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Azole resistance in *aspergillus fumigatus*: Virulence evaluation in invertebrate models.

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Introduction

The emergence of azole resistance in *Aspergillus fumigatus*, a ubiquitous environmental mold and opportunistic human pathogen, poses a growing threat to global health. Azoles—especially itraconazole, voriconazole, and posaconazole—are frontline antifungal agents used to treat invasive aspergillosis. However, resistance to these drugs has been increasingly reported, complicating treatment outcomes and raising concerns about environmental and clinical drivers of resistance. To better understand the pathogenic potential of resistant strains, invertebrate models such as *Galleria mellonella* (wax moth larvae) and *Caenorhabditis elegans* have emerged as valuable tools for virulence evaluation [1].

Azole resistance in *A. fumigatus* is primarily driven by mutations in the cyp51A gene, which encodes the target enzyme 14α-demethylase. Common mutations include TR34/L98H and TR46/Y121F/T289A, often associated with environmental exposure to agricultural azole fungicides. These mutations reduce drug binding affinity, rendering treatment ineffective. Resistance can also arise through overexpression of efflux pumps, biofilm formation, and stress response pathways. Epidemiological studies have documented resistant strains in soil, compost, and hospital environments, suggesting a dual origin—environmental and clinical—for resistance development [2].

Invasive aspergillosis primarily affects immunocompromised individuals, including those undergoing chemotherapy, organ transplantation, or suffering from chronic lung diseases. Azole-resistant *A. fumigatus* infections are associated with higher mortality rates, prolonged hospital stays, and limited therapeutic options. Amphotericin B and echinocandins serve as alternatives, but they come with increased toxicity and reduced efficacy against certain fungal forms. Early detection of resistance is crucial. Molecular diagnostics targeting cyp51A mutations and antifungal susceptibility testing are recommended for high-risk patients. However, these methods are not universally available, especially in resource-limited settings [3].

Traditional mammalian models, while informative, are costly, ethically complex, and time-consuming. Invertebrate models offer a practical alternative for high-throughput virulence screening and antifungal efficacy testing. The wax moth larva has gained popularity due to its ease of handling, low maintenance, and innate immune system that mimics aspects of mammalian immunity. Larvae can be infected via injection, and survival curves, melanization, and histopathology provide insights into fungal virulence. Studies have shown that azole-resistant strains of *A. fumigatus* exhibit variable virulence in *G. mellonella*. Some resistant isolates retain full pathogenic potential, while others show attenuated virulence, suggesting that resistance mechanisms may incur fitness costs [4].

This nematode model is genetically tractable and suitable for studying host-pathogen interactions. *C. elegans* can be exposed to fungal spores on agar plates, and endpoints such as survival, locomotion, and reproductive output are measured. Although less commonly used for filamentous fungi, *C. elegans* has demonstrated utility in assessing fungal toxicity and immune responses. Its transparent body allows for real-time imaging of fungal invasion and host defense activation. Virulence in

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A. fumigatus is multifactorial, involving thermotolerance, conidial surface proteins, proteases, and secondary metabolites like gliotoxin. Azole resistance may influence the expression of these factors. Transcriptomic analyses reveal that resistant strains often upregulate stress response genes and downregulate metabolic pathways, potentially affecting virulence. For example, the TR34/L98H mutation has been linked to altered cell wall composition and immune evasion. Invertebrate models help dissect these changes by providing a controlled environment to compare wild-type and resistant strains under identical conditions [5].

Conclusion

Azole resistance in *Aspergillus fumigatus* represents a formidable challenge in clinical mycology. Invertebrate models such as *Galleria mellonella* and *C. elegans* offer powerful platforms to evaluate the virulence of resistant strains and test antifungal strategies. As resistance continues to rise, integrating these models into research pipelines will be essential for understanding fungal pathogenesis and guiding therapeutic development.

References

1. HerniaSurge Group. International guidelines for groin hernia management. Hernia. 2018;22(1):1-165.
2. Kingsnorth A, LeBlanc K. Hernias: inguinal and incisional.Lancet. 2003;362:1561-71.
3. Köckerling F, Sheen AJ, Berrevoet F, et al. The reality of general surgery training and increased complexity of abdominal wall hernia surgery. Hernia. 2019;23(6):1081-91.
4. Chibata M, Daronch OT. Assessment of postoperative risk of complications on inguinal hernioplasty and its relation to risk factors. Rev Assoc Med Bras (1992). 2020;66(5):623-29.
5. Stylianides N, Slade DA. Abdominal wall reconstruction. Br J Hosp Med (Lond). 2016;77(3):151-6.

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