated that these genetic mechanisms can act independently or synergistically in conferring resistance. While *ERG11* overexpression generally exerts a more pronounced effect than *ERG11* mutations alone, as confirmed in several previous studies [4-9, 16, 17], their interaction is complex.

Although an additive effect of *ERG11* overexpression and mutations might be anticipated, our data reveal that certain mutations can attenuate the impact of *ERG11* overexpression. This resulted in a noticeable reduction in the overall effect of *ERG11* overexpression in our *C. albicans* strain collection. However, it is not recommended to generalize this observation to all instances of genetically mediated resistance in *C. albicans*; rather, this finding is interpreted as a potential characteristic specific to the strains included in this study.

The observation of high triazole resistance in *C. albicans* strains lacking *ERG11* alterations suggests that other resistance mechanisms are also operative. For example, overexpression of efflux pump genes, such as *CDR1*, *CDR2* and *MDR1*, has been reported [4, 5], although their relative contributions to resistance remain to be fully quantified.

The analysis of variance accounted for the contribution of both *ERG11* overexpression and mutation to the population-level variation in triazole susceptibility among *C. albicans* strains. While both mechanisms

contribute, the results indicate that *ERG11* mutations play a dominant role in shaping this phenotypic diversity.

Evaluating the biological and medical significance of the overexpression and mutations of the *ERG11* gene in *C. albicans* strains, it was observed that *ERG11* overexpression and the associated lanosterol-14α-demethylase hyperproduction serve as a far more effective defense mechanism against the harmful effects of triazole antifungals than the synthesis of genetically modified enzyme variants. However, non-synonymous point mutations in *ERG11* clearly contribute to the increased biological diversity of this yeast-like fungus, without necessarily causing a dramatic, short-term increase in its clinical threat. Therefore, from a practical perspective, identifying *ERG11* overexpression may be a more appropriate initial strategy for predicting the immediate risk of triazole resistance in *C. albicans* isolates.

Conclusion

1. Triazole resistance in *C. albicans* strains arises from the combined effects of *ERG11* overexpression and mutation.

2. *ERG11* overexpression has a significantly greater impact on resistance levels than its non-synonymous mutations.

3. Mutations within the *ERG11* gene are a more significant driver of population-level triazole resistance diversity in *C. albicans* than *ERG11* overexpression.

4. It is recommended to test strains for *ERG11* overexpression to predict the emergence of triazole resistance in *C. albicans*.

СПИСОК ИСТОЧНИКОВ | REFERENCES

1. Xiong L., Wang X., Wang Y., et al. Molecular mechanisms underlying bacterial resistance to ceftazidime/avibactam. *WIREs Mech. Dis.* 2022;14(6):e1571. DOI: https://doi.org/10.1002/wsbm.1571
2. Azargun R., Gholizadeh P., Sadeghi V., et al. Molecular mechanisms associated with quinolone resistance in *Enterobacteriaceae*: review and update. *Trans. R. Soc. Trop. Med. Hyg.* 2020; 114(10):770–81. DOI: https://doi.org/10.1093/trstmh/traa041
3. Gogry F.A., Siddiqui M.T., Sultan I., Haq Q.M.R. Current update on intrinsic and acquired colistin resistance mechanisms in bacteria. *Front. Med. (Lausanne).* 2021;8:677720. DOI: https://doi.org/10.3389/fmed.2021.677720
4. Biswas C., Chen S.C., Halliday C., et al. Identification of genetic markers of resistance to echinocandins, azoles and 5-fluorocytosine in *Candida glabrata* by next-generation sequencing: a feasibility study. *Clin. Microbiol. Infect.* 2017;23(9):676.e7–10. DOI: https://doi.org/10.1016/j.cmi.2017.03.014
5. Cernicka J., Subik J. Resistance mechanisms in fluconazole-resistant *Candida albicans* isolates from vaginal candidiasis. *Int. J. Antimicrob. Agents.* 2006;27(5):403–8. DOI: https://doi.org/10.1016/j.ijantimicag.2005.12.005
6. Lim H.J., Shin J.H., Kim M.N., et al. Evaluation of two commercial broth microdilution methods using different interpretive criteria for the detection of molecular mechanisms of acquired azole and echinocandin resistance in four common *Candida* species. *Antimicrob. Agents Chemother.* 2020;64(11):e00740-20. DOI: https://doi.org/10.1128/AAC.00740-20
7. Lopes W., Vainstein M.H., Schrank A. Revealing colonial characteristics of *Candida tropicalis* by high-resolution scanning electron microscopy. *Clin. Microbiol. Infect.* 2019;25 (2):188–9. DOI: https://doi.org/10.1016/j.cmi.2018.06.032
8. Pappas P.G., Kauffman C.A., Andes D.R., et al. Clinical practice guideline for the management of candidiasis: 2016 update by the infectious diseases society of America. *Clin. Infect. Dis.* 2016;62(4):e1–50. DOI: https://doi.org/10.1093/cid/civ933
9. Castanheira M., Deshpande L.M., Messer S.A., et al. Analysis of global antifungal surveillance results reveals predominance of Erg11 *Y132F* alteration among azole-resistant *Candida parapsilosis* and *Candida tropicalis* and country-specific isolate dissemination. *Int. J. Antimicrob. Agents*. 2020;55(1):105799. DOI: https://doi.org/10.1016/j.ijantimicag.2019.09.003
10. Несвижский Ю.В., Афанасьев С.С., Воропаев А.Д. и др. Спектр и функциональные свойства мутаций гена *ERG11* флуконазол-резистентныйх грибов *Candida albicans*, выделенных от ВИЧ-инфицированных пациентов. *Журнал микробиологии, эпидемиологии и иммунобиологии. 2023;*100(4):285–92. Nesvizhsky Yu.V., Afanasiev S.S., Voropaev A.D., et al. Spectrum and functional properties of ERG11 gene mutations in fluconazole-resistant *Candida albicans* strains isolated from HIV-infected patients. *Journal of Microbiology, Epidemiology and Immunobiology.* 2023;100(4):285–92. DOI: https://doi.org/10.36233/0372-9311-407 EDN: https://elibrary.ru/pxrovi
11. Godinho C.P., Sá-Correia I. Physiological genomics of multistress resistance in the yeast cell model and factory: aocus on MDR/MXR transporters. In: Sá-Correia I., eds. *Yeasts in Biotechnology and Human Health. Progress in Molecular and Subcellular Biology, Volume 58.* Cham;2019:1–35. DOI: https://doi.org/10.1007/978-3-030-13035-0_1
12. Xu Y., Chen L., Li C. Susceptibility of clinical isolates of *Candida* species to fluconazole and detection of *Candida albicans* ERG11 mutations. *J. Antimicrob. Chemother.* 2008;61(4):798-804. DOI: https://doi.org/10.1093/jac/dkn015
13. Kakeya H., Miyazaki Y., Miyazaki H., et al. Genetic analysis of azole resistance in the Darlington strain of *Candida albicans*. *Antimicrob. Agents Chemother.* 2000;44(11):2985–90. DOI: https://doi.org/10.1128/AAC.44.11.2985-2990.2000
14. Finkina E.I., Bogdanov I.V., Ignatova A.A., et al. Antifungal activity, structural stability, and immunomodulatory effects on human immune cells of defensin from the lentil *Lens culinaris*. *Membranes (Basel)*. 2022;12(9):855. DOI: https://doi.org/10.3390/membranes12090855
15. Lee Y., Puumala E., Robbins N., Cowen L.E. Antifungal drug resistance: molecular mechanisms in *Candida albicans* and beyond. *Chem. Rev.* 2021;121(6):3390–411. DOI: https://doi.org/10.1021/acs.chemrev.0c00199
16. Katsipoulaki M., Stappers M.H.T., Malavia-Jones D., et al. *Candida albicans* and *Candida glabrata*: global priority pathogens. *Microbiol. Mol. Biol. Rev.* 2024;88(2):e0002123. DOI: https://doi.org/10.1128/mmbr.00021-23
17. Mahdizade A.H., Hoseinnejad A., Ghazanfari M., et al. The *TAC1* gene in *Candida albicans*: structure, function, and role in azole resistance: a mini-review. *Microb. Drug Resist.* 2024;30(7): 288–96. DOI: https://doi.org/10.1089/mdr.2023.0334

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