DMykG

Deutschsprachige Mykologische Gesellschaft

ÖGMM

60th Scientific Conference of the German-speaking Mycological Society (DMykG) e. V.

ABSTRACTS



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Myk2026

17–19 September | Graz

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Talks

Session 1 • Clinical management of acute and chronic fungal diseases

S1-03

Invasive candidiasis in 2024–2026: treatment patterns and outcomes in a multinational real-world cohort

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Objectives

Invasive *Candida* infection causes significant morbidity and mortality, particularly among immunocompromised and critically ill patients. The FungiScope *Candida* Campaign collects real-world data on risk factors, management, and outcomes across various centers worldwide.

Materials & Methods

Anonymized patient data were collected via an online questionnaire (Clinicalsurveys.net and Carelane.io). Only adult patients with invasive *Candida* infection diagnosed between 2024 and 2025 were included in the study.

Results

As of April 2026, 2535 patients were enrolled (median age 67 years [range 18–102]; 62.2% male). The majority of cases originated from Germany (n = 1214), followed by Spain (n = 504) and United States (n = 417).

Among the patients included, central venous catheter use (60.0%) was the most prevalent risk factor, followed by chronic cardiovascular disease (44.3%), hematological or oncological disease (39.4%) and major surgery (33.1%). Only 2.3% of patients had no identified underlying condition.

First-line treatment was dominated by caspofungin (49%), followed by fluconazole (17.4%) and anidulafungin (16.8%), with notable variation across countries. Caspofungin predominated in Germany (75.7%), anidulafungin in Spain (45.1%), micafungin in the US (60.4%), and fluconazole in Austria (42.5%). Rezafungin was predominantly used as a salvage option, accounting for 0.4% of first-line and 5.5% of second-line cases. Cox regression analysis revealed that first-line antifungal choice influenced survival ($p<0.001$), with fluconazole associated with lower mortality risk (HR=0.734) compared to anidulafungin (HR=1.277) and micafungin (HR=1.295), and cumulative survival declining steeply within the first 100 days to approximately 40%.

Conclusion

Invasive *Candida* infections predominantly affected high-risk patients, with caspofungin as the most used first-line agent globally, although fluconazole was associated with lower mortality risk compared to echinocandins.

Session 2 • Fungal virulence and impact of climate change

S1-04

ECMM Candida IV – epidemiology, species distribution, and clinical outcomes in candidemia caused by non-*albicans Candida* species

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Objectives

For over 25 years, the European Confederation of Medical Mycology (ECMM) has conducted multicentre studies on invasive *Candida* infections, documenting shifts in species distribution, rising antifungal

resistance, and persistently high mortality rates. Building on this, the ongoing ECMM Candida IV study collects global data exclusively on blood-culture-proven candidemia caused by non-*albicans Candida* species.

Methods & Materials

Patient data has been collected from 81 hospitals globally, with no limit on the number of participating centres or cases submitted. The observation period ran from April 1, 2024 to September 30, 2025, followed by a phase for data entry and shipment of isolates. The primary objectives are to analyse epidemiological trends and evaluate patient outcomes.

Results

By the end of April 2026, data had been provided by 81 hospitals from 35 countries. To date, 2019 patient entries have been completed. Preliminary outcomes show a demographic breakdown of 59% male and 41% female patients. The age distribution is: 3.7% < 18 years, 3.1% 19-29 years, 10.4% 30-49 years, 36.7% 50–69 years, 42.4% 70–89 years, and 3.6% >90 years. The majority of infections were caused by *Candida parapsilosis* (33.7%), followed by *Nakaseomyces glabrata*(32.0%), *Candida tropicalis* (11.8%) and *Candida auris* (9.6%). The species distribution and participating countries are shown in Figures 1 and 2. 48.7% of patients were in the ICU at the time of the first positive blood culture. The 30-day mortality was 41.4% (801/1934 patients) and 180-day mortality was 66.4% (1100/1657 patients).

Conclusion

The ECMM Candida IV study is the first global, multicentre study focusing exclusively on non-*albicans Candida* species. Preliminary results show the distribution of age, sex and species as well as a persistently high 180-day mortality rate.

Figure 1 Preliminary overview of participating countries and number of enrolling hospitals (April 2026).

Figure 2 Reported fungal species (%).

Figure 1

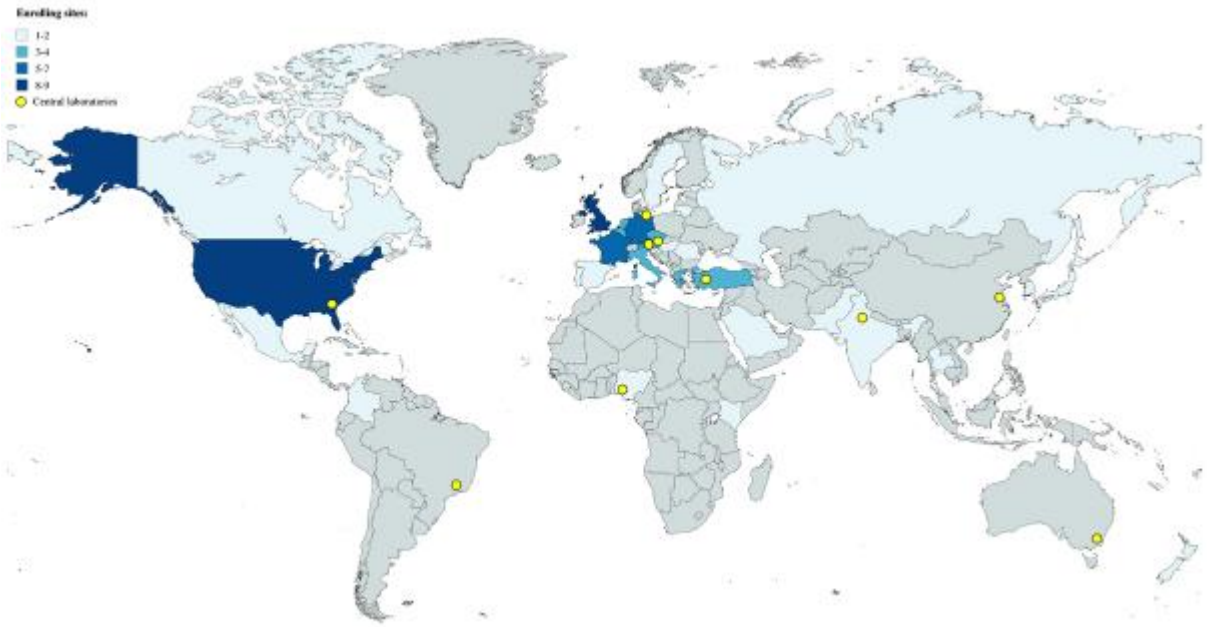
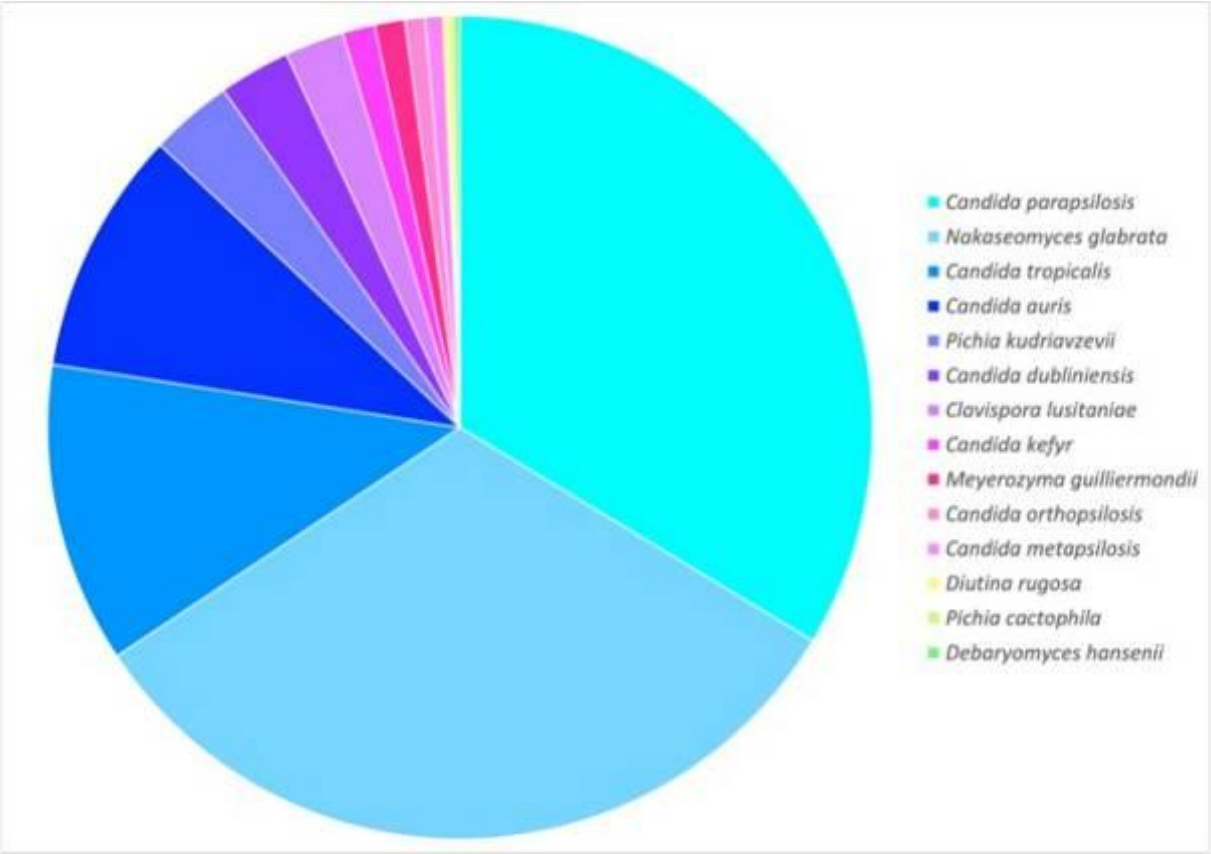


Figure 2



S2-02

Heme availability impacts azole susceptibility and ergosterol biosynthesis in *Aspergillus fumigatus*

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Introduction

Aspergillus fumigatus is a major fungal pathogen, with rising azole resistance threatening first-line therapy. Azoles target the heme-containing sterol C14-demethylase Cyp51 in ergosterol biosynthesis, linking heme metabolism to azole efficacy. Heme biosynthesis depends on iron and oxygen, thereby connecting cofactor availability to sterol homeostasis and azole susceptibility. Emerging evidence further associates elevated intracellular heme levels with itraconazole resistance, highlighting heme metabolism as a potential driver of antifungal resistance.

Objectives

We aim to investigate the role of heme biosynthesis in regulating sterol homeostasis and azole susceptibility in *A. fumigatus*.

Materials & Methods

Conditional gene expression mutants targeting distinct steps of the heme biosynthetic pathway were generated using CRISPR/Cas9-mediated genome editing. Fungal growth, sterol profiles, and antifungal susceptibility were assessed under controlled modulation of heme-gene expression. In parallel, we examined how iron limitation and hypoxic conditions constrains heme-dependent processes.

Results

Disruption of heme biosynthesis impairs growth, alters sterol composition similar to azole treatment, and markedly increases azole susceptibility. Conversely, overexpression of a key pathway component promotes azole resistance. We are currently investigating the mechanistic basis of this relationship, focusing on how heme availability influences sterol homeostasis and antifungal stress adaptation, and how iron limitation and hypoxia further modulate these heme-dependent effects.

Conclusion

Intracellular heme is a critical determinant of azole susceptibility in *A. fumigatus*, coordinating sterol metabolism and antifungal stress responses. Targeting heme biosynthesis may represent a promising therapeutic avenue and strategy to overcome antifungal resistance.

S2-03

Antifungal susceptibility and condition-dependent proteomic profiling of *Neocosmospora keratoplastica* from clinical and environmental origins

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Introduction

N. keratoplastica, member of the *Fusarium solani* species complex (FSSC), is an emerging opportunistic pathogen of increasing clinical relevance.

Objectives

This study aimed to investigate distribution, antifungal susceptibility, and condition-dependent proteomic profile of clinical and environmental *N. keratoplastica* isolates.

Materials & Methods

A total of 28 isolates were analysed, including clinical strains (n=12) from Croatia and Austria and environmental isolates (n=16) from drain systems. Identification was performed using ITS, *TEF1* and *RPB2* sequencing; MALDI-TOF reliably assigned isolates to the FSSC. Antifungal susceptibility to amphotericin B, voriconazole, posaconazole, isavuconazole, olorofim and manogepix was assessed using CLSI guidelines. For proteomics, one clinical and one environmental strain were cultured in SDB and RPMI (±HS) at 25°C, 37°C and 37°C + CO_2, followed by analysis using TripleTOF® 6600+ (Sciex).

Results

Most isolates showed high MICs to azoles. Amphotericin B showed MIC ranged from 1–8 mg/L, with one isolate >16 mg/L. Olorofim showed limited efficacy (MIC<16 mg/L). Manogepix exhibited low MIC50 values in most isolates, ranging from <0.03–1 mg/L (n=18), with higher values observed in a smaller subset (2–4 mg/L, n=2; 8–16 mg/L, n=5). Proteomic analysis identified more than 750 proteins, including those involved in cell wall integrity and host interaction (WSC, CFEM), stress response (SOD, Hsp), signalling (calmodulin, MAPK), intracellular trafficking (SEC), transport (MFS, ABC) and

secondary metabolism (PKS-EN). Several proteins/isoforms appeared exclusively at 37 °C, indicating temperature-driven proteostasis and stress adaptation.

Conclusion

N. keratoplastica exhibits proteomic adaptation to environmental and host-like conditions with conserved core functions and strain-dependent differences. Its widespread presence and azole resistance underline clinical relevance, while manogepix shows therapeutic potential.

Acknowledgement: The research was funded by the Croatian Science Foundation (HRZZ-IP-2022-10-8062).

S2-04

ARGiS – Azole-Resistant fungi: Gradients in Soils

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Fungal pathogens threaten human life directly and indirectly as they are responsible for about 1.5 million human deaths annually and for up to 30% pre- and post-harvest yield losses[1]. Azoles are antimycotic agents used in both, agriculture and medicine. This dual use harbors the risk of cross-resistance development within azole antifungals[2]. Azoles inhibit the lanosterol 14α-demethylase (Cyp51) in the ergosterol biosynthesis and hence influence cell wall stability. Resistances were found to be due to mutations in the encoding gene *cyp51*, besides overexpression of the Cyp51 and drug efflux pumps[3]. The development of azole resistance has been linked to the exposure of fungi to azoles in agriculture[2]. Yet, the role of other environmental factors and azole burden as well as the diversity of azole resistant fungi in soils remain unclear and will therefore be assessed in this work by culture-based and molecular approaches. So far, we isolated 300 azole resistant morphotypes from over 1000 azole resistant isolates. Azole resistant isolates have been retrieved from all studied soils no matter the land-use and represent a variety of fungal taxa and some yet undescribed species. In our further research we aim to establish a soil functional biodiversity index for resistance by correlating azole burden, abiotic soil parameters, fungal biodiversity and diversity of the *cyp51*.

1. Stukenbrock, E. G. S. Address the growing urgency of fungal disease in crops. *Nature* **617**, 31–34 (2023).

2. Verweij, P. E. *et al.* Dual use of antifungals in medicine and agriculture: How do we help prevent resistance developing in human pathogens? *Drug Resistance Updates* **65**, 100885 (2022).

3. Dladla, M., Gyzenhout, M., Marias, G. & Ghosh, S. Azole resistance in Aspergillus fumigatus-comprehensive review. *Archives of Microbiology* vol. 206 Preprint at https://doi.org/10.1007/s00203-024-04026-z (2024).

S2-05

Macrophage inflammatory responses shape *C. albicans* adaptations to host-imposed stresses

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Adaptation to new host niches and changing environments is crucial for microbial success and persistence within the host. *Candida albicans* is an opportunistic pathogen which commonly colonizes mucosal surfaces of healthy individuals as part as their microbiome. Its coexistence as a commensal, has fostered the co-evolution of adaptation strategies to evade and escape host immune defenses.

We investigate how inflammatory responses mounted upon infection impact fungal adaptation using an *in vitro* inflammation-adaptation model. Briefly, we stimulate human macrophages with heat-killed *C. albicans*, and use the supernatants of this interaction as surrogate inflammatory environments to which we expose the fungus and evaluate its fitness when encountering immune cells. We observed increased tolerance to fever-like and oxidative stresses, as well as augmented escape from macrophage-mediated clearance, when *C. albicans* was stimulated with supernatants of macrophages that responded to heat-killed hyphae *Candida* (HKH), compared to supernatants from resting macrophages.

By performing fungal transcriptomics, we identified five intriguing candidate genes that were specifically upregulated in the HKH-stimulated macrophage supernatant. Validation of *C. albicans* deletion mutants of these differentially regulated genes revealed altered tolerance to fever-like- (40°C) and oxidative-stress, highlighting their importance in the adaptation to the host-imposed stresses. We currently are dissecting the underlying mechanisms of how these genes mediate *C. albicans* stress adaptation, and whether they affect fungal fitness when encountering host immune cells.

Collectively, we show that specific inflammatory responses can shape *C. albicans* adaptation to resist stress and that a select set of differentially regulated genes is key to overcome host-imposed stresses.

Session 3 • Mycobiome and fungal colonization

S3-02

Modeling of intravenous caspofungin administration using an intestine-on-chip reveals altered *Candida albicans*microcolonies and pathogenicity

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The human intestine is a major reservoir of the commensal fungus *Candida albicans* and a potential source of life-threatening systemic candidiasis. While 2D *in vitro* models are commonly used to study fungal–host interactions, they lack biological complexity and are limited in assessing antifungal drug transport across multilayered tissue barriers. To address this, a 3D intestine-on-chip model was used to investigate fungal–host interactions and the efficacy of antifungal caspofungin treatment.

The model features a vascular compartment containing endothelial and immune cells and an intestinal compartment formed by intestinal epithelial cells, both under peristaltic flow. Epithelial infection was

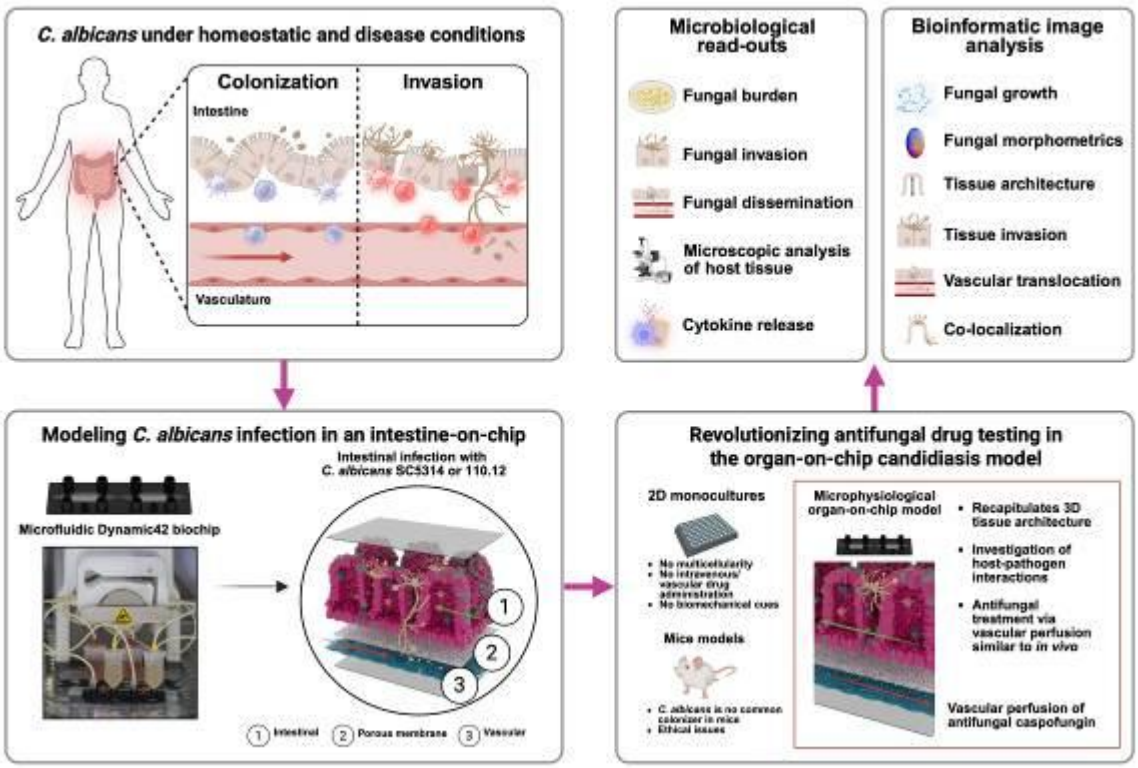
performed using either a wild-type (SC5314) or a caspofungin-resistant (110.12) *C. albicans* strain. Caspofungin was administered via vascular perfusion to mimic intravenous treatment. Alongside biomolecular analyses, an automated 3D image analysis pipeline was developed to characterize fungal morphology, quantify epithelial architecture, and assess fungal invasion, tissue interaction, and translocation.

Results showed that *C. albicans* invades epithelial tissue and translocates into the vascular compartment, causing severe host tissue damage by disrupting cell–cell contacts, increasing permeability, and inducing inflammation. Caspofungin restored tissue integrity, reducing fungal burden, invasion, and translocation in a concentration-dependent manner, along with decreased inflammation. Image analysis revealed reduced fungal biomass, more compact microcolonies, and a lower surface-to-volume ratio, indicating decreased exposure to epithelial tissue after treatment. In contrast, caspofungin had limited effects on the resistant clinical isolate.

Overall, this intestine-on-chip model enables detailed *in situ* analysis of antifungal efficacy, emerging drug resistance, and alterations in host–pathogen interactions.

Figure 1: Graphical outline of the candidiasis-on-chip model.

Figure 1



S3-03

Unravelling the infection dynamics of *Candida albicans* clinical isolates on gut epithelial cells

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Candida albicans is a common, harmless commensal of the human gastrointestinal tract, but under certain conditions, it can shift to a pathogenic lifestyle. Although epithelial cell responses to *C. albicans* infection have been well characterized, the activation of inflammatory and/or non-inflammatory cell death pathways remains unexplored. Additionally, nearly all studies so far have been performed with the reference strain SC5314, but conclusions based solely on this strain may mask variations in the interactions between *C. albicans* and host epithelial cells. Therefore, to better understand the range of these interactions, we screened 64 isolates from various sources for their damage potential. We then selected isolates with similar or higher levels of damage than SC5314 for further assays.

To monitor host responses, we employed fluorescent reporter cell lines: a mitochondrial redox sensor (mt-roGFP2), a caspase-3/7-mRuby3 reporter for apoptosis, and an ASC-LmCerulean reporter for inflammasome activation to allow precise temporal tracking of host responses. Fungal behaviour was also assessed by measuring adhesion, invasion, translocation, and epithelial barrier integrity.

These readouts varied greatly among *C. albicans* isolates, stressing a broad range of phenotypes among these strains. For instance, the mt-roGFP2 reporter revealed strain-specific mitochondrial redox responses, with distinct strains (among them SC5314) showing a strong shift to more oxidative conditions, while the apoptosis reporter indicated increased caspase-3/7 activation at late time points in several strains. The ASC-inflammasome reporter showed *C. albicans* subgroups of strong early and delayed inducers.

This work demonstrates that *C. albicans* should not be regarded as a single prototype pathogen, but rather as a species with strain-specific phenotypes. It may also underscore the importance of studying multiple isolates to capture the full spectrum of *C. albicans* behaviour and host interactions.

S3-04

Single-cell transcriptomic profiling of the pulmonary landscape during *Candida albicans* colonization and bacterial superinfection

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Introduction

Candida albicans is a common commensal fungus that colonizes mucosal surfaces and is frequently isolated from the lungs of mechanically ventilated patients. While it rarely causes pneumonia and does not invade via the lungs, its presence can alter responses to bacterial pathogens. In a mouse model of *C. albicans* colonization followed by *S. aureus* infection, we found that *C. albicans* reduced the severity and invasiveness of subsequent *S. aureus* infection.

Objectives

We aimed to characterize how *C. albicans* influences single-cell transcriptional responses to *S. aureus* within the mouse lung.

Materials & Methods

Mice were administered *C. albicans* intranasally at Day 0 and then infected at Day 1 with *S. aureus*. Single microbe and mock controls were included. At Day 2, isolated lung cells were processed using Parse Biosciences Evercode Cell Fixation and WT v3 kits, then sequenced on an Illumina NovaSeqXplus platform.

Results

Our analysis captured all major lung cell types (immune and non-immune), including a highly resolved neutrophil compartment. Pathway analysis of differentially expressed genes between the *C. albicans*/*S. aureus* versus *S. aureus* only groups indicated that *C. albicans* strongly downregulated pathways such as TNF signalling, PI3K/AKT/mTOR signalling, interferon responses and glycolysis in alveolar macrophages, suggesting suppression of inflammatory responses. In contrast, *C. albicans* upregulated pathways associated with inflammatory and antimicrobial responses in neutrophils but also upregulated TGF-beta signalling, wound healing and apical junction signalling pathways, suggesting a regulatory feedback loop that may enhance mucosal barrier integrity. Together this response allowed for bacterial containment while preventing excessive pathology.

Conclusion

These data show that *C. albicans* drives myeloid cell reprogramming, further clarifying the molecular mechanisms by which it reduces the severity of *S. aureus* pneumonia.

S3-05

Candidozyma auris in Austria: Evidence for Repeated Importation and Implications for Infection Control

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Introduction

Candidozyma auris has emerged as a major global public health threat due to its ability to cause healthcare-associated outbreaks. The pathogen frequently exhibits multidrug-resistance, posing substantial challenges for infection prevention and control. We provide an overview of the current epidemiological situation in Austria and data on the antifungal efficacy of commercial products for skin, wound and mucous membrane antisepsis and environmental disinfection.

Methods

Epidemiological data and whole-genome sequencing were analyzed to identify *C. auris* transmission routes and reconstruct phylogenetic relationships. Antifungal susceptibility testing was performed by broth-microdilution (EUCAST) and quantitative suspension assays (EN13624:2013) were conducted to evaluate the efficacy of antiseptics and disinfectants.

Results

To date, 21 cases of *C. auris* were reported to the Austrian National Reference Centre for Yeasts and Moulds. Most were linked to prior travel and hospitalization abroad, with Greece accounting for six cases; single cases were linked to Spain, India, Romania, Serbia, South Africa, China and Turkey. Three patients reported frequent travel (Turkey, India, USA); one was an outpatient. No travel history was available for four individuals. Except for one otitis externa and one candidemia case, all detections represented colonization. Whole-genome sequencing assigned isolates to clade I, clade III and clade IV, indicating multiple independent introductions rather than local transmission. Antiseptic efficacy testings are currently ongoing.

Conclusion

Most cases in Austria are linked to importation via international travel and prior hospitalization abroad, highlighting the need for systematic screening of transferred patients. Given the global rise of *C. auris* and its role in nosocomial outbreaks, effective hygiene and infection control measures are of critical importance in healthcare environments to minimize the risk of transmission.

Session 4 • Pediatric fungal infections

S4-02

Mitochondrial intoxication by macrophage-derived reactive oxygen species mediates echinocandin tolerance of intramacrophage *Candida glabrata*

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Question

Although antifungal resistance is known to drive therapeutic failure, yet a significant population of patients infected with susceptible fungi experience antifungal therapeutic failure. Further, unlike the prevalent paradigm that macrophage and echinocandins synergistically cooperate to contain the infection, we previously noted that intramacrophage *Candida glabrata* cells are 500-fold more tolerant to echinocandins and are more prone to develop echinocandin resistance. As such, we propose that one of the major armories of immunity antagonizes the efficacy of echinocandins, which partially explains why patients infected with susceptible fungal cells develop therapeutic failure. Despite its importance, why and how macrophages antagonize the efficacy of echinocandins remain unknown.

Methods

Herein, by leveraging transcriptomic, metabolomic, functional genetic, biochemical studies, and extensive phenotypic and ex-vivo studies, we address this question.

Results

Mechanistically, our transcriptomic and functional genetic studies show that intramacrophage *C. glabrata* show hallmarks of oxidative stress and macrophage ROS level and echinocandin tolerance are positively correlated. Our biochemical, metabolomic, and functional genetic studies indicate that ROS produced by macrophages inhibits two major Krebs cycle enzymes, which drives mitochondrial collapse and growth-arrest of intramacrophage *C. glabrata* cells. Our extensive phenotypic studies show that exogenous

administration of pyruvate could restore the efficacy of echinocandins against ROS-exposed *C. auris*, *C. albicans*, *C. parapsilosis*, and *C. glabrata* cells. Our comprehensive phenotypic and functional genetic studies delineate that pyruvate-mediated enhanced echinocandin efficacy is mainly driven by scavenging ROS.

Conclusions

Our study unravels a mechanistic insight into host-mediated antifungal therapeutic failure and proposes a practical framework to restore the echinocandin efficacy during infection.

S4-03

Emergence of a High-Risk ST11 Lineage and Early Azole Resistance in Clinical *Candida parapsilosis* Isolates

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Introduction

Candida parapsilosis is an important cause of invasive candidiasis, associated with nosocomial transmission and emerging azole resistance. Following an increase in *C. parapsilosis* detection from 18 isolates (18 patients) in 2022 to 47 isolates (24 patients) in 2023–2024 at our institution, a detailed investigation was initiated.

Objectives

The aim of this study was to characterize antifungal susceptibility, genetic relatedness, and resistance mechanisms of clinical *C. parapsilosis* isolates.

Materials & Methods

Forty-seven clinical isolates obtained from 24 patients between February and July 2024 were analyzed. Susceptibility to fluconazole and anidulafungin was determined using the Clinical & Laboratory Standards Institute (CLSI) broth microdilution and gradient diffusion (Etest). Whole-genome sequencing (WGS) was applied for SNP-based phylogeny and multilocus sequence typing (MLST). Resistance-associated mutations were investigated in non-susceptible isolates.

Results

WGS of the 47 isolates revealed no single clonal outbreak but a genetically heterogeneous population belonging to nine sequence types (STs), six SNP clusters and ten singletons. A notable cluster included closely related ST11 isolates detected in three patients and linked to previously described epidemic lineages. Fluconazole non-susceptibility was confined to isolates from one patient within this cluster. These isolates harbored predominantly heterozygous variants consistent with early polygenic resistance. Method-dependent discrepancies were observed for anidulafungin, while fluconazole showed higher concordance.

Conclusion

Integration of WGS with susceptibility testing distinguished increased prevalence from clonal spread, identified a high-risk ST11 lineage, and highlighted early resistance evolution. These findings support molecular surveillance and careful interpretation of susceptibility results for infection control and antifungal stewardship.

S4-04

From Bananas to the Clinic: Emerging Clinical Relevance of Fusarium musae within the Fusarium fujikuroi Species Complex

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Introduction

The Fusarium fujikuroi species complex (FFSC) includes environmentally widespread fungi increasingly recognized as opportunistic human pathogens. Among them, Fusarium musae is strongly associated with banana-related environments and may represent a source of human exposure.

Objectives

This study aimed to investigate the distribution of F. musae within the FFSC and to evaluate its antifungal susceptibility profile in comparison with other members of the complex

Materials & Methods

Ninety FFSC isolates (45 clinical, 45 environmental) were analysed. Clinical isolates originated from respiratory samples, sinus secretions and wounds, while environmental isolates were recovered from cereals, kitchen drainage, banana fruits and peels. Species identification was performed using MALDI-TOF MS and TEF1-α/RPB2 sequencing. Antifungal susceptibility testing according to CLSI guidelines included amphotericin B, voriconazole, posaconazole, isavuconazole, olorofim and manogepix.

Results

The most prevalent species were F. musae (n=30), F. verticillioides (n=29) and F. annulatum (n=23). F. musae predominated in banana-associated samples (24/30), while six isolates originated from clinical specimens. Voriconazole (MIC 1–4 mg/L in 63 isolates) and posaconazole (MIC 0.25–4 mg/L in 49 isolates) showed the most favourable activity, whereas isavuconazole showed consistently elevated MICs. Six isolates exhibited elevated MICs (8 to >16 mg/L) across all tested antifungals. Similar susceptibility patterns were observed between F. musae and other FFSC species. Olorofim showed near-complete growth inhibition (MIC90–100), particularly against F. annulatum. Manogepix activity was reflected by low MIC50 values and marked hyphal alterations across most FFSC isolates.

Conclusion

F. musae predominated in banana-associated environments but was also recovered from clinical samples, supporting a food-associated environmental reservoir with possible transition into clinical settings.

This work has been supported by the Croatian Science Foundation (HRZZ-IP-2022-10-8062; DOK-NPOO-2023-10-2348).

S4-05

An Early Decision Point in Alveolar Macrophages Shapes the Outcome of Pulmonary *Aspergillus* Infection

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Invasive aspergillosis, mainly caused by *Aspergillus fumigatus*, poses a major global health threat [1,2]. Although humans inhale hundreds of *A. fumigatus* conidia daily, most are efficiently cleared in the alveoli [3,4]. How early host-fungus interactions determine whether clearance or progression occurs remains unclear.

Using intratracheal *A. fumigatus* infection in immunocompetent BALB/c mice, we show that alveolar macrophages (AMs) mount a rapid and decisive antifungal response, achieving fungal clearance within 10 hours, prior to recruitment of neutrophils and monocytes. This phase featured AM activation, elevated pro-inflammatory cytokines (TNF-α, IL-1α, IL-6), reduced IL-10 and chemokine profiles consistent with antifungal immunity. Concurrently, AMs upregulated adhesion molecules (CD29, CD54) and downregulated the inhibitory receptor SIRP1α/CD172a, coinciding with enhanced intracellular killing capacity marked by increased Cathepsin B activity.

These findings identify AMs as key arbiters of an early immunological decision point determining whether *A. fumigatus* is cleared at the alveolar surface or progresses to invasive disease. Targeting this initial macrophage-driven phase may offer new strategies to strengthen early host defence.

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Session 5 • Novel fungal diagnostics

S5-02

Unmasking Occult Fungaemia and Fungal Meningitis in Bacteria-Positive Blood Culture Bottles

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Introduction

Fungaemia and fungal meningitis are severe invasive mycoses associated with high morbidity and mortality. However, culture-based diagnosis remains limited, particularly in cases of low fungal burden or competing bacterial growth in blood culture bottles. In a routine setting, blood culture (BC) incubation is discontinued once bacterial growth is detected. Fungal growth can subsequently be missed.

Objective

To determine the diagnostic yield and clinical relevance of expanded mycological work-up of bacteria-positive BC bottles.

Methods

In this prospective two-year study, all BC bottles positive for bacterial growth were subjected to prolonged incubation and visually inspected for fungal growth, including hyphal ball formation. After seven days, bottles were subcultured on Sabouraud agar and incubated for at least four additional days. Bacteria-positive BC bottles used for cerebrospinal fluid culture were also included. All isolates were identified by MALDI-TOF MS.

Results

Among 2,067 bacteria-positive BC bottles, two showed additional growth of *Candida glabrata* (0.1%). Both patients had enterococcal bloodstream infection and required intensive care treatment. In one case, *C. glabrata* was also detected in another BC bottle without enterococcal growth; in the other, fungaemia would have remained undiagnosed without the expanded protocol. Among 88 bacteria-positive BC bottles used for CSF culture, *Cryptococcus deneoformans* was detected in one case. This infection would likely have been missed or misclassified as contamination due to overgrowth by *Staphylococcus haemolyticus*.

Conclusion

Expanded mycological work-up of bacteria-positive BC bottles showed a low but clinically relevant diagnostic yield, identifying invasive fungal infections that would otherwise have been missed or misclassified. Targeted use in high-risk patients may therefore improve culture-based diagnostics.

S5-03

False-positive galactomannan values in bronchoalveolar lavage fluid are significantly more common in critically ill patients after aspiration

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Objectives

Invasive pulmonary aspergillosis (IPA) is increasingly diagnosed in non-neutropenic ICU patients. In this population, galactomannan (GM) in bronchoalveolar lavage fluid (BALF) has become the most important microbiological parameter. However, there is evidence that a considerable number of false-positive BALF

GM tests lead to misdiagnosis. In this study, we examined if aspiration is causing false-positive BALF GM tests.

Methods

All adult, non-surgical ICU patients who underwent BAL with GM testing (Platelia Aspergillus Ag Assay, BioRad), mycological culture, and Aspergillus PCR (AsperGenious, PathoNostics) from 11/2020 until 09/2025 were retrospectively included. Additional data were collected to classify patients for IPA following the FUNDICU or EORTC/MSGERC 2020 criteria. The likelihood of previous aspiration was assessed clinically (blinded review of bronchoscopy report and patient records) and based on 17 known risk factors.

Results

404 BALF specimens from 206 ICU patients were included. 66 BALF specimens (16.3%) were GM positive at a cutoff-value of ≥ 1.0 AU. 39 (59%) of GM-positive BALF specimens were only GM positive (PCR and culture negative); in those patients aspiration was significantly more common than in patients with positive GM and positive culture or PCR. Mean BALF-GM in patients with aspiration was significantly higher than in patients without aspiration (1.8 vs 0.6 AU; p<0,001), while Aspergillus-PCR and serum GM were not. Proven and probable IPA were diagnosed in 2 and 16 patients. Aspiration rate in patients with proven or probable IPA was significantly lower than in patients without IPA (50.0% vs 65.5%; p=0.02). 69.7% of patients without IPA had more than 1 risk factor compared to 0% in patients with IPA (p=0.001).

Conclusion

Aspiration is more common in GM-positive patients without IPA. Two or more risk factors for aspiration strongly argue towards a false-positive GM value and against proven or probable IPA.

S5-04

ImmunoPET and LSFM-based Imaging for Early Diagnosis of Invasive Aspergillosis Using Fc-Modified Anti-*Aspergillus fumigatus* Antibodies

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Introduction

Aspergillus fumigatus causes invasive aspergillosis (IA), a life-threatening infection in immunocompromised individuals and increasingly in COVID-19 patients. IA is difficult to diagnose early due to nonspecific symptoms and limited tools, with mortality rates exceeding 40%.

Objective

To establish a non-invasive imaging approach for early IA detection and therapy monitoring using immunoPET with Fc-modified antibody tracers.

Materials & Methods

The JF5 antibody, targeting an *A. fumigatus* hyphal antigen, was Fc-modified to reduce FcRn binding and circulation time while preserving antigen affinity. Variants were radiolabeled with copper-64 and tested in a murine IA model. PET/MR assessed tracer biodistribution; LSFM validated binding and fungal burden at tissue level.

Results

Fc-modified JF5 tracers showed improved pharmacokinetics with reduced background signal and enhanced signal-to-noise ratios compared to the unmodified antibody. PET imaging indicated specific accumulation at infection sites.

Conclusion

Fc-engineered JF5-based immunoPET enables specific, non-invasive monitoring of IA and therapy response. The method supports early diagnosis and individualized antifungal treatment with high potential for clinical translation.

Figure 1

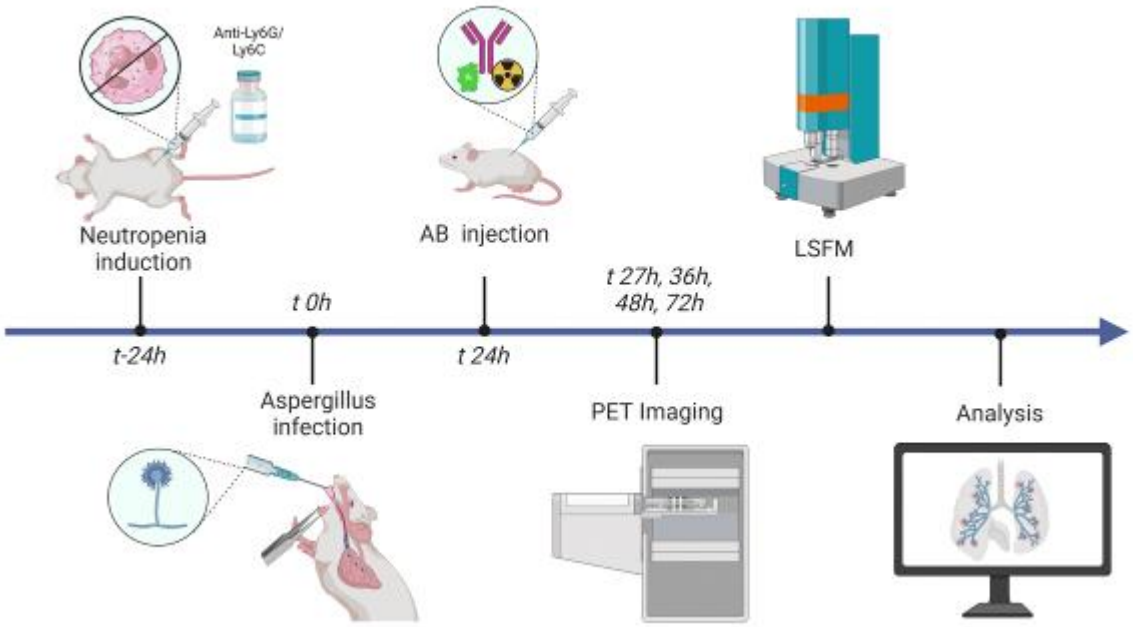
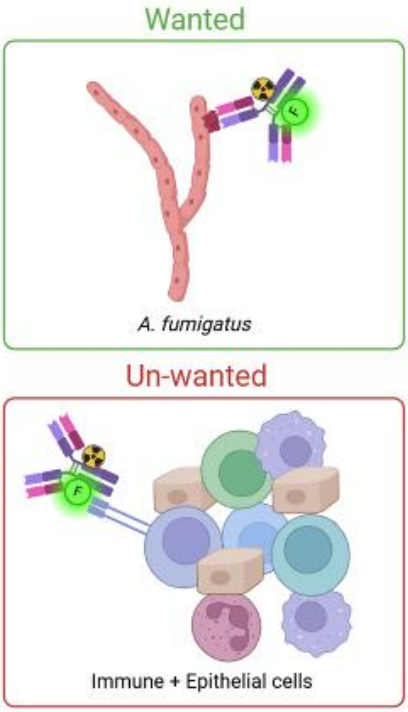


Figure 2



S5-05

Blood PCR for Mucorales in Patients with suspected Invasive Mould Infection: Findings from a Single Center

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Background

Mucormycosis is a life-threatening fungal infection that is difficult to diagnose due to the low sensitivity of microscopy and culture. This study evaluated the MucorGenius® PCR assay in blood samples from high-risk patients with probable or proven invasive aspergillosis (IA), mucormycosis, or possible invasive mold infections (IMIs).

Methods

In this single-center cohort study at the Medical University of Graz, Austria, 20 blood samples (serum and plasma) from 20 patients with clinical suspicion of IMI were analyzed. Samples were tested with the MucorGenius® PCR assay in ISO-certified laboratories, and results were compared with standard fungal diagnostic methods.

Results

Patient characteristics are summarized in Table 1. Of the 20 patients, 11 (55%) were male and 9 (45%) female. The median age was 69 years (range, 24–78 years). According to the 2020 EORTC/MSGERC criteria, patients were classified as: 1 proven IA, 2 proven mucormycosis, 10 probable IA, 2 probable COVID-19-associated pulmonary aspergillosis, and 7 possible IMIs. Mucorales DNA was detected in 2/20 samples (10%). Sensitivity for proven mucormycosis was 50% (1/2). Both PCR-positive results occurred in patients classified as probable IA. One of these patients also fulfilled criteria for proven mucormycosis, while in the other case no mucormycosis was identified by routine diagnostics. In this patient, antifungal therapy was started with caspofungin and later switched to posaconazole due to clinical deterioration. The patient died two days after sample collection.

Conclusion

The MucorGenius® PCR may serve as a supplementary diagnostic tool in high-risk patients, detecting Mucorales DNA when routine methods were negative. However, due to the small sample size and limited number of proven mucormycosis cases, findings should be interpreted cautiously. Larger studies are needed to clarify the clinical utility of blood-based PCR testing for early detection of mucormycosis.

Figure 1

Table 1: Patient Characteristics and MucorGenius® PCR Results

Variables	Cohort n=20 (%)
Sex	
Male	11 (55)
Female	9 (45)
Age	
Years	Median 69 (range 24–78)
Clinical classification (EORTC/MSGERC 2020)	
Proven IA	1 (5)
Probable IA	10 (50)
Possible IFI	7 (35)
Probable CAPA	2 (10)
Proven mucormycosis	2 (10)
Mixed Fungal infection	2 (10)
Underlying Diseases	
Acute myeloid leukemia	4 (20)
Acute lymphoblastic leukemia	3 (15)
Myelodysplastic syndrome	2 (10)
Chronic lymphocytic leukemia	1 (5)
Lymphoma	2 (10)
Multiple myeloma	2 (10)
No underlying disease	4(20)
Unknown	2(10)
Variables	**MucorGenius® PCR positive samples (n=2)**
Routine diagnostic	
Rhizopus spp. detection via ITS sequencing from biopsy	1
GM positive and lungs showing radiological signs	1
Routine diagnostic	**MucorGenius® PCR negative sample but positive in the routine (n=1)**
Mucor circinelloides detection via ITS sequencing from biopsy	1

Session 6 • Host-fungal pathogen interactions

S6-02

Galectin-3 regulates macrophage antifungal immunity and host susceptibility to invasive pulmonary aspergillosis

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Introduction

Invasive pulmonary aspergillosis (IPA) is a severe fungal infection primarily affecting immunocompromised patients and increasingly reported in severe respiratory viral infections. Galectin-3, encoded by the *LGALS3* gene, has emerged as a key regulator of innate antifungal immunity, modulating pathogen recognition and inflammatory responses.

Objectives

This study aimed to elucidate the role of galectin-3 and the impact of genetic variation within its encoding gene on antifungal immune responses.

Methods

Functional analyses were performed using human monocyte-derived macrophages stratified by the rs4644 SNP in *LGALS3* following *in vitro* infection with *A. fumigatus*.

Results

Our findings identified a significant association between the rs4644 SNP in *LGALS3* and susceptibility to IPA. Human macrophages carrying the risk genotype exhibited reduced galectin-3 expression compared with wild-type counterparts. Notably, this variant impaired the interaction between galectin-3 and dectin-1, leading to defective fungal recognition and phagocytosis, accompanied by attenuated PI3K/Akt signaling. We further demonstrated that galectin-3 is recruited to phagosomes containing conidia, highlighting its critical role in antifungal host defense. Macrophages from risk-allele carriers displayed impaired phagolysosomal fusion and increased fungal germination. Proteomic analysis of isolated conidia-containing phagolysosomes further revealed that this genetic variant reshapes the phagosomal proteome, characterized by persistent membrane stress, defective Rab-mediated trafficking, and activation of lysosomal stress-response pathways.

Conclusions

These findings establish galectin-3 and its genetic variation as critical determinants of antifungal immunity, orchestrating fungal recognition, phagosomal dynamics, and pathogen clearance, thereby modulating susceptibility to IPA.

S6-03

M-CSF–stimulated alveolar macrophages safeguard from invasive aspergillosis

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Background and objectives

Invasive pulmonary aspergillosis caused by *Aspergillus fumigatus* is a major cause of mortality after allogeneic hematopoietic cell transplantation (allo-HCT), with innate immune mechanisms remaining poorly defined. We investigated how alveolar macrophages (AMs), as first-line tissue-resident sentinels, control pulmonary infection and how CSF-1R ligands M-CSF and IL-34 modulate AM function and protection against invasive aspergillosis after allo-HCT.

Methods

We used super-resolution and confocal microscopy to assess the effects of M-CSF and IL-34 on AM phenotype and migration in vitro. In vivo, a murine allo-HCT model with intratracheal *A. fumigatus* infection was used to evaluate cytokine stimulation. Mice survival was monitored, and host–pathogen interactions were analyzed by flow cytometry and light-sheet fluorescence microscopy.

Results

We identified alveolar macrophages (AMs) as key mediators of pulmonary antifungal defense. In immunocompromised mice, AMs protected against lethal aspergillosis at day 6, but not day 4, post–allo-HCT. Compared with neutrophils and monocytes, AMs showed the highest abundance, proliferation, and phagocytic activity, indicating a dominant role in controlling *A. fumigatus*. This was confirmed by AM depletion, which led to uncontrolled infection.

To enhance AM function at the earlier time point, we tested cytokine-based interventions and found that M-CSF—but not IL-34—enhanced AM migration, versatility, phagolysosomal function, and fungal killing, consistent in murine and human AMs. In vivo, M-CSF expanded AMs (~1.5-fold), improved antifungal activity, and protected 90% of allo-HCT mice from lethal infection at day 4. This effect was AM-dependent and associated with preserved lung integrity and reduced inflammation.

Conclusions

Tissue-resident AMs are key mediators of pulmonary antifungal immunity. M-CSF enhances AM function and represents a promising strategy to improve early host defense after allo-HCT.

S6-04

Mitochondrial metabolism tunes hyphoptosis susceptibility in macrophages – A dysfunctional checkpoint in primary immunodeficiencies?

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Filamentation is a virulence attribute, used by many fungal pathogens to invade tissues and infect susceptible hosts. Particularly in *Candida albicans*, hyphal formation is linked to pathogenicity, rendering hyphae a primary threat that tissue-resident macrophage sentinels have to disarm in early stages of

infection. In this context, we have discovered the cell death "hyphoptosis" as an integral constituent of the macrophage-hyphae interplay that not only terminates the initial interaction by death of the macrophage, but beyond shapes subsequent interactions of *C. albicans* with innate immune cells. Host-pathogen interactions centrally involve metabolic competition, forcing immune cells to adapt their metabolism to mount effective responses. Therefore, we hypothesized that cellular immunometabolism is also a key determinant, whether to engage hyphoptosis.

Thus, we analyzed macrophage metabolism during interaction with *C. albicans* hyphae by untargeted intra- and extracellular metabolomics, Seahorse, ELISA and live-cell imaging, and modulated metabolism using targeted inhibitors.

We observed considerable pathway intertwinement between hyphoptosis induction and mitochondrial metabolism. While mitochondrial energy supply was crucial for cytokine release and to restrain hyphoptotic cell death, mitochondrial ROS production was detrimental for macrophage survival. To connect those findings to a clinical setting, we assessed the hyphoptosis response and the associated mitochondrial activation in macrophages of primary immunodeficiency patients at risk of fungal infection. Both, Chronic Granulomatous Disease and Hyper IgE Syndrome patient macrophages, on different levels, showed aberrant mitochondrial responses and increased activation of hyphoptosis.

Thereby, we identified another mechanistic layer in those immunodeficiency patients that helps explain their lifelong susceptibility to fungal infection, and might serve as a target for novel host-directed therapies.

Session 7 • Rethinking risk: Fungal infections in non-classical hosts

S7-03

Influenza-associated pulmonary aspergillosis: incidence, outcomes and implications for targeted antifungal prophylaxis

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Introduction

Influenza-associated pulmonary aspergillosis (IAPA) is a frequent, serious complication among critically ill patients suffering from severe influenza, but its epidemiological burden and optimal prevention strategies remain unclear.

Aims

To assess incidence and fatality rate across publications between 2000 and 2025 and the role of antifungal prophylaxis based on published evidence.

Methods

A structured literature review of PubMed/Medline was conducted, including primary studies on IAPA. 53 studies were included in the final analysis. Study characteristics, epidemiological outcomes and data on antifungal prophylaxis and its effects were extracted.

Results

Substantial heterogeneity across studies was observed. IAPA incidence values range from 1.91% to 46.15%, with a median of 14.55% (95% CI 11.16-19.21), fatality rates range from 0.00% to 100.00% (median = 50%, 95% CI 42.86-58.54). No statistically significant differences were revealed for diagnostic criteria, but incidence and fatality rate were statistically significantly higher in ICU settings than hospital-wide studies. Larger studies reported lower incidence estimates. No significant survival benefit of universal antifungal prophylaxis in severe influenza was demonstrated across available evidence.

Conclusions

Current literature shows a considerable epidemiological burden of IAPA with high incidence and fatality rates. The high heterogeneity complicates comparability between different publications. Current literature cannot provide a definitive recommendation for universal antifungal prophylaxis within severe influenza. A targeted, risk-factor-based therapy like a genetic-susceptibility-guided regime may provide clinical benefit while reducing unnecessary antifungal exposure.

Figure 1

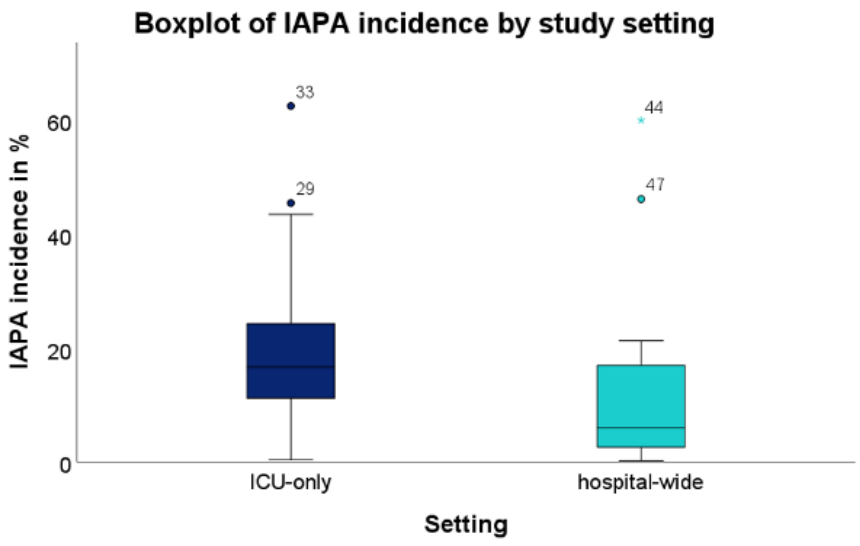
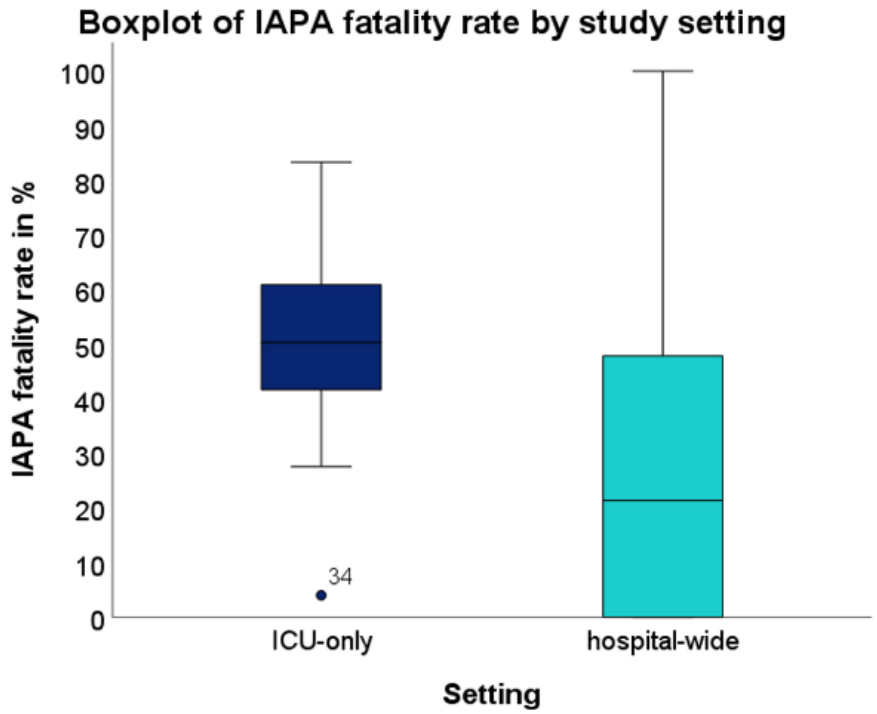


Figure 2



S7-04

Rare Invasive Fungal Infections in Patients with Hematological Malignancies: Epidemiology, Clinical Course, and Outcomes

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Introduction

Climate change promotes fungal growth and, together with rising numbers of immunosuppressed patients, drives a global increase in invasive fungal infections (IFIs). IFIs are associated with high mortality, especially in severely immunocompromised patients. Rare fungal pathogens pose major challenges due to limited evidence-based guidelines, restricted treatment options, and increasing antifungal resistance.

Objectives

This study aimed to characterize rare IFIs in patients with hematologic malignancies regarding epidemiology, clinical course, treatment and outcomes, and to contribute data to the *FungiScope* registry.

Patients & Methods

We conducted a retrospective single-center analysis of patients with *proven* or *probable* IFIs (EORTC/MSG criteria) caused by rare pathogens, treated between 2010 and 2025 at the Department of Hematology and Oncology of the LMU University Hospital Munich. Rare IFIs were defined as mold or yeast infections with an incidence ≤1/100.000. Clinical, microbiological, therapeutic and outcome data were analyzed descriptively.

Results

45 patients were included; 73.3% had *proven* and 26.7% *probable* IFIs. Median time from admission to IFI diagnosis was 33.5 days and 6.2 months from malignancy diagnosis to IFI onset. 49.9% of IFIs were molds, 51.1% yeasts. The most frequent pathogens were *Magnusiomyces spp*. (31.1%) and *Mucorales* (24.2%), detected predominantly via blood cultures (42.2%) and respiratory specimens (15.6%). Acute myeloid leukemia (46.7%) and non-Hodgkin lymphoma (28.9%) were the most frequent malignancies; 44.4% had undergone allogeneic hematopoietic stem cell transplantation. Overall mortality was 75.6%, with 46.7% attributable to IFIs.

Conclusion

Rare IFIs are associated with very high mortality and mainly affect severely immunocompromised patients with hematologic malignancies, highlighting the need for earlier diagnosis, better risk stratification, and more effective, evidence-based treatment strategies.

S7-05

Coccidioidomycosis in Germany: Case series after work-associated travel to Arizona

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Introduction

Coccidioidomycosis (CM) often manifests as community acquired pneumonia in highly endemic regions. They are predominantly diagnosed by antibody detection using sensitive tests (ELISA, complement fixation) unavailable outside endemic regions. In Germany, infections are typically diagnosed after travel, often as proven infection after cultivation potentially leading to underestimation of cases.

Objective

To describe microbiology results and clinical presentation in a cohort of patients with CM, after work-related travel to Arizona.

Methods

Review of clinical presentation from laboratory forms. Antibodies for CM were tested by lateral flow assay (lfa, IMMY™). LFA positive samples also by immune diffusion (ID, IMMY™) using TP (IGM) and CF (IGG) antigen with titration of CF positive samples.

Results

The Index case (male, 47 years old) presented with pneumonia and cerebral infarctions. CM was established by cultivation of *C. posadasii* from BAL and antibody detection by lfa and ID (TP and CF antigen; CF (titer 1:4), six weeks after travel to Arizona. Cerebrospinal fluid (csf) was not available for confirmation of central nervous system infection.

Eight additional patients were hospitalized for suspected CM, 2-4 months after travel due to persisting symptoms for invasive testing of BAL (n=8) and csf (n=2). Antibodies against *Coccidioides* were detected in six (75%) by lfa, none by ID. Diagnostic testing from BAL (microscopy, culture, qPCR) and CSF (culture, qPCR, lfa) did not show evidence for CM.

LFA detected antibodies in additional 7/90 (8%), ID in 1/90 (1%) non-hospitalized subjects with travel history that were asymptomatic or without symptoms specified on laboratory forms.

Conclusion

This cluster suggests superior *Coccidioides* antibody detection by lfa as compared to ID for imported CM. Microbiologic testing from invasive sampling may miss the majority of hospitalized CM cases. Additional serologic tests such as ELISA may improve early diagnosis.

S7-06

The Epidemiology of Cryptococcosis in Germany, 2018-2025: A Retrospective Study

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Introduction

Cryptococcosis is a fungal infection caused by *Cryptococcus neoformans and C. gattii*, primarily affecting the central nervous system.

Objective

To describe the epidemiology and mycological features of cryptococcosis in Germany.

Methods

Retrospective analysis of confirmed cases in Germany (2018-2025). Patient characteristics are described; species identification, antifungal susceptibility testing (yeast one microdilution, method specific epidemiologic cut offs) and molecular typing (MLST) were performed.

Results

We included 248 cases (male 71 %, female 29 %), aged 1 to 97 years (Median: 53). Underlying diseases included AIDS (30%), immunosuppression (13%), malignancy (11%), organ transplantation (7%), chronic liver disease (6%) or undefined (18%). Isolates were isolated from the central nervous system (CNS) (42%), blood (25%), respiratory tract (13%), skin and soft tissue (10%), urinary tract (3 %) and bone (2%). Infections were disseminated (81,5%) as suggested by cultivation site.

Cryptococcus neoformans var. grubii predominated (70 %), followed by *C. neoformans var. neoformans* (21 %), *intervarietal hybrids* (5%) and rarely *C. gattii* species complex (n=2, 1%). Some samples were culture negative precluding species identification and resistance testing (3 %). *In vitro* resistance documented MIC above the epidemiologic cutoff for 5 FC (>8 µg/ml; 16/211, 8%) and fluconazole (>8 µg/ml; 8/211, 4%). Common sequence types (ST) included ST63 (18%), ST23 (15%), ST5 (8%), ST93 (4%).

Conclusions

C. neoformans var. grubii, mostly worldwide distributed STs predominates in Germany as agent of cryptococcosis. *C. gattii* is rarely identified. Indicators for in vitro resistance are infrequently documented. Infections were increasingly diagnosed in non-AIDS patients and manifested as disseminated infections.

S8-03

Fungi and antifungals: an overlooked gap in wastewater surveillance and reuse regulation

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Introduction

The recast EU Urban Wastewater Treatment Directive (EU) 2024/3019 strengthens treatment and formalises wastewater-based surveillance but does not explicitly include fungal pathogens or antifungal residues; despite exposure pathways during effluent discharge and reclaimed-water reuse.

Objectives

To highlight this surveillance/regulatory gap and propose a pragmatic, risk-based addition of fungi and antifungals to wastewater monitoring.

Materials & Methods

Key elements of the new EU wastewater framework with current evidence on fungal wastewater surveillance, antifungal residues (selection pressure) and the use of predicted no-effect concentrations (PNECs), complemented from hospital-sewershed monitoring.

Results

Existing reuse criteria typically rely on bacterial indicators (e.g., E. coli) and omit fungi/antifungals. Global initiatives (e.g., GloWACON) prioritise *Candida auris* and *Aspergillus fumigatus sensu stricto* for environmental wastewater surveillance. PNECs provide a practical basis to prioritise antifungals and define acceptable levels in effluents/reclaimed water, supporting integrated monitoring of targets plus residues.

Conclusion

Adding fungal targets and antifungal residues as a tiered module (qPCR screening, culture/AST where feasible, sequencing as needed) would better align wastewater surveillance with One Health risk management and reclaimed-water safety, while enabling threshold-setting as QMRA evidence emerges.

Acknowledgement

FCT for grant UID/00329/2025 https://doi.org/10.54499/UID/00329/2025

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S8-04

Antifungal Tolerance detection in Non-*albicans Candida* Bloodstream Isolates from Innsbruck: An Analysis within the ECMM *Candida* IV Study

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Introduction

Non-albicans *Candida* (NAC) species are increasingly implicated in candidemia and often exhibit antifungal resistance. Antifungal tolerance has recently emerged as an additional complicating factor, enabling growth above the minimal inhibitory concentration (MIC) without MIC changes, making it difficult to detect with standard susceptibility testing and contributing to treatment failure.

Aim

To detect tolerance to fluconazole (FLC) and anidulafungin (ANI) among NAC bloodstream isolates.

Methods

A total of 45 NAC bloodstream isolates from 21 patients were analyzed. Antifungal susceptibility testing was performed using E-test and EUCAST methods to identify potential microcolonies (MCs) within the inhibition zone and to determine supra-MIC growth (SMG) values as an indicator of tolerance. Additionally, growth kinetics under antifungal exposure were assessed to further characterize tolerance.

Results

15 isolates produced 60 MCs in the E-test: *C. glabrata* (n=7), *C. parapsilosis* (n=6), and *C. orthopsilosis* (n=2). In *C. glabrata*, two isolates showed heterogenic MCs, with MICs above 16 mg/L (n=5) and below (n=3). Resistant MCs had elevated SMG values (0.17–0.26). All *C. parapsilosis* MCs were FLC-susceptible. Among *C. orthopsilosis*, one isolate produced only susceptible MCs, while the other yielded two susceptible and four resistant MCs with SMG 0.13–0.21. For ANI, all MCs were susceptible except one *C. glabrata* isolate with two resistant MCs (SMG 0.29–0.32). Growth kinetics showed slower growth of MCs and differences in area-under-the-curve calculations.

Conclusion

NAC isolates generate MCs with heterogeneous susceptibility profiles; subsets exhibit increased resistance relative to the parental strain, while others demonstrate tolerance, reflected by elevated SMG and altered growth kinetics. As these phenotypes are not detected by standard susceptibility testing, their identification may be critical to prevent treatment failure.

Session 10 • Systems biology of fungal infections

S10-02

Exploring the role of extracellular vesicles in fungal immunity in human macrophages

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Histoplasma capsulatum (Hc) is a fungus causing pulmonary to systemic mycoses. Hc resides in alveolar macrophages that promote formation of hypoxic granulomas. In low oxygen environments, macrophages stabilize hypoxia-inducible factor (HIF-)1α, a transcriptional regulator of innate immunometabolism. In prior work, exaggerated HIF-1α enhanced killing of Hc in human monocyte-derived macrophages (MΦ) by abolishing host autophagy. In MΦ, extracellular vesicles (EV) are mediators of intercellular immunity.

We hypothesized, HIF-1α alters the content of EV from HIF-stabilized Hc-infected MΦ, thereby modulating the fungicidal ability of neighboring MΦ.

Human MΦ were infected w/o chemical HIF-1α-stabilization (IOX2) for 3 h. Further, infected cells were treated with either supernatant or EV from infected MΦ (MHc-EV) or infected MΦ treated with IOX2 (IOX2-EV) for 3 h. HIF-1α and LC3-II protein amounts were assessed by Western blot, TNF-α, IL-1β, and GLUT1 expression by qRT-PCR, and fungal survival by killing assays.

HIF-1α, GLUT1 and IL-1β were enhanced while LC3-II was diminished by IOX2 during infection compared to infected controls. Survival of Hc was decreased in IOX2-treated infected MΦ.

Treatment of infected MΦ with supernatant from IOX2-treated infected MΦ increased HIF-1α stabilization compared to infected MΦ treated with supernatant from infected controls. The supernatant of IOX2-treated infected MΦ further reduced Hc survival in infected MΦ compared to IOX2-treated infected MΦ.

In infected MΦ treated with IOX2-EV, HIF-1α and IL-1β were enhanced while LC3-II was diminished compared to Hc-infected MΦ treated with MHc-EV. Both, IOX2-EV and MHc-EV, enhanced GLUT1 and TNF-α in infected MΦ compared to infected controls. Furthermore, IOX2-EV enhanced killing in infected MΦ compared to MHc-EV-treated MΦ.

These findings demonstrated that HIF-1α boosted EV-mediated proinflammatory priming and antifungal immunity in MΦ. In future, proteomics of the EV will be performed.

S10-03

Cholesterol metabolism regulates phagosome biogenesis and maturation during *Aspergillus fumigatus* infection

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Introduction

Invasive pulmonary aspergillosis (IPA) is a life-threatening infection primarily caused by the opportunistic fungal pathogen *Aspergillus fumigatus* and mainly affects immunocompromised patients. Cholesterol homeostasis plays a pivotal role in maintaining immune cell function, and its dysregulation has increasingly been implicated in the pathogenesis of several infectious diseases.

Objectives

This study aimed to investigate the role of cholesterol metabolism in antifungal immunity and susceptibility to IPA.

Methods

Functional analyses were performed using human monocyte-derived macrophages infected *in vitro* with *A. fumigatus* and treated with cholesterol-lowering agents.

Results

Our results show that infection of macrophages with *A. fumigatus* activates genes involved in the cholesterol biosynthesis pathway, accompanied by increased intracellular cholesterol levels. Notably, we found that elevated cholesterol levels impair the antifungal effector functions of macrophages, particularly their ability to eliminate the fungus. At the molecular level, inhibition of cholesterol biosynthesis enhanced the recruitment of key proteins required for the maturation of *A. fumigatus*-containing phagosomes and promoted phagolysosomal fusion. This, in turn, improved control of fungal growth and reduced susceptibility to infection. Furthermore, proteomic analysis of isolated conidia-containing phagolysosomes revealed that FDFT1, an enzyme involved in cholesterol biosynthesis, is recruited to these compartments. Ongoing work is focused on understanding why this metabolic enzyme localizes to the phagosome and whether its recruitment contributes to the detrimental effects of cholesterol on antifungal immunity.

Conclusions

Our findings propose a novel pathogenic mechanism for IPA and highlight cholesterol modulation as a promising strategy for its clinical management.

S10-04

Human Organ-on-Chip Platforms for Assessing Efficacy and Toxicity of Nanoparticle Antifungal Therapies

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Introduction

Invasive fungal infections (IFIs) have high mortality and are difficult to treat. Antifungal drug development remains slow, partly due to the limited predictive power of conventional in vitro systems and animal models. Organ-on-chip technologies offer controlled, human-relevant models of infection, drug response, and organ-specific toxicity.

Objectives

This study evaluates the efficacy and toxicity of nanoparticle-based antifungal formulations and their corresponding free drug using human-relevant organ-on-chip systems.

Materials & Methods

Drug-loaded nanoparticles, developed within the ATHANA (Antifungal therapeutic approaches through nanoparticle-based targeting of drugs) consortium, and free drug controls were investigated in a human lung-on-chip dynamic infection model to assess antifungal efficacy. In addition, a human liver-on-chip model was employed to evaluate cytotoxicity. In the lung model, antifungal activity was determined by fungal load quantification and epithelial integrity markers, while liver toxicity was assessed using hepatic marker expression and LDH release.

Results

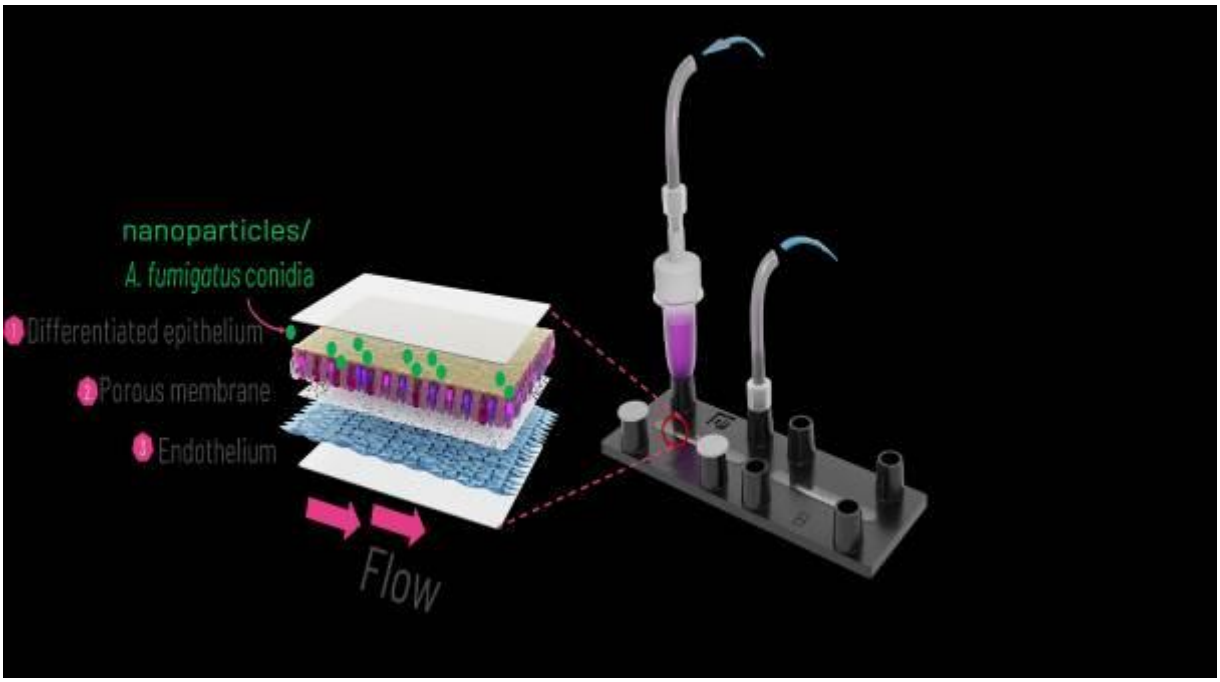
In the lung-on-chip infection model, both formulations showed good biocompatibility without detectable epithelial damage or cytotoxic effects. The nanoparticle formulation reduced fungal burden compared to untreated controls and demonstrated comparable antifungal efficacy to the free drug. In the liver-on-chip

model, nanoparticle-treated samples showed improved preservation of hepatic markers and tissue integrity compared to free drug exposure, particularly under higher treatment conditions. Consistently, LDH release was lower in nanoparticle-treated samples, indicating reduced cytotoxicity.

Conclusion

Organ-on-chip systems enable functionally distinct assessment of antifungal efficacy and toxicity. Nanoparticle-based formulations demonstrate the potential to maintain antifungal activity while reducing cytotoxicity in human-relevant models.

Figure 1



S10-05

Itaconate impairs macrophage effector functions and increases susceptibility to invasive pulmonary aspergillosis

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Introduction

Invasive pulmonary aspergillosis (IPA) is a severe fungal infection primarily caused by the opportunistic fungus *Aspergillus fumigatus*, and it predominantly affects immunocompromised patients. Itaconate, a metabolite derived from the tricarboxylic acid (TCA) cycle, has gained attention for its multiple immunoregulatory properties and shows considerable potential for therapeutic modulation across several diseases.

Objectives

This study aimed to elucidate the role of itaconate during *A. fumigatus* infection.

Methods

Functional analyses were conducted using both murine and human macrophages, alongside *in vivo* models of *A. fumigatus* infection.

Results

Our findings demonstrate that the Acod1/itaconate axis is upregulated in both murine and human macrophages during *A. fumigatus* infection. Of note, we found that activation of this axis impairs fungal internalization and elimination, consistent with the increased resistance to infection observed in *Acod1/-* mice in an experimental model of aspergillosis. In human macrophages, the rs9530614 SNP in *ACOD1*, which is associated with reduced gene expression, was also linked to enhanced antifungal immune responses. Mechanistically, ACOD1-deficient macrophages exhibited increased production of reactive oxygen species (ROS), both under basal conditions and following fungal infection. This phenotype was associated with distinct metabolic reprogramming, including alterations in lipid metabolism and oxidative stress pathways, ultimately leading to improved fungal clearance.

Conclusions

These findings reveal a detrimental role for the Acod1/itaconate axis in modulating innate immune responses against *A. fumigatus*, highlighting its potential as a therapeutic target for IPA.

Session 11 • Mucosal fungal interactions

S11-02

An organ-on-chip model to study vulvovaginal candidiasis and the interplay between fungal pathogenicity and inflammation

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Vulvovaginal candidiasis (VVC) is one of the principal mucosal yeast infections, which causes vaginal and vulvar inflammation. Approximately three quarters of women suffer from this infection at least once during their reproductive years, and a subset suffers from recurrent infections that dramatically impact their quality of life. The pathogenesis of recurrent VVC (RVVC) is linked to a complex interplay between fungal pathogenicity and excessive innate immune responses associated with neutrophilic inflammation rather than compromised immunity. The current knowledge of (R)VVC pathogenesis is established based on patient studies, animal models and *in vitro* cell culture infection models. However, traditional epithelial infection models are limited in their capacity to simulate neutrophil-mediated inflammation and exacerbation, a hallmark of (R)VVC pathogenesis.

Microfluidic organ-on-a-chip technology enabled us to establish a vaginal-candidiasis (VC)-on-chip that models infection of vaginal mucosa by *Candida albicans* and can be used to study innate immune responses driving neutrophil-mediated inflammation. Upon *C. albicans* infection of the (VC)-on-chip model, recruitment of neutrophils from the vascular compartment to the infected epithelial compartment induced by proinflammatory immune responses was observed under microscopy. We found that the influx of neutrophils also exacerbated proinflammatory cytokine responses via cytokine measurements.

Overall, this VC-on-chip model can be used to dissect mechanisms driving neutrophil-mediated immunopathology of a poorly understood but widespread disease that demands thorough understanding in order to proceed to proper treatment. This model will serve as a platform for studying host-pathogen interactions at the vaginal epithelial interphase and evaluating novel pathogen- as well as host-directed therapies.

S11-03

Spatial Analysis of *Candida albicans* and *Candida auris* in Co-Cultivation on Human Intestinal Organoid-Derived Monolayers

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Introduction

Infections caused by *Candida* pose a growing global health challenge. WHO specifically prioritizes research on *C. albicans* and *C. auris*. The latter has gained attention due to biofilm formation on (a-)biotic surfaces and rising antibiotic resistance, posing a threat in healthcare units. However, research has mainly relied on animal models. Only few studies have used human tissue, such as skin biopsies or isolated immune cells. Although both pathogens are highly relevant for human health, host-pathogen (h-p) and pathogen-pathogen (p-p) interactions are poorly understood. Direct interactions of both *Candida spec*. during co-cultivation have not yet been investigated.

Objectives

We established human intestinal duodenal organoid-derived monolayers (ODM) as a novel infection model for *Candida spp*. and examined model stability as well as p-p and h-p interactions by live-cell imaging and staining of colonized ODMs.

Methods

ODMs were co-cultivated with *C. auris* and/or *C. albicans* and monitored by live-cell imaging. Transepithelial electric resistance (TEER) measurements assessed barrier function during fungal colonization. We utilized fluorescence in situ hybridization (FISH) to identify and localize fungal cells within the ODM.

Results

Human ODMs exhibited no barrier breakdown throughout the experiment. Moreover, TEER values increased in co-cultivation with both pathogens. FISH analysis showed close spatial association of both *Candida spec.* in cell aggregates on the apical site of the monolayer.

Conclusion

We present a novel physiological human infection model to assess intestinal epithelial barrier responses during *Candida* colonization. The model revealed close spatial association of *C. auris* and *C. albicans*, indicating interaction between these fungi. To our knowledge, this is the first study to observe co-aggregation of *C. albicans* and *C. auris* during co-colonization of human intestinal epithelial cells.

S11-04

Cross-kingdom interaction between *Candida albicans* and *Akkermansia muciniphila* in an enterocyte infection model

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Candida albicans is a natural member of the fungal human gut microbiota, where it typically exists as a harmless commensal. However, under favorable conditions, such as antibiotic treatment that reduces resident anaerobic bacteria, fungal outgrowth can lead to dissemination and infection. *Akkermansia muciniphila* is an abundant mucin-degrading anaerobic gut bacterium with experimentally demonstrated health benefits.

In this study we employed an enterocyte infection model to determine whether *A. muciniphila* impacts the cytotoxicity and proliferation of two *C. albicans* strains, SC5314 and 101, representing strains with differing virulence potential. Our results show that metabolically active *A. muciniphila* markedly reduce fungal host cell damage and impair *C. albicans* hyphal formation under hypoxic conditions. This effect is accompanied by the ability of *A. muciniphila* to bind to fungal hyphae. Additionally, during co-culture conditions we observed an initial ~2-fold increase in *A. muciniphila* abundance, along with a slight increase in *C. albicans* strain 101 and a slight decrease in *C. albicans* strain SC5314. Using *C. albicans* deletion mutants, we found that this inhibition is independent of the fungal hyphae-associated adhesins Hpw1 and Als3. Analysis of the fungal cell wall revealed that the presence of *A. muciniphila* leads to exposure of β-glucan, likely associated with mannan alteration. These changes were also observed in the absence of enterocytes but were less pronounced. We hypothesize that the resulting structural alterations limit hyphal development and thereby reduce fungal pathogenicity.

In conclusion, *A. muciniphila* can modulate *C. albicans* pathogenic potential during enterocyte infection by reducing filamentation through a yet-unidentified mechanism.

S11-05

Elucidating alternative virulence strategies in *Candida albicans* clinical isolates

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Despite its normally commensal nature, *Candida albicans* can cause severe diseases in predisposed humans, as the fungus possesses a set of virulence factors to establish infections. However, the vast majority of studies of *C. albicans* virulence relies mostly on SC5314, a potent producer of the peptide toxin candidalysin, described as more virulent than most other strains.

To decipher not only how the fungus can damage intestinal epithelial cells, but also how the host responds to it, we screened over 60 *C. albicans* isolates from different body sites and clades for their damage potential. Importantly, we found that almost one third of these strains is at least as damaging as SC5314.

In this study we focused on C227, a blood isolate, that causes as much damage, redox stress, apoptosis and inflammasome activation in intestinal epithelial cells as SC5314. Surprisingly, we observed strongly reduced levels of adhesion, invasion, and translocation for C227 compared to SC5314. However, C227 shows unusually high expression levels of many virulence genes, including members of the hyphal-

associated secreted aspartic protease genes *SAP4-6*. A C227 mutant lacking *SAP4-6* (*sap4-6*ΔΔ) showed reduced damage compared to the wild-type. Interestingly, the candidalysin variant of C227 belongs to the low-damaging family I, and staining with a nanobody exhibited low candidalysin secretion, suggesting that toxin production is not as relevant for this strain. While the damage capacity of C227 to intestinal epithelial is on par with SC5314, this virulence attribute is more specific, as C227 shows no damage in other cell types.

We believe that C227 represents a group of clinical isolates that manage to establish infection in different ways than SC5314, depending less on invasion and candidalysin secretion. Our study is shedding light on alternative ways that *C. albicans* damages and infects the host and help us better understand fungal pathogenicity and the unexplored natural variations of it.

Session 12 • Dermatomykologie

S12-03

Comparison of PCR tests for the detection of dermatophytes in onychomycosis

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Introduction

Onychomycosis is a fungal infection affecting the toenails and fingernails, occurring in 2–18% of the population. Dermatophytes, particularly *Trichophyton (T.) rubrum* and *T. interdigitale*, are the primary causative agents.

Objective

This study evaluated the performance of the "EurobioPlex DermaScreen" RT-PCR assay for the identification of the most common dermatophyte species. Additionally, other dermatophyte RT-PCR tests were compared with regard to their sensitivity for the detection of *T. rubrum* and *T. interdigitale* in nail samples.

Materials & Methods

79 nail samples were extracted (QIAamp DNA Mini QIAcube Kit) and analysed using various RT-PCR kits on a CFX96 analyser. DermaGenius® 3.0 Complete (PathoNostics B.V.) served as the reference. The following RT-PCR kits were used: DermaScreen RT-PCR (EurobioScientific S.A.); "Dermatophyte and C. albicans RT-PCR" (SSI); Novaplex™ Dermatophyte Assay (Seegene).

Results

Using the reference kit, 14 negative samples were detected; 55 samples were positive for *T. rubrum*/Pan-Derma; 10 samples were positive for *T. interdigitale*/Pan-Derma. The DermaScreen kit yielded identical results to the reference in all samples. "Dermatophyte and C. albicans" yielded 14 negative samples, 55 positive samples for *T. rubrum*/Pan-Derma and 10 samples were positive for Pan-Derma. The Novaplex™ test yielded 21 negative results, 48 samples positive for the *T. rubrum* complex and 10 samples positive for the *T. mentagrophytes* complex.

Conclusion

"DermaScreen" and "Dermatophyte and C. albicans" detected all nails infected with dermatophytes. The Novaplex™ RT-PCR correctly identified 10 *T. interdigitale* samples as positive for the *T. mentagrophytes* complex. However, 7 *T. rubrum*-positive samples were not detected, suggesting lower sensitivity for this dermatophyte.

S12-04

Trichophyton indotineae auf dem Vormarsch?Resistenzsituation und epidemiologische Daten aus Österreich

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Einleitung

In den letzten Jahren wurde Trichophyton indotineae als wichtige Ursache therapieresistenter Dermatophytosen, identifiziert. Ursprünglich überwiegend in Asien beschrieben, wurden inzwischen auch Fälle in Europa einschließlich Österreich berichtet. Die Terbinafin-Resistenz ist hauptsächlich mit Mutationen im Gen der Squalenepoxidase (SQLE) assoziiert. Ziel der Studie war die Untersuchung epidemiologischer Merkmale, des SQLE-Mutationsstatus sowie der antimykotischen Empfindlichkeit österreichischer Isolate.

Methoden

Untersucht wurden 33 als T. indotineae identifizierte Dermatophyten-Isolate. Epidemiologische Daten zu Alter, Geschlecht und Infektionslokalisation wurden erhoben. Die Sequenzierung der internal transcribed spacer (ITS)-Region der ribosomalen DNA wurde als Referenzmethode zur definitiven Speziesidentifikation durchgeführt. Zusätzlich erfolgte die Identifikation mittels MALDI-TOF MS (Bruker, Bremen, Deutschland). Der SQLE-Mutationsstatus wurde mittels DermaGenius Resistance Multiplex Real-Time PCR bestimmt. Die antimykotische Empfindlichkeit wurde gegenüber Terbinafin, Itraconazol, Fluconazol, Amorolfin, Miconazol, Ciclopirox, Griseofulvin und Naftifin getestet; die MHK-Werte wurden nach EUCAST-Mikrodilution bestimmt.

Ergebnisse

Das Durchschnittsalter betrug 37,6 Jahre, 72 % waren männlich. Die häufigste Manifestation war Tinea corporis (~75 %). Alle Isolate wurden mittels ITS-Sequenzierung (≥99 % Übereinstimmung in BLAST) als T. indotineae identifiziert, jedoch durch MALDI-TOF als T. mentagrophytes-Komplex klassifiziert. Eine ausgeprägte Terbinafin-Resistenz zeigte sich in ~80 % der Isolate (MHK ≥ 1 µg/mL). Itraconazol und Amorolfin waren am wirksamsten, Fluconazol am wenigsten aktiv. SQLE-Mutationen lagen in 84 % der Isolate vor, 16 % waren Wildtyp; nur ein Wildtyp-Isolat war resistent. Schlussfolgerung: Es zeigt sich eine hohe Prävalenz terbinafinresistenter T. Indotineae Isolate in Österreich mit starker Assoziation zu SQLE-Mutationen. Die eingeschränkte Differenzierung durch MALDI-TOF unterstreicht die Bedeutung molekularer Referenzmethoden. Therapeutische Anpassungen sowie verstärkte epidemiologische Surveillance sind erforderlich.

Rapid Fire Session

RFS-1

RttA – a Novel Regulator of Sterol Homeostasis and Azole Resistance in *Aspergillus fumigatus*

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Background

Azole antifungals are frontline therapeutics for treating invasive aspergillosis, a life-threatening fungal disease. Their mode of action relies on inhibition of sterol C14-demethylase (Cyp51), a key enzyme in ergosterol biosynthesis. *Aspergillus fumigatus* encodes two Cyp51 isoenzymes, Cyp51A and Cyp51B, with most known azole resistance mechanisms arising from mutations in *cyp51A*. The transcription factors SrbA and AtrR are major regulators of ergosterol biosynthetic genes, including *cyp51A*, and are essential for maintaining sterol homeostasis.

Objective

This study aimed to identify and characterize additional regulatory factors involved in sterol homeostasis and azole resistance in *A. fumigatus*.

Methods

The protein RttA was analyzed as a candidate Zn_2Cys_6-type transcription factor with structural similarity to *Saccharomyces cerevisiae* Upc2 and *Neurospora crassa* NcSR, both known regulators of sterol metabolism and azole resistance. Functional analyses included gene deletion, overexpression, transcriptome profiling, susceptibility testing, and growth assays.

Results

Our results demonstrate that RttA acts as a key regulator of sterol homeostasis and azole resistance by activating *erg6* (encoding sterol C24-methyltransferase) and genes encoding azole efflux pumps. Furthermore, *rttA* expression depends on both AtrR and SrbA, indicating regulatory interconnectivity among these transcription factors.

Conclusions

Together, our findings identify RttA as a novel transcriptional regulator contributing to azole resistance in *A. fumigatus*. Ongoing work aims to further elucidate the biological role of RttA, its downstream targets, and its broader impact on fungal physiology and antifungal resistance.

RFS-2

Rhizopus arrhizus infection rewires host RNA splicing

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Fungal infections increasingly threaten human health with current antifungals limited by host toxicity, drug resistance, and poor efficacy in at-risk immunocompromised patients. Immunomodulatory approaches may complement antifungal treatment but require a better understanding of host immunity in response to fungal invaders. While fungal infections elicit complex host responses, alterations in RNA processing and modification are poorly understood. Preliminary analysis of a public dataset that previously recognized a core host transcriptomic response to three clinically relevant fungal pathogens[1] revealed adenosine-to-inosine (A-to-I) RNA editing (hyper-editing) and aberrant RNA splicing in response to *R. arrhizus* but not *Aspergillus fumigatus* or *Candida albicans* infection.

We hypothesized *that R. arrhizus,* one of the major causal agents of life-threatening mucormycosis, induces pathogen-driven changes in host RNA splicing and A-to-I hyper-editing in human peripheral blood mononuclear cells (PBMCs).

We generated high-depth long non-coding RNA sequencing (lncRNA-seq) data from human PBMCs exposed to *R. arrhizus* and characterized RNA splicing and A-to-I hyper-editing using several computational tools. Analysis of our lncRNA-seq dataset confirmed extensive global changes in host splicing, including immune- and apoptosis-related genes, increased A-to-I hyper-editing in response to fixed, but not viable, *R. arrhizus*, and differential regulation of lncRNAs.

Together, these preliminary findings reveal a previously unrecognized post-transcriptional response to *R. arrhizus* that appears dependent on the strength of initial immune stimulus. Although elucidation of the molecular mechanism is in progress, these data already highlight RNA processing as a candidate layer of host regulation during mucormycosis that may inform future development of immunomodulatory approaches.

References:

[1] Bruno M, *et al*. *Comput Struct Biotechnol J*. 2020 Dec 26;19:647-663.

RFS-3

ATHANA – Antifungal therapeutic approaches through nanoparticle-based targeting of drugs

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Introduction

Invasive fungal infections (IFIs), affecting in particular immunocompromised patients, are still an often underestimated problem and associated with unacceptable high mortality rates up to 95%. These infections are estimated with an annual incidence of 6.5 Mio, resulting in 3.8 Mio deaths. Limited treatment options in combination with an increasing number of resistant strains against the currently available drugs further highlights the importance of this topic.

Aim

The aim of the project was to develop nanoparticles (NPs) for the treatment of IFIs

Materials & Methods

NPs were evaluated regarding their composition, fungal targeting on the NP surface, antfungal drugs encapsulated in the NP for efficient transport, and their ability to be nebulized for inhalative therapy. The NPs were evaluated with a broad range of assays, starting from cell mono culture, to more advanced methods like organ-on-chip, up to *in vivo* animal experiments.

Results

The ATHANA consortium developed a platform technology for the production and testing of drug-loaded NPs that can recognize pathogen-specific structures. Thereby, a frontrunner-NP targeting *Aspergillus* spp. and displaying increased efficiency compared to the pristine antifungal substance was developed as inhalative application to treat invasive aspergillosis.

Conclusion

Encapsulation of a drug within a 'nanocarrier' is a strategy employed to prevent premature degradation and facilitate controlled release at the targeted location. This approach increases the efficiency and reduces systemic side effects. The toolbox approach facilitates the flexible, systematic and accelerated production of therapeutic NPs with different functionalities for gradual expansion to accommodate new applications. Furthermore, the use of NPs would open the application of pharmacologic problematic substances, as the pharmacological properties in these formulations are dominated by the carrier system and not by the drug itself.

RFS-4

Designer Self-Immolative Linkers for Prodruging Antifungals

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[5] Faculty of Science, Charles University, Prague, Czech Republic

Invasive fungal pathogens impose a severe global burden, resulting in 1.5 million deaths annually. Susceptible individuals, e.g., patients undergoing cancer treatment, organ transplants, or immunocompromised patients, are among the most vulnerable. The number of currently approved antifungal drugs is limited, and these drugs often exhibit severe off-target effects and toxicity, making long-term therapies complicated.

Phosphorus self-immolative linkers, previously developed in our lab, offer an excellent opportunity to develop novel prodrugs that can potentially evade drug resistance or reduce the toxicity of current antifungals.

In our search for novel ways to target pathogenic fungi, we applied designer phosphorus SI linkers to the polyene macrocycles amphotericin B and voriconazole to reduce their off-target effects (toxicity). We prepared four new amphotericin B prodrugs that demonstrate efficacy and toxicity comparable to those of advanced FDA−approved formulations of amphotericin B. Selected voriconazole prodrugs show excellent efficacy in the G. mellonella infection model compared with the parent voriconazole. The chemistry and function of phosphorus SI linkers will be discussed.

Our research was funded by the Charles University Cooperatio program SCI, the Czech Science Foundation (O.B., grant number 23-05752S), and by Strategie AV21 project "VP33 MycoLife - the world of fungi" of the Czech Academy of Sciences. Microscopy was performed at the Laboratory of Confocal and Fluorescence Microscopy co-financed by the European Regional Development Fund and the state budget of the Czech Republic, projects numbers CZ.1.05/4.1.00/16.0347 and CZ.2.16/3.1.00/21515 and funded by the Czech-BioImaging large RI project LM2015062.

RFS-5

Antifungal susceptibility testing of olorofim and manogepix for *Fusarium*, *Scedosporium* and rare fungal pathogens

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The clinical management of fungal infections is impaired by the limited availability of antifungal substances from only three major classes - azoles, polyenes and echinocandins - and the limited intrinsic susceptibility of multiple fungal taxa to these compounds. Additionally, resistance acquired in the environment or under treatment further complicates antifungal therapy. Therefore, novel antifungal agents with new modes of action are urgently needed. Two such agents are the novel antifungals olorofim, targeting pyrimidine synthesis by inhibition of the dihydroorotate dehydrogenase, and manogepix, which inhibits GPI-anchor biosynthesis. Recent studies already showed a broad antifungal activity of manogepix, except for Mucorales, as well as a potent activity of olorofim against many molds, underlining their clinical potential. However, data regarding species-and taxon-specific susceptibility patterns and activity against rare fungal pathogens remain incomplete. To address this gap, we performed EUCAST microdilution testing of both compounds on clinical isolates available at the NRZMyk, which have been molecularly identified to the species level. In addition to *Fusarium* and *Scedosporium* species, the panel included isolates from rare pathogens, such as *Purpureocillium*, *Talaromyces*, *Trichoderma* or the Onygenales. While we confirmed broad activity for manogepix with few exceptions, a more nuanced pattern was observed for olorofim, with several taxa showing intrinsic resistance or elevated MIC values. Exemplary for such a pattern is *Fusarium*, where susceptibility is species complex-dependent. Taken together, these data further define the activity spectrum of both novel antifungals and their potential clinical applicability, while also underlining the importance of reliable fungal identification, ideally to species level.

RFS-6

Grand Escape - How fungi outsmart the human complement system by binding to factor H – A review of 30 years of research

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Fungal diseases remain a significant cause of mortality and morbidity worldwide. Complement is a critical component in the defense against pathogens and despite their great differences, viruses, bacteria, protists and of course also fungi have all developed similar mechanisms of evasion from human complement (1). A recent review has summarized an update of different mechanisms of evasion, which can be grouped as avoidance of recognition, avoidance of eradication and avoidance of activation and function of complement used either in a defensive (own protection) or aggressive (invasion of the host) way (2), a classification already proposed in 1999 (1).

A very sophisticated way of evasion lies in the employment of host (human) complement, especially its major regulators, such as factor H and its family.

It all started almost 30 years ago, when both serum-sensitive and -resistant Borrelia were found (3) and this was attributed to a differential factor H binding (4,5). For Candida, factor H binding was published in 2002, 24 years ago (6) and several factor H binding molecules have been published since, all with multiple functions, summarized in (7-10). Eventually, binding of factor H to Aspergillus spp. has been detected (11).

A full review of the history is given at the conference.

References: 1, Mol Immunol 36,249,1999; 2, Immunobiology 230,153126,2025; 3, Med Microbiol Immunol 185:253,1997; 4, Eur J Immunol 31:1674,2001; 5, Infect Immun 69:3685,2001; 6, Infect Immun 70:5185,2002; 7, J Infect Dis 204:802,2011; 8, Front Microbiol 9:3319,2019; 9, Front Immunol 11:1471,2020; 10, Antibiotics 11:257,2022; 11, Mol Immunol 45:1485,2008

RFS-7

Targeting TNFR2 to Enhance Innate Immunity Against Pulmonary Aspergillus Infection

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Introduction

Tumor necrosis factor (TNF) regulates inflammation and homeostasis through TNFR1 and TNFR2[1,2]. TNFR1 drives pro-inflammatory signalling and cell death, whereas TNFR2 supports immunoregulation[2]. Macrophages express both receptors and are key TNF producers[3].

Recent studies highlight TNFR2 agonists as promising therapies to prevent graft-versus-host disease (GvHD)[4-6]. Because immunocompromised patients are particularly vulnerable to invasive aspergillosis, it remains essential to clarify whether TNFR2 activation strengthens innate immunity or impairs antifungal host defense.

Objectives

We investigated whether TNFR2 activation reshapes pulmonary innate immunity to promote effective antifungal defense against *A. fumigatus*, with a focus on alveolar macrophages (AMs).

Materials & Methods

AMs were isolated from wild-type BALB/c (WT) mice and stimulated *in vitro* with the murine TNFR2 agonist NewSTAR25 prior to infection with Af293 *A. fumigatus* WT or FLARE[7] conidia (MOI5). Wild-type mice were injected with NewSTAR2 and were infected with $5x10^4$ conidia.

Results

TNFR2 stimulation enhanced AM antifungal activity *in vitro*, increasing phagocytosis, cathepsin B activity, and lysosomal acidification. Systemic NewSTAR2 increased frequencies of AMs, interstitial macrophages, neutrophils and monocytes. Prophylactic NewSTAR2 improved phagocytosis of FLARE conidia without reducing AM killing capacity. Notably, pre-treatment before hematopoietic cell transplantation reduced weight loss and improved outcomes after *A. fumigatus* challenge.

Conclusion

TNFR2 targeting does not compromise antifungal host defense, it enhances pulmonary innate immunity. These findings support TNFR2 agonists for GvHD prevention without increasing susceptibility to invasive fungal infections.

References

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RFS-8

Proposal and validation of a new Candidozyma auris core genome Multilocus Sequence Typing (cgMLST) scheme

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Background

Candidozyma auris is a drug-resistant fungal pathogen, leading to frequent outbreaks in healthcare settings. WGS-based typing methods are essential for high-resolution molecular epidemiology. However, the lack of a standardized approach aggravates comparability, consistent surveillance and outbreak detection. Thus, we propose a novel core genome multilocus sequence typing (cgMLST) scheme overcoming interlaboratory comparability challenges.

Methods

A stable cgMLST scheme was developed using the reference genome B11220 (clade II) and a total of 2,822 high-quality whole-genome data sets extracted from public databases. The novel scheme was afterwards evaluated using WGS data from nine outbreak and non-outbreak investigations over four continents and comprising 185 isolates. Utility was further validated through re-analysis of own German epidemiological data (2015–2024). For scheme calibration minimum-spanning-tree (MST) analysis with pairwise distance calculation was used assessing genetic relatedness and defining outbreak cutoffs.

Results

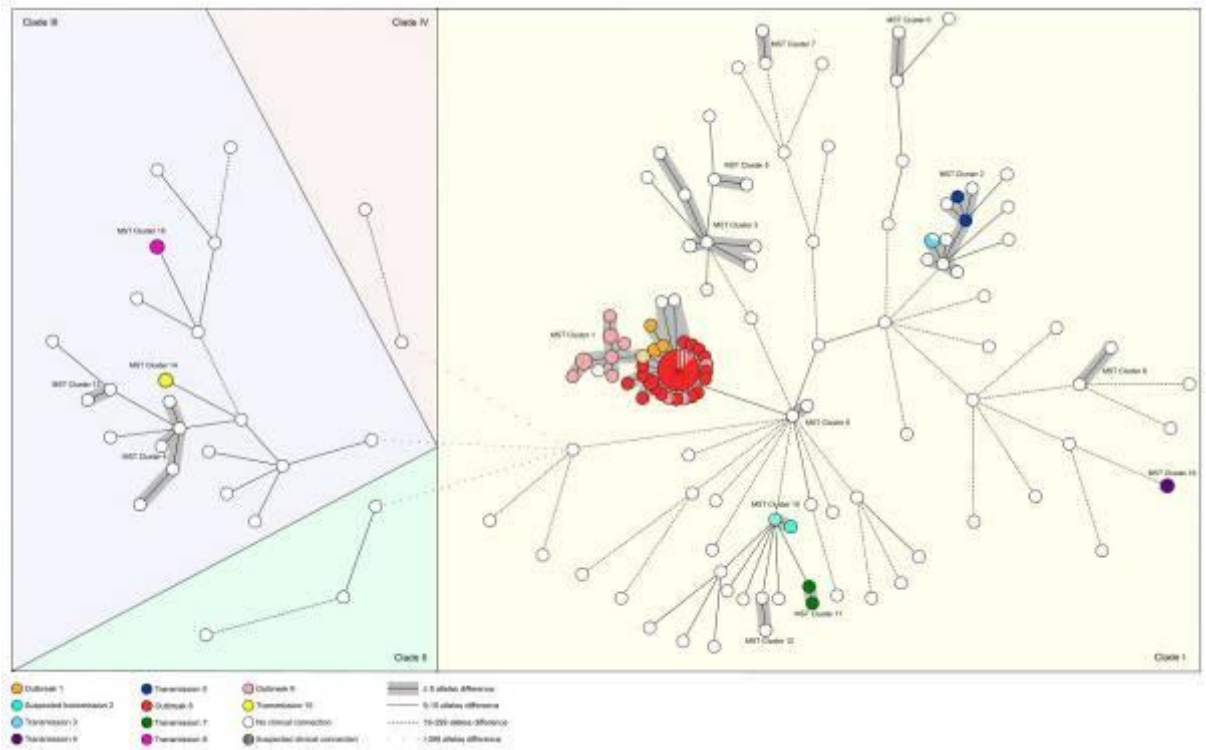
The novel cgMLST scheme covers 69% of the seed genome’s target genes and 44% of its nucleotide content. Analysis of 185 isolates from outbreak and non-outbreak settings gave comparable results to previous typing efforts with the ability to successfully discriminate outbreak clusters from unrelated isolates.

It accurately resolved known outbreaks in Riyadh, Hong Kong (both clade 1), Johannesburg, Nairobi (both clade 3), Chicago (clade 4), while correctly identifying unlinked isolates (e.g., Japan (clade 2), Iran (clade 5), Singapore (clade 6). MST analysis of German national data (2015–2024) revealed distinct genetic clusters, enabling reconstruction of transmission dynamics.

Conclusion

We present a scalable and reproducible cgMLST scheme that enables standardization of molecular surveillance and outbreak investigations, allowing a better understanding of C. auris genomic epidemiology and facilitating interlaboratory comparisons.

Figure 1



RFS-9

Using human airway and alveolar organoid-derived monolayers for quantification of Cryptococcus-host interactions

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Background and aims

Cryptococci are environmental fungi that cause localized or disseminated infections typically after uptake via the respiratory tract. Studies on pathogenicity are based on animal models, cancer cell lines or immune cells. However, to understand pathomechanisms novel models are required.

Methods

We cocultured cryptococcal reference strains (C. gattii VGII/R265 and C. neoformans VNI/H99) with organoid-derived monolayers (ODMs) originating from adult stem cells of proximal (= Airway) and distal (= Alveoli) human respiratory tissue. Barrier function of ODMs was probed by measuring the transepithelial electrical resistance. Internalization of fungi into respiratory cells was visualized by immunofluorescence stainings. Fungal viability was assessed by cell counting and cultivation. Ink stainings were used to assess fungal cell morphology.

Results

While barrier function of airway ODMs was maintained, cryptococci induced a barrier breakdown in alveolar ODMs. Immunofluorescence stainings revealed that cryptococcal adhesion and internalization events to and into airway ODMs were rare, while alveolar ODMs showed an increased susceptibility towards cryptococcal internalization. Both cryptococcal strains were able to proliferate on ODMs. Analysis of fungal morphology revealed strain specific fungal adaptation with giant cells in C. gattii and pseudohyphal growth for C. neoformans while cocultured with alveolar, but not with airway ODMs.

Conclusions

Studying interactions of cryptococci with primary human cells of the respiratory tissue is feasible and suggests different fungal-host interactions of C. gattii and C. neoformans and distinct tissue reaction in proximal versus distal tissues. The model enables future studies in the tissue response leading to barrier breakdown and analysis of related fungal subpopulations, as well as immunologic reactions of epithelial tissues.

Poster

Poster Session 1

PP-1-01

Posaconazole-induced Excess Mineralocorticoid Syndrome – Observations in Three Pediatric Patients

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Background

Posaconazole is well tolerated and effective in prophylaxis and treatment of opportunistic invasive fungal diseases (IFDs) and recommended for high-risk pediatric patients with hematological malignancies (HM) and following allogeneic hematopoietic cell transplantation (HCT). Excess mineralocorticoid syndrome or pseudohyperaldosteronism is a rare but potentially significant adverse event.

Methods: Single-center, retrospective observational study of cases of posaconazole-induced pseudohyperaldosteronism (PIPH) patients with descriptive analysis of clinical and laboratory characteristics and outcome.

Results

Three pediatric patients (5,6, and 16 years) with lymphoblastic lymphoma (2) or status post allo-HCT (1) and PIPH were identified who received posaconazole tablets for antifungal prophylaxis (1) and for

treatment of proven or probable invasive aspergillosis (2), respectively, according to a previously validated dosing scheme (Tragiannidis et al., J Antimicrob Chemother 2019). All presented with the new onset of hypertension and hypokalemia within 2 to 9 weeks after initiation of posaconazole. Laboratory investigations revealed decreased plasma aldosterone levels in all and elevated serum 11-deoxycortisol levels in one patient in whom it was examined. Posaconazole trough concentrations in serum were moderately elevated and ranged from 1.8 to 7.16 ug/mL (median: 3.0). Following dose-reduction (2) and discontinuation (1) of posaconazole, hypertension and hypokalemia were reversible in all patients.

Conclusions

Posaconazole may be associated with secondary hypertension and hypokalemia, consistent with pseudohyperaldosteronism, and its development appears to be associated with higher serum posaconazole concentrations.

Figure 1

Clinical and laboratory characteristics of three patients with PIHA

Case	1	2	3
Age (years)	6	16	5
Sex	M	M	F
Primary underlying condition	B-lymphoblastic lymphoma	T-lymphoblastic lymphoma	s/p allo HCT
Indication for posaconazole	proven IPA	probable IPA	antifungal prophylaxis
Posaconazole dose	300 mg QD tablet	300 mg QD tablet	300 mg QD tablet
Baseline blood pressure	95/52	122/82	100/59
Hypertension (BP >95th percentile)	+	+	+
Max. reported BP with posaconazole	137/86	146/97	140/80
Time to onset of hypertension	3 weeks	9 weeks	2 weeks
Hypokalemia (≤3mEq/L)	+	+	+
Plasma aldosterone (nl: 32-353 pg/mL)	< 10 pg/mL	< 10 pg/mL	15.5 pg/mL
Plasma cortisole (nl:11-97 ng/mL)	120 ng/mL	110 ng/mL	96.1 ng/mL
Serum 11-deoxycortisole (nl:0.1-10 ug/L)	n.d.	n.d.	31.6 ug/L
Antihypertensive therapy	Amlodipine	Amlodipine/Metoprolole	Amlodipine
Dose and posaconazole trough levels (ug/mL)	300 mg: 1.8, 2.3, 5.3 200 mg: 3.1, 2.1	n.d.	300 mg: 2.3, 3.0,7.2 200 mg: 6.3 100mg: 1.7

PP-1-02

Invasive Aspergillosis in ICU patients with Influenza during the 2025/26 season: a multicenter study in Austria

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Introduction

Influenza-associated pulmonary aspergillosis (IAPA) affects up to 20% of critically ill influenza patients and is associated with mortality rates of approximately 50%. Early diagnosis remains challenging, often leading to delayed antifungal therapy. Universal antifungal prophylaxis has shown limited benefit, highlighting the need for personalized strategies to identify patients at highest risk. This study aims to describe the incidence, and outcomes of IAPA in critically ill influenza patients and to support the evaluation of LGALS3 genetic variation as a potential biomarker for risk stratification.

Methods

Patients in 7 institutions (Medical University of Graz, LKH Graz West, Medical University of Vienna, Kepler University Hospital, Linz, LKH Eastern Styria, Hartberg, LKH Eastern Styria, Feldbach, and LKH Eastern Styria, Fürstenfeld) in Austria were enrolled during the 2025/26 influenza season as part of the ongoing multicenter study GALACTIC (04/2025–04/2028) which enrolls critically ill influenza patients admitted to intensive care units to validate genetic variation in the *LGALS3* gene as a biomarker for risk stratification for IAPA. A descriptive analysis of IAPA incidence, demographics, and outcomes was performed.

Results

A total of 41 patients with influenza were included, of whom 2 (5.1%) developed IAPA. The median age was 69 years (range 24–88). Overall, 27 (65.9%) patients survived and 14 (34.1%) died. Both patients with IAPA died (100%).

Conclusion

In this preliminary cohort, IAPA occurred in a small proportion of critically ill influenza patients but was associated with very high mortality, as both affected patients died. These preliminary data highlight the importance of early risk stratification and support ongoing efforts to identify biomarkers, such as LGALS3 genetic variation, to guide targeted preventive strategies.

PP-1-03

Life-threatening Invasive Fungal Infections in Patients With T-Cell Large Granular Lymphocytic Leukemia

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Introduction

T-cell large granular lymphocytic leukemia (T-LGLL) is a rare chronic lymphoproliferative disorder characterized by clonal expansion of cytotoxic T cells. Disease inherent or treatment-related severe neutropenia (absolute neutrophil count <0.5 × 10^9/L) occurs in 10 to 45% of patients predisposing to

serious infections, the leading cause of death in T-LGLL. Although prolonged neutropenia is a recognized risk factor for invasive fungal infections (IFI), evidence for IFI in T-LGLL is limited to case reports.

Objectives

To describe IFI in patients with T-LGLL and raise the question whether antifungal prophylaxis should be considered in selected patients.

Patients & Methods

Three patients with T-LGLL treated at our tertiary care center within one year who developed life-threatening IFI during prolonged neutropenia.

Results

All patients presented with neutropenic fever refractory to broad-spectrum antibiotics. Patient 1 (63-y/o female) developed disseminated pan-susceptible *Candida albicans* infection with cutaneous and deep-seated muscle abscesses and was successfully treated with surgical drainage, caspofungin, and prolonged fluconazole. Patients 2 and 3 developed invasive pulmonary aspergillosis (IPA). Patient 2 (34 y/o male) presented with pulmonary nodules and halo sign on CT, without microbiological species identification. He achieved radiologic resolution with voriconazole but was switched to isavuconazole due to adverse effects. Patient 3 (61 y/o female) developed mixed IPA due to *A. fumigatus* and *A. flavus*, requiring treatment switch from liposomal amphotericin B to isavuconazole. She succumbed to bacterial sepsis.

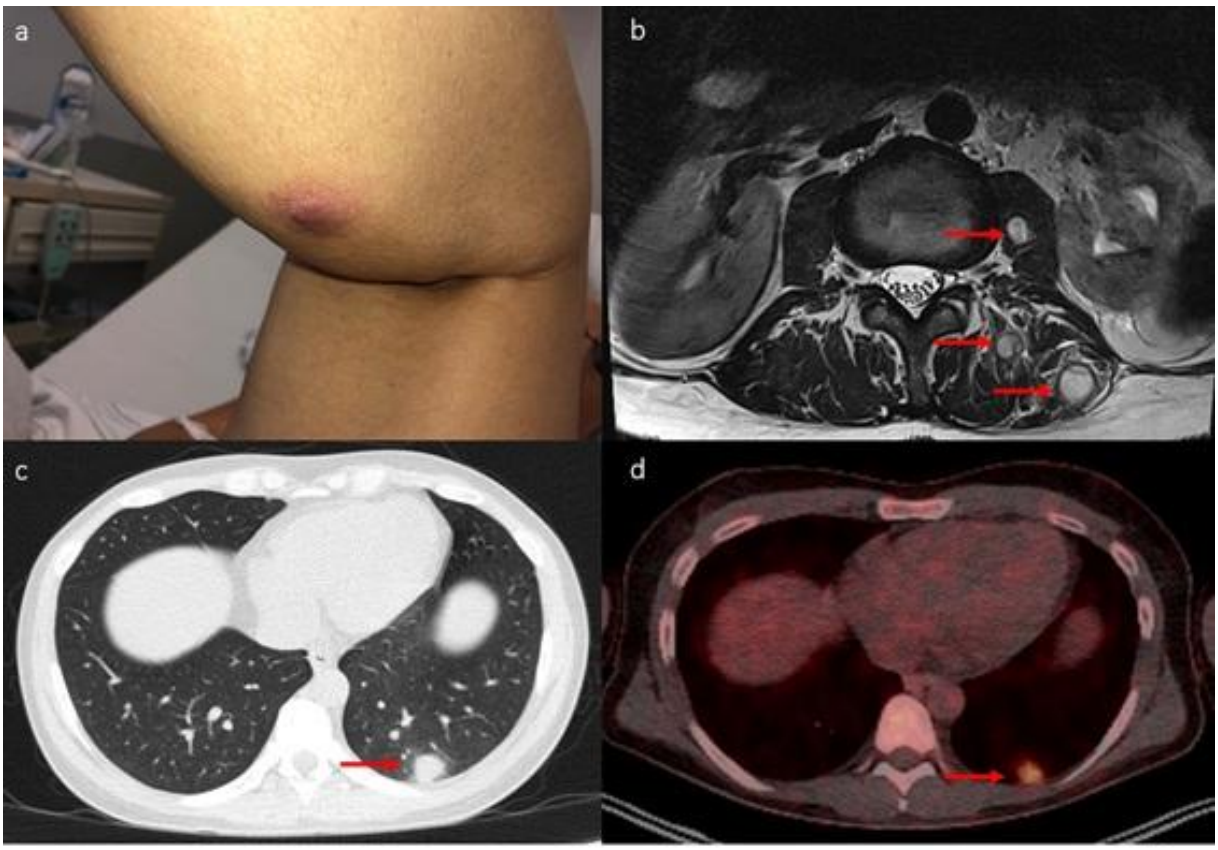
Conclusion

We highlight the underrecognized risk of IFI in T-LGLL patients with prolonged neutropenia. Mold-active antifungal prophylaxis may be considered in selected high-risk patients, balancing benefits against toxicity, drug interactions, and cost. Prospective data are needed to improve IFI risk stratification in T-LGLL.

Figure 1

Category	Patient 1	Patient 2	Patient 3
Demographics	63-year-old female	34-year-old male	61-year-old female
Underlying disease	T-LGLL	T-LGLL	T-LGLL
Duration of neutropenia prior to IFI	more than one year	more than eight months	more than four years
Comorbidities / risk factors	Rheumatoid arthritis	Ulcerative colitis; primary sclerosing cholangitis; hidradenitis suppurativa; anti-granulocyte antibodies	Rheumatoid arthritis; small-vessel vasculitis
IFI diagnosis	EORTC/MSG proven invasive candidiasis	EORTC/MSG possible invasive pulmonary aspergillosis	EORTC/MSG probable invasive pulmonary aspergillosis
IFI species and susceptibility testing	*Candida albicans* (pansusceptible)	No pathogen detected	*Aspergillus fumigatus* (wild-type):
Antifungal treatment	Caspofungin (4 weeks); fluconazole (ongoing, 7 months)	Voriconazole (3 months); isavuconazole (ongoing, 1 month)	Liposomal amphotericin B (one week); isavuconazole (five months, until death)
Outcome	Alive at 8-month follow-up; PET-CT shows no hypermetabolic activity in previously affected sites	Alive at 5-month follow-up; chest CT lesions resolved after 3 months of voriconazole treatment	Death due to septic shock caused by necrotizing gram-negative soft tissue infection of a lower limb ulcer

Figure 2



a) Cutaneous abscess of the lower limb caused by disseminated candidiasis with *Candida* albicans (patient 1)
b) Abscesses of the lower back and psoas muscle due to *Candida albicans* (patient 1)
c) Chest CT showing pulmonary nodule compatible with invasive pulmonary aspergillosis (patient 2)
d) PET-CT detecting hypermetabolic 18F-FDG uptake in the corresponding lesion (patient 2)

PP-1-04

Implementation of an international weekly expert case conference for invasive fungal diseases – an initiative of the ECMM Excellence Center Cologne

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Objectives

To provide structured consultation for patients with invasive fungal diseases (IFD); to facilitate a network of consulting physicians, laboratories, and specialized departments; to improve patient care and outcome of IFD.

Methods

The ECMM Excellence Center for Invasive Mycoses at the University Hospital Cologne offers a consultation service for complex IFD as an interdisciplinary virtual mycology case conference. Cases can be submitted via standardized request form and are discussed with participation from Infectious Diseases, Hematology, Microbiology, and Radiology. Data collection includes patient demographics and information on the consulting departments, underlying disease, microbiological pathogen detection, available imaging, prior antifungal therapy, and patient outcome.

Results

In 2025, 129 consultations were reviewed and discussed, submitted by 20 different disciplines, most frequently Infectious Diseases (28.7%), and Pulmonology (8.5%). Additionally, a structured interdisciplinary written consultation was provided on another 25 cases when case presentation was urgent. The most commonly diagnosed fungal species were Aspergillus fumigatus (16.28%), Candida glabrata (6.98%), and Fusarium spp. (6.98%). Rare molds or yeasts were detected in 32.5% of cases, and multiple fungal species in 10.5%. Lungs (46.51%), liver (20.93%), spleen (18.60%), CNS (13.95%), blood stream (9.30%), and bones (9.30%) were most frequently affected sites of IFD. The most common consultation question concerned pharmacological therapy and treatment duration (48.8%). In 96.9% of cases, patients were hospitalized.

Conclusion

The mycology case conference provides access to expert opinion and guideline-concordant diagnostic and therapeutic approaches for patients with rare and complex infections which are encountered more and more frequently. Whether consultation improves patient outcome and health economic endpoints will be addressed in future case–control analyses.

PP-1-05

Bioassay zur Olorofim-Bestimmung im Serum: eine Alternative im Vergleich zu LC-MS/MS?

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Einführung

Olorofim (OLO) ist ein neues Antimykotikum zur Behandlung therapieresistenter Pilzinfektionen. Da nicht jedes Labor Zugang zu LC MS/MS hat, könnte eine spezifische und einfache Analysemethode zum therapeutischen Drug Monitoring mittels Bioassay eine Alternative zur Bestimmung der OLO-Konzentrationen im Serum darstellen.

Zielsetzung

Validierung der Leistungsfähigkeit des Bioassays, Vergleich mit LC-MS/MS.

Materialien & Methoden

Ein OLO-sensibler *Paecilomyces varioti* (McFarland 1.0) wird auf Sabouraud-Agar aufgetragen. Serum von Patienten unter Therapie im Verlauf (n = 4), 5 OLO-Standardkonzentrationen (MedChemExpress, USA) und 5 Qualitätskontrollen (QK) werden auf in den Agar vorgestanzte Löcher pipettiert. Nach Inkubation wird der Hemmhofdurchmesser der Standards gemessen und eine Kalibrationskurve erstellt, anhand derer die Konzentrationen der zu testenden Seren abgelesen werden können.

Ergebnisse

Die Linearität der Standardkurve des Bioassays erzielte eine R^2-Wert von 0,898 im Vergleich zur LC-MS/MS (R^2 = 0,996). Die untere Quantifizierungsgrenze des Bioassays beträgt 0,5 µg/ml, > 4 µg/ml kann keine Linearität nachgewiesen werden. Die Intra-Assay-Genauigkeit des Bioassays für QK war wie folgt: 0,5 µg/ml = 0,481 ± 0,21; 0,75 µg/ml = 1,040 ± 0,15; 1,5 µg/ml = 2,031 ± 0,1; 3 µg/ml = 2,879 ± 0,170 (Mittelwert ± Standardabweichung). Die Inter-Assay-Genauigkeit des Bioassays für die QKs war ähnlich. Die OLO-Konzentrationen der Patient*innen wurden mittels Bioassay tendenziell höher bestimmt als mittels LC MS/MS (Mittelwert = 0,624 µg/ml versus 0,473 µg/ml). Eine parallele Gabe anderer Antimykotika, die zu den erhöhten OLO-Konzentrationen geführt haben konnte, wurde mittels Multi-Azol-LC-MS/MS ausgeschlossen.

Schlussfolgerung

Im Bereich 0,5 bis 4 µg/ml zeigt der Bioassay eine gute Linearität im Vergleich zur LC MS/MS. Der Bioassay ist nicht OLO-spezifisch, sondern reagiert auch bei Therapie mit anderen Antimykotika. Weitere Analysen und Optimierungen folgen.

PP-1-06

Fluconazol-Bestimmung aus Speichel unter Anwendung von Volumetric Absorptive Microsampling (VAMS) und isokratischer HPLC-UV – Projekt der PharMSchool Münster

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Einführung

Fluconazol ist ein Triazol-Antimykotikum und wird zur Prophylaxe von Candida-Infektionen bei Kindern mit hämatologischen Neoplasien eingesetzt. [1] Nach Aussage einer niederländischen Publikation weisen krebskranke Kinder häufig subtherapeutische Fluconazol-Spiegel (< 11 mg/L) auf, weshalb ein

therapeutisches Drug Monitoring (TDM) empfohlen wird, um unzureichende Konzentrationen festzustellen. [2]

Zielsetzung

Im Rahmen der PharMSchool-Projekte der Universität Münster hat eine Gruppe von Pharmaziestudierenden sich das Ziel gesetzt, die Fluconazol-Bestimmung aus Speichel zu untersuchen, um insbesondere Kindern ein schmerzfreies TDM unter Vermeidung einer Blutabnahme zu ermöglichen. Die Abnahme der Speichelflüssigkeit sollte mittels der Volumetric Aborptive Microsampling (VAMS)-Technologie unter Anwendung von sogenannter Mitra® (Neoteryx by Trayan, Torrance, USA) durchgeführt werden (Probenvolumen:10 µL).

Patienten & Methoden

Für die Analyse aus Speichel wurden 10 unterschiedliche Probenpaare (EDTA-Vollblut und entsprechende Speichelprobe) hergestellt sowie 4 Patientenprobenpaare gesammelt und vermessen. Als Grundlage für die Probenverarbeitung und Analyse diente die Methode von *Zimbelmann* et al. [3]

Ergebnisse

Sowohl die gespikten Proben- als auch Patientenprobenpaare sind erfolgreich vermessen worden und lieferten nach Korrelationsanalyse einen durchschnittlichen Umrechnungsfaktor von 1,2.

Schlussfolgerung

Die erfolgreiche Fluconazol-Bestimmung aus Speichel lässt darauf schließen, dass unter Anwendung von Mitra® ein TDM auch ohne eine den Patienten belastende Blutabnahme funktionieren kann. Die Konzentrationsbestimmung aus Speichel muss noch mit weiteren Patientenproben klinisch validiert werden, um eine sichere und präzise Anwendbarkeit zu zeigen.

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PP-1-07

Cardiac and ophthalmic involvement in candidaemia: results from the ECMM Candida III study

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Introduction

Candida spp. are among the most common fungal pathogens. In *Candida* bloodstream infections, hematogenous complications such as endocarditis and endophthalmitis must be considered. Antifungal resistance and limited tissue penetration remain major therapeutic challenges.

Objectives

To assess the frequency and characteristics of endocardial and ocular complications in candidaemia and the influence of antifungal therapy.

Methods

Subgroup analysis of the Candida III study. Echocardiographic and ophthalmologic findings were analyzed alongside clinical characteristics, outcomes and antifungal therapy.

Results

Echocardiography and ophthalmologic examination were performed in 226 (35.8%) and 170 (26.9%) of 632 patients. Findings consistent with endocarditis and ocular involvement occurred in 16/226 (7.1%) and 16/170 (9.4%) examined patients, respectively, including 3 patients presenting with both.

Among patients with endocarditis or ocular involvement, echinocandins were the initial treatment in 19/29 (65.5%). Overall 180-day-fatality was 37.9% (11/29) versus 41.6% (250/601, p = .153).

180-day-fatality was higher in patients without than with echocardiography (47.4% vs. 31.0%, OR 0.50, 95% CI 0.36–0.71; p < .001), while 180-day-fatality in patients with endocarditis-consistent findings was 50.0% (95% CI 22.5–77.5%).

Conclusions

Endocardial and ocular involvement occurred in a relevant proportion of candidaemia patients. Given limited evidence underlying current guideline recommendations, the observed rate of endocardial and ocular involvement among selectively screened patients raises concern for underdiagnosis.

Higher fatality rates in patients without echocardiography, approaching rates observed in patients with endocarditis-consistent findings, may indicate undetected cardiac involvement. These findings suggest a potential clinical relevance of systematic screening, although causal inferences are limited by the observational design.

Figure 1

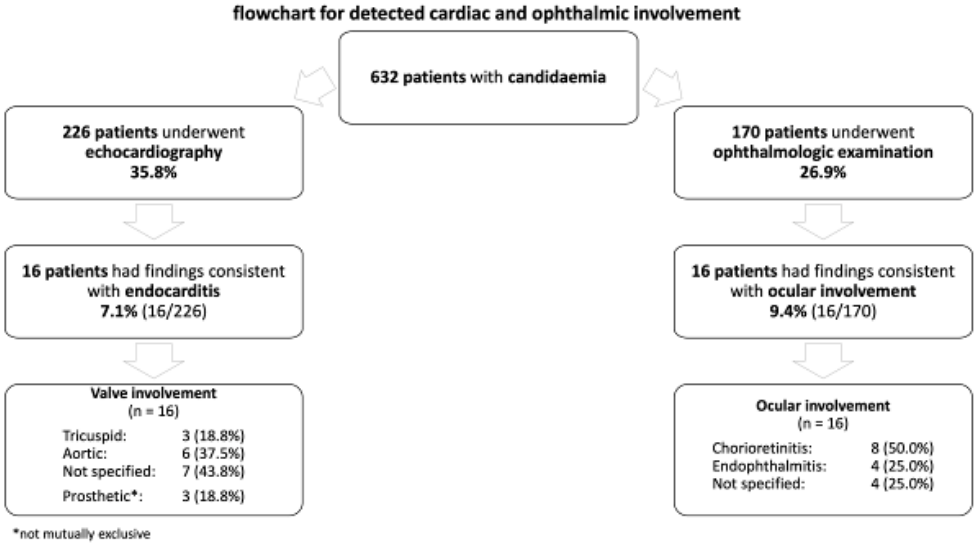
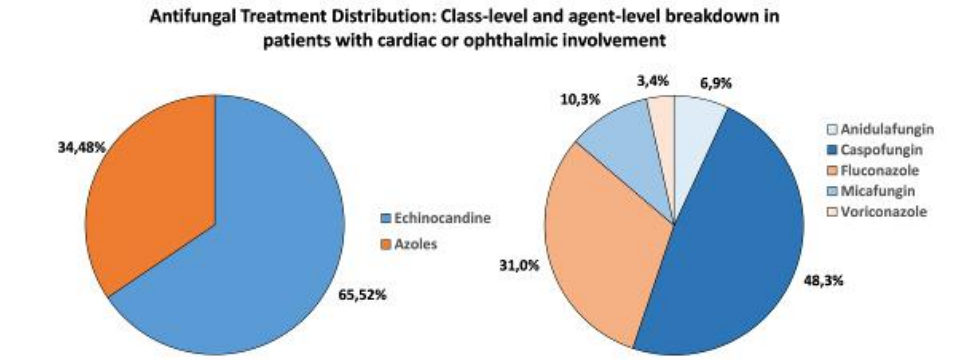


Figure 2



PP-1-08

***Petromyces alliaceus* – Erstmals als Erreger einer Onychomykose nachgewiesen**

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Die Onychomykose ist weltweit die häufigste Pilzinfektion beim Menschen. Nicht immer sind Dermatophyten die Auslöser.

Wir berichten über den erstmaligen Nachweis von *Petromyces (P.) alliaceus* (früher *Aspergillus (A.) alliaceus*) als Auslöser einer Nagelmykose.

Bei einer sonst gesunden 64-jährige Patienten mit klinisch vermuteter Zehennagelmykose wurde der aus dem Nagelmaterial isolierte Erreger konventionell mykologisch charakterisiert. Kulturmaterial wurde histologisch untersucht und genetisch klassifiziert (durch Prof. Gräser, Berlin und das NRZMyk). Eine Literaturrecherche wurde zur Biologie, Verbreitung und medizinischen Bedeutung von *P.alliaceus* durchgeführt.

Der in mehrfachen zeitlich versetzten Nagelproben alleinig nachgewiesene rasch wachsende Fadenpilz bildete typische Aspergillusköpfchen aus, später entwickelten sich außerdem schwarze harte Körperchen auf der Thallusoberfläche, die anfangs solide waren, innerhalb von Wochen aber eine Umstrukturierung des enthaltenen Zellverbandes erfuhren. Genetisch wurde der Erreger als *P.alliaceus* identifiziert. Eine antimykotische Therapie führte zu nachhaltiger Abheilung.

P. alliaceus gehört zur *A. flavus*-Gruppe, kann Pflanzen schädigen und Toxine bilden. Bemerkenswert ist die Fruktifikation von *P. alliaceus*. Unter geeigneten Bedingungen werden neben der *Aspergillus*-typischen vegetativen Sporenbildung zunächst Sklerotien-artige harte Körperchen auf der Thallusoberfläche gebildet, in denen sich innerhalb von Wochen fertile cleistothecienartige Ascocarpe entwickeln können. Diese homothallische perfekte Form des Erregers wurde erst spät allgemein wahrgenommen. Die taxonomisch engsten Verwandten sind *A. lanosus* und *A. vandermerwei*.

In der Humanmedizin wurde *P. alliaceus* nur selten als Krankheitserreger nachgewiesen, so bei pulmonaler Aspergillose abwehrgeschwächter Patienten. Unser Fall zeigt jedoch, daß *P. alliaceus* sogar bei immunkompetenten Patienten eine Onychomykose verursachen kann.

PP-1-09

Itraconazole-resistant *Trichophyton rubrum* isolates showed transcriptional up regulation of sterol 14-α demethylase genes *Erg11A* and *Erg11B* compared to sensitive wild type strains

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Recently, *T. rubrum* isolates were obtained from a patient who failed therapy with itraconazole, voriconazole and terbinafine1. MLN methods were adapted according to the EUCASTE.Def11.02 and comparable protocols for itraconazole susceptibility testing for several *Trichophyton* species including sensitive and resistant isolates of *T. rubrum*2. Resistant *T. rubrum* strains showed increased inhibitory concentrations against itraconazole, while retaining single-copy status of both *Erg11B* and *Erg11A* genes3. Expression analyses of sterol 14-α demethylase genes were performed as previously described4 and demonstrated upregulation of both *Erg11A* and *Erg11B* in resistant *T. rubrum* strains compared with sensitive isolates. In contrast, *T. indotineae* strains showed overexpression only of *Erg11B*4, which was at least partly associated with increased copy numbers caused by different types of gene amplification5. These findings suggest that prolonged exposure to sublethal antifungals concentrations during patient treatment generated similar selective pressure in *T. rubrum* and *T. indotineae* leading to the evolution of novel resistance mechanisms. However, the distinct molecular patterns indicate independent evolution of azole resistance in the two species.

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PP-1-10

An overview of the pathogen spectrum in 2025 in molecular dermatophyte diagnostics in private dermatology practices

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Introduction

In German dermatology practices, the general identification of dermatophytes using microscopy and culture has a long tradition. For several years now, there has been an increasing use of molecular methods.

Objectives

This study aims to give an impression of the distribution of DNA-based dermatophyte results in German dermatology practices.

Patients & Methods

2161 molecular test results, were generated 2025 in 12 dermatology practices by an outpatient laboratory service in the state of Baden-Württemberg. The analysis was done using the DermaGenius® 3.0 Complete RT-PCR test on the BMS MIC system.

Results

Out of 2161 samples, 1462 were dermatophyte-negative (68%) and 699 dermatophyte-positive (32%). The detected dermatophytes are listed in table 1:

Conclusion

Patient samples analyzed by RT-PCR in 12 dermatology practices resulted in 68% negatives. *Trichophyton (T.) rubrum* and *T. interdigitale/ T. mentagrophytes* contributed to 97% of all positives. Similar results were reported by Uhrlass et al. (2023) in a laboratory setting and could be expected based on several prevalence studies.

Figure 1: Dermatophyte spectrum in 12 private dermatology practices

Figure 1

Dermatophytes	n	Percentage of positive samples (n=699)
Trichophyton (T.) rubrum	610	87
T. interdigitale/ T. mentagrophytes	70	10
Trichophyton tonsurans	6	0.9
Epidermophyton floccosum	4	0.6
Nannizzia gypsea	4	0.6
Trichophyton benhamiae	1	0.1
Microsporum canis	1	0.1
T. quinckeanum/ T. schoenleinii	1	0.1
Trichophyton violaceum	1	0.1
Trichophyton verrucosum	1	0.1

PP-1-11

Pilot evaluation of the EurobioPlex two-step PCR strategy for dermatophyte diagnostics

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Introduction

Dermatophytosis affects up to 1.7 billion people worldwide. Conventional diagnostics are limited by reduced sensitivity, especially after antifungal exposure, overgrowth by contaminants, and long turnaround times. Reimbursement for dermatophyte PCR in Switzerland (2026) enables broader use of molecular diagnostics and evaluation of a two-step PCR workflow (EurobioPlex).

Objectives

To assess the performance and real-world applicability of a two-step dermatophyte PCR compared with culture.

Materials & Methods

We retrospectively analyzed 47 routine specimens (skin, nail, swabs) collected between September 2025 and January 2026. All samples underwent parallel culture and PCR testing. Samples with persistent PCR inhibition were excluded. Discordant PCR-positive/culture-negative results were evaluated by expert adjudication using clinical and microbiological data.

Results

47 specimens from 45 patients (median age 58 years) were included. Culture detected dermatophytes in 6/47 samples (4 Trichophyton rubrum, 2 T. interdigitale); 31 were negative and 10 showed non-dermatophyte fungi. PCR confirmed 5/6 culture-positive cases; one false-negative was attributed to

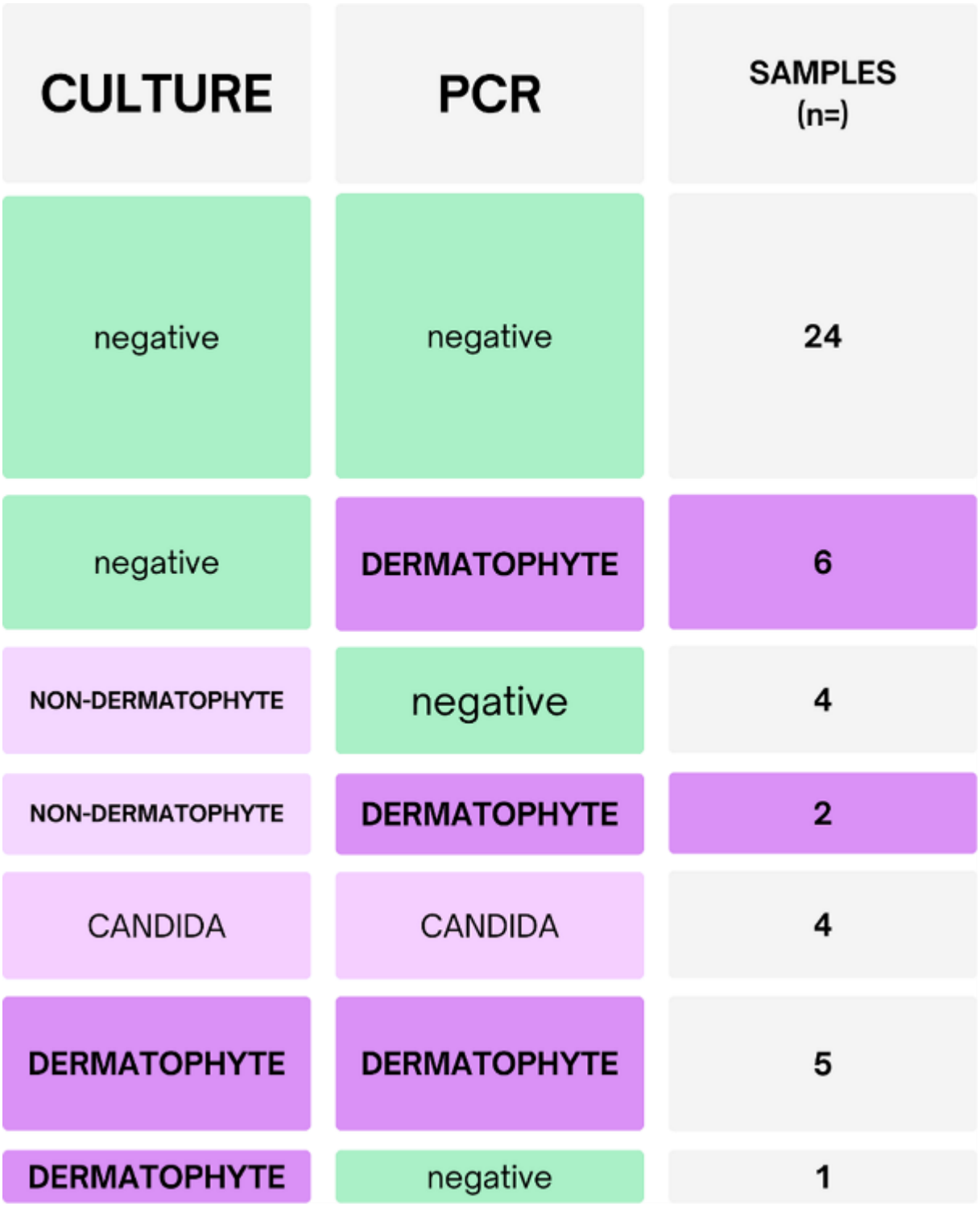
insufficient material. PCR detected dermatophytes in 8 additional culture-negative samples; the remainder were concordantly negative. Expert adjudication showed near-complete consensus.

Conclusion

PCR improves dermatophyte detection compared with culture while reducing turnaround time. It is a valuable complementary tool and may serve as a primary method in selected patients with high pretest probability and negative culture.

Table: Diagnostic yield of PCR versus culture in routine samples.

Figure 1



PP-1-12

Prävalenz von Dermatophyten bei Haustieren: Auswertung der kulturellen Diagnostik von Hautpilzen in einem veterinärmedizinischen Diagnostiklabor in 2025

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Zwischen Menschen und Haustieren besteht oft ein enger Kontakt. Hunde, Katzen und Kleinsäuger können symptomatische als auch asymptomatische Träger von Dermatophyten sein und stellen somit ein Zoonoserisiko dar.

Ziel dieser Studie ist die retrospektive Auswertung kultureller mykologischer Untersuchungen von Haut- und Haarproben aus dem Jahr 2025 aus einem veterinärmedizinischen Diagnostiklabor. Analysiert wurden Häufigkeit und Verteilung der Dermatophyten *Microsporum (M.) canis*, *Trichophyton (T).mentagrophytes* und *T. mentagrophytes var. benhamiae* bei Hunden, Katzen und Kleinsäugern (Meerschwein, Kaninchen, Ratte, Hamster) unter Berücksichtigung der Haltung (Privathaushalt vs. Tierheim/Tierschutzeinrichtung) sowie bei Hund und Katze zusätzlich des Alters (< 1 Jahr vs. > 1 Jahr).

Es erfolgte eine Anzucht auf Selektivnährböden bei 28°C bis zu 28 Tage mit anschließender morphologischer und bei Bedarf mikroskopischer oder massenspektrometrischer (Maldi-ToF) Identifikation.

Die Gesamtprävalenz der analysierten Dermatophyten bei den Haustieren betrug 11,5 % (557/4837). Beim Hund waren 3,2 % der Tiere positiv (78/2410), 5,4 % der Hunde aus Tierheimen (n=2/37) und 7,0 % innerhalb der Jungtiere (n=19/271) waren positiv. Bei insgesamt 18,4 % der Katzen wurden Hautpilze nachgewiesen (337/1831). 36,2 % der Katzen aus Tierheimen (n=47/130) und 38,7 % der Tiere innerhalb der Jungtierpopulation war positiv (n=163/421). Bei Hunden und Katzen wurde hauptsächlich *M. canis* nachgewiesen (n=43, 55,1 % bzw. n=282, 83,7 %). Unter den Kleinsäugern waren 23,8 % positiv (142/596), 19,4 % der Tierheimtiere waren betroffen (n=6/31). *T. mentagrophytes var. benhamiae* (124/142) dominierte beim Meerschwein.

Katzen und Meerschweinchen zeigen hohe Prävalenzen für zoonotische Hautpilze. Jungtiere und Tiere aus Tierheimen sind oft betroffen. Der Kontakt zu insbesondere diesen Tieren sollte daher berücksichtigt werden, wenn Patienten mit Dermatophytosen in der dermatologischen Praxis vorstellig werden.

PP-1-13

Performance of a Candida Mannan Antigen lateral flow assay in Diagnosing Candidemia and Invasive Candidiasis

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Background

Invasive candidiasis is a severe, potentially life-threatening infection in which delayed diagnosis increases mortality. Culture-based methods are often slow and lack sensitivity, highlighting need for rapid diagnostics.

This study compared the *Candida* mannan antigen lateral flow assay (CAN-AG LFA) with the standard Mannan antigen ELISA (ELISA) in patients with confirmed *Candida* infections.

Methods

Seventeen samples from 15 patients with confirmed *Candida* infections were collected at the Medical University of Graz, Austria. Candidemia was identified in 12 patients by blood cultures, and non-candidemic invasive candidiasis in three patients using swabs or punctates. One patient with candidemia contributed three samples, resulting in 17 total samples. Serum samples were tested using the CAN-AG LFA (TECO® Fast Candida Mannan Antigen LFA, TECOmedical AG, Switzerland) and Mannan ELISA (Platelia Candida Ag Plus, Bio-Rad, USA). β-D-glucan (BDG) results from routine diagnostics were available for all patients. Concordance was assessed using Cohen"s Kappa and Chi-square tests; correlations using Pearson"s and Spearman"s coefficients.

Results

The CAN-AG LFA detected 14/17 (82.4%) of samples as positive. The ELISA identified 2 samples as positive, 2 as borderline, and 13 as negative. Concordance between the two assays was low, with 3/17 (17.6%) samples showing agreement. No significant association (Chi-square = 0.201) was observed and agreement beyond chance (Cohen"s Kappa = −0.102, p = 0.201). Moderate positive trends were found between assays (Pearson r = 0.426, p = 0.088; Spearman ρ = 0.430, p = 0.085), without statistical significance. BDG positivity occurred in 5/17 samples (29.4%), fewer than detected by CAN-AG LFA.

Conclusion

CAN-AG LFA showed the highest sensitivity versus culture, but lacked agreement with ELISA and showed limited concordance with BDG results. Specificity should be evaluated in future studies.

Figure 1

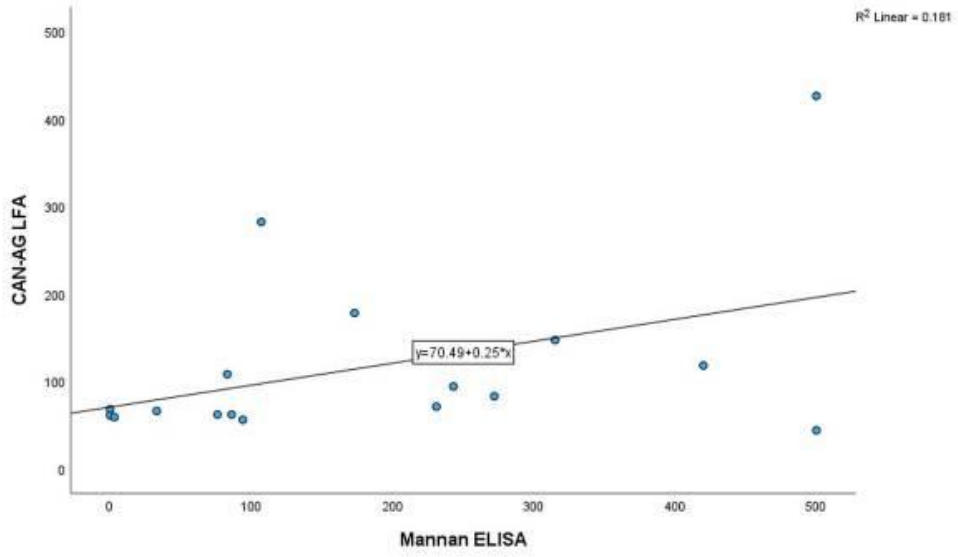


Figure 1 Scatter plot highlighting the correlation of the two assays

PP-1-14

Candi-MAG study: Evaluation of a *Candida* Mannan Antigen Lateral Flow Assay for the Diagnosis of Candidemia

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Background

Candida bloodstream infections carry high mortality. Early antifungal therapy is critical, yet diagnosis remains challenging; therefore, rapid and reliable diagnostic tests are needed. This study evaluated a novel lateral flow assay (LFA) detecting *Candida* mannan (*Candi*-MAG) versus blood culture (BC) and 1,3-β-D-glucan (BDG) in patients at risk of candidemia from three Austrian centres.

Methods

Prospectively, consecutive serum samples (n=254) from 134 patients (median age 64 (20-86) years; 34.3% female) with suspected candidemia from three Austrian centres (Graz, Wels, Innsbruck) were included. All samples underwent serum *Candi*-MAG testing (TECOmedical), and BDG (Fungitell) testing; BC served as reference. McNemar and $\chi 2$-tests were used.

Results

Prevalence of candidemia by BC was 12.6% (32/254). Relative to BC, *Candi*-MAG showed lower sensitivity (37.5% (12/32) vs. 71.9% (23/32)), but higher specificity (68.5% (152/222) vs. 5.9% (13/222)) than BDG. Positive and negative predictive values were higher for *Candi*-MAG (14.6% (12/82) vs. 9.9% (23/232) and 88.4% (152/172) vs. 59.1% (13/22), respectively). Overall accuracy was 64.6% (164/254) for *Candi*-MAG, and 14.2% (36/254) for BDG. Antigen assays were significantly discordant ($p<0.001$).

Conclusion

Candi-MAG showed modest specificity but low sensitivity, missing about two-thirds of BC-positive candidemia. For a life-threatening condition, this is clinically insufficient. A negative result cannot reliably exclude infection and may delay therapy. The high NPV mainly reflects the low prevalence rather than strong test performance, limiting its rule-out value. Using BC as the sole reference likely underestimates performance; a composite reference standard with clinical criteria would be more robust. Potential earlier positivity vs. BC and effect on time-to-therapy need further studies. Limitations include low prevalence of candidemia in this cohort and low sensitivity of BC as the reference standard.

PP-1-16

Fosmanogepix expanded access in patients with invasive mould infections from Germany, Austria and Switzerland

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Background

Fosmanogepix (FMGX) is available via expanded access (EA) for treating serious fungal infections in patients with drug resistance, lack of response, and/or intolerance to standard antifungal therapy.

Methods

Standardised data from patients with an invasive mould infection (IMI) treated with FMGX via EA were collected and analysed to describe demographic data and assess treatment response according to MSG-EORTC criteria.

Results

Between Feb-24 and Jan-26, 20 patients (5 female; median age 55.5 [range, 7–71] years) completed FMGX treatment from Germany (14), Austria (3) and Switzerland (3). Of the patients, 65% (13/20) had underlying malignancies (mostly haematological conditions) and 35% (7/20) had other conditions (**Tab. 1**). Patients with malignancies presented with invasive fusariosis (9), aspergillosis (3), and mucormycosis (1); organ manifestations included bloodstream (7), disseminated IMI (6), and skin-soft tissue (6), pulmonary (5). Patients with non-malignant underlying conditions presented with invasive fusariosis (2), aspergillosis (2), mucormycosis (1), scedosporiosis (1), and lomentosporiosis (1); organ manifestations included lung (3), sinus (2) and bone/joint (2) disseminated IMI (1). Favourable responses were reported for 69% (9/13) of patients with underlying malignancies and 71% (5/7) with non-malignant underlying conditions. All-cause mortality at 6 weeks was 31% (4/13) in patients with underlying malignancies and 29% (2/7) in patients with non-malignant underlying conditions (Fig. 1). Three patients discontinued treatment due to nausea, liver function test elevations. or central nervous system events.

Conclusion

This case series highlights the unmet need for new antifungals in patients with complex underlying conditions and IMI, where resistance, lack of response, or intolerance limit standard therapies. FMGX showed efficacy and tolerability across diverse patient groups.

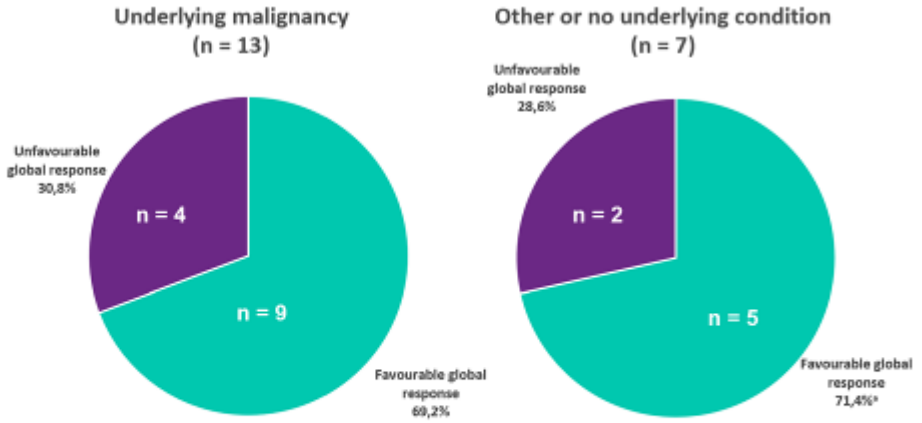
Figure 1

Table 1. Reasons for requesting EA with fosmanogepix

Underlying condition	Resistant pathogen	Refractory to SOC	Intolerance to SOC
Malignancies (n = 13)	10	5	6
Other or no underlying conditions (n = 7)	4	4	6

EA, expanded access; SOC, standard of care

Figure 2



	Malignant underlying conditions	Other or no underlying condition
Treatment duration, days		
Median (range)	69 (17–205)	52 (3–393)
All-cause mortality, 6 weeks		
% (n/N)	31% (4/13)	29% (2/7)

PP-1-17

Development of a complex in vitro cell culture system for investigating antifungal drug delivery approaches

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Introduction

Invasive aspergillosis (IA) remains a serious clinical challenge, particularly in immunocompromised individuals, with mortality rates up to 95%. This underlines importance of novel antifungal therapies, which are needed urgently as an alternative therapeutic approach. Nanoparticles could offer a targeted antifungal strategy by addressing limitations of conventional antifungals. However, this approach requires trustable *in vitro* testing systems, mimicking *in vivo* conditions. Air-liquid interface (ALI) provides physiologically relevant conditions for pulmonary drug delivery testing in a time-efficient manner.

Objectives

This study aims to establish and optimize an *in vitro* lung model with various pulmonary cell lines for testing of infection models with novel antifungal drug delivery systems like nanoparticles.

Materials & Methods

Human alveolar epithelial A549/H441 cells were cultured on ALI inserts and then exposed to air after 4 days of cultivation, to promote cell differentiation. BLaER1/THP-1 macrophages were then added on the epithelial cells. Transepithelial electrical resistance (TEER) was performed to evaluate barrier integrity. For infection, *A. fumigatus* spores were used and treated with different antifungal formulations. Fluorescent microscopy was utilized to determine cell type-specific markers and to assess infection.

Results

Epithelial cell differentiation under ALI conditions was confirmed by fluorescence microscopy using cell type–specific markers for type I and type II pneumocytes, as well as macrophages. In addition, barrier

integrity of the cells was confirmed with TEER measurements. Infection model with *A. fumigatus* conidia and successful treatment with both pristine drugs and nanoparticle formulations was established.

Conclusion

A functional ALI co-culture model was established to investigate antifungal drug delivery systems, contributing to the development of novel strategies for combating invasive aspergillosis.

PP-1-18

MedicalGuideline.org – a Collaborative Web-Based Platform for Structured Clinical Guideline Development – Concept, Implementation and Application

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Background

Clinical guidelines are traditionally created using spreadsheet-based tables, with collaboration managed via email and file sharing leading to inconsistent formatting, limited version control and difficulties coordinating distributed expert groups. MedicalGuideline.org was developed as an AI-assisted online platform for structured, collaborative guideline authoring.

Objectives

To develop and implement a web-based platform for collaborative clinical guideline creation; to provide integrated tools for literature management, structured authoring, and AI-assisted text drafting.

Methods

MedicalGuideline.org is a globally accessible, account-based system with role and group management. Key features include structured chapter and outline management with formatting templates, inline guidance and training content and a comment and issue-tracking system. A personal inbox allows members to track changes, new entries and comments across projects. A literature management system with AI-assisted variable extraction supports evidence synthesis. An integrated AI module enables literature summarization, interactive literature chat, and text drafting based on table entries and cited references. The platform supports version control with tracked changes and revision comparisons and export to presentation slides and formatted word files with linked references and author affiliations.

Results

Five guidelines are currently in progress on the platform. The aspergillosis guideline, a joint initiative of the European Confederation of Medical Mycology (ECMM), the International Society for Human and Animal Mycology (ISHAM) and the American Society for Microbiology (ASM), was already in development and

became the first to continue in 2024 within MedicalGuideline.org. Further guidelines include molds in burns (ECMM) and three guidelines by the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology (AGIHO): Diagnostics and Treatment of Invasive Fungal Diseases, Central Venous Catheter Infections and Antibacterial and Pneumocystis jirovecii Pneumonia Prophylaxis.

The platform currently has over 200 registered active members from multiple countries. Across all projects, approximately 250 chapters have been structured, with around 2,000 table entries and 175 text entries recorded. Compared to conventional manual workflows, the platform reduces redundant communication, eliminates formatting inconsistencies and accelerates review and revision cycles.

Conclusion

MedicalGuideline.org provides an infrastructure for international clinical guideline development, integrating collaborative authoring, AI-assisted tools, structured formatting, and standardized export into a single platform. Five active guideline initiatives and over 200 members from multiple international societies reflect broad acceptance across the medical mycology community.

Keywords: clinical guidelines, collaborative platform, guideline development, medical informatics, aspergillosis, mycology, digital tools, artificial intelligence

PP-1-19

Association between 1,3-Beta-D-Glucan and immune dysregulation in liver cirrhosis

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Objectives

Liver cirrhosis is a severe systemic disease with a high global prevalence across low-, middle-, and high-income countries. The aim of the present study was to investigate the association between serum levels of 1,3-beta-D-glucan (BDG) in patients with liver cirrhosis and soluble immuneinflammatory markers, reflecting immune dysregulation associated with cirrhosis.

Methods

In this non-interventional, single-center observational study conducted at the Medical University of Graz, 76 patients and four healthy donors were analyzed. Correlation between various biomarkers was calculated using Spearman's rho correlation analysis due to the nonnormal data distributions. Correlation matrices were graphically depicted as heat diagrams. Logistic regression was used to assess predictors of positive 1,3 BDG serum levels (≥80 pg/mL). Immune profiling was performed using the ProcartaPlex™ Human Immune Monitoring Panel for MAGPIX (65-plex), a bead-based multiplex immunoassay employing Luminex xMAP technology for the simultaneous quantification of 65 cytokines, chemokines, and growth factors in human serum samples. All statistical analyses were performed using R software, version 4.6.0 (R Development Core Team).

Results

In univariate analysis, patients with cirrhosis Child-Pugh class (CPC) B and CPC-C had 3.2-fold higher odds (95% CI 1.009–10.1, p = 0.04) for a positive BDG (i.e., >80 pg/mL) result compared to CPC-A. Luminex analysis should differential expression of various immune-related cytokines across the different stages of liver cirrhosis, with several cytokines showing increased expression in CPB and C as compared to healthy donor or CPA (**Figure 1**). Heatmap of cytokines and BDG levels (**Figure 2**) for CPC indicated significant correlations between positive BDG and Hepatocyte Growth Factor (ρ 0.26, p < 0.02) and Macrophage Inflammatory Protein-1 alpha (ρ 0.30, p < 0.01).

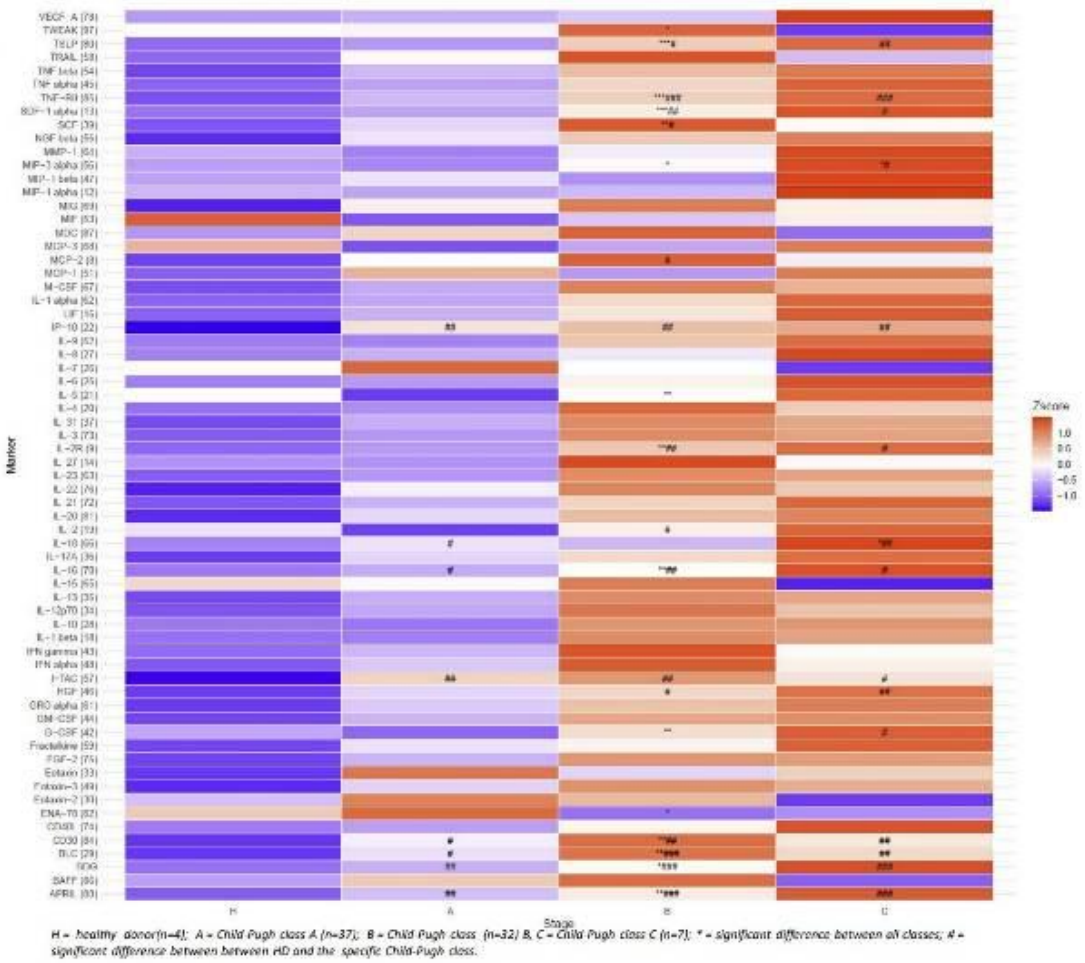
Conclusions

We observed trends for increased fungal translocation depending on the severity of liver cirrhosis and association of BDG with an immune-inflammatory environment.To gain more in-depth knowledge about (fungal-)dysbiosis and its detrimental consequences in the setting of liver cirrhosis, these trends need to be studied in moredetail including mycobiome analyses. This will further elucidate complex host–pathogen interactions and potentially introduce points of application for therapeuticinterventions.

Figure 1. Differential expression of cytokines, chemokines and various soluble factors across different stages of liver cirrhosis.

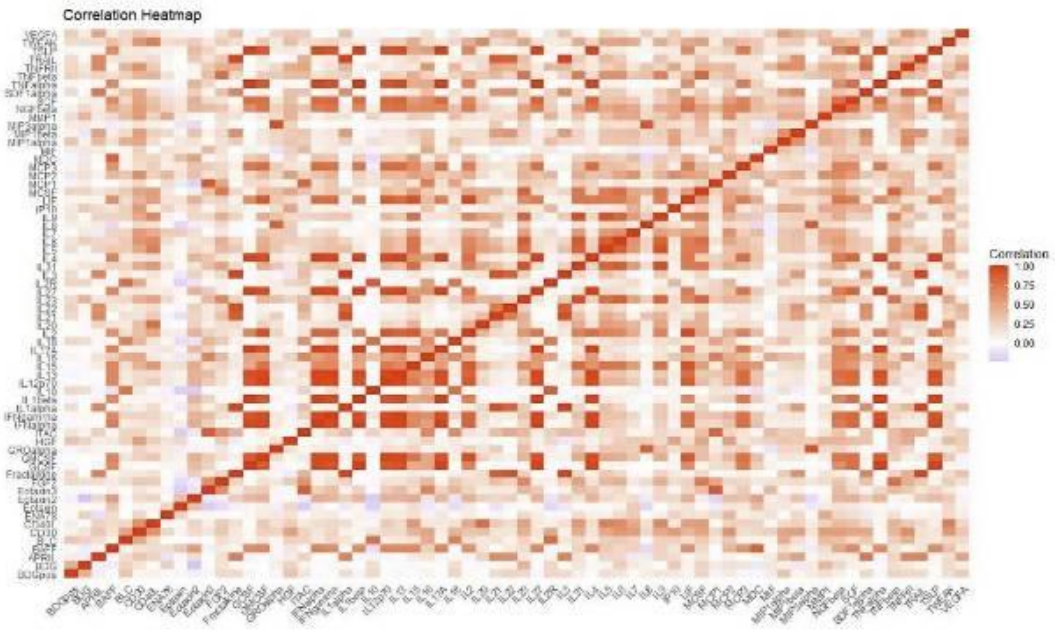
Figure 2. Correlation matrix of 1,3-Beta-D-Glucan and various cytokines

Figure 1



H = healthy donor(n=4); A = Child Pugh class A (n=37); B = Child Pugh class (n=32) B, C = Child Pugh class C (n=7); * = significant difference between all classes; # = significant difference between between HD and the specific Child-Pugh class.

Figure 2



P1-20

Population pharmacokinetic of fluconazole in paediatric patients with allogeneic haematopoietic cell transplantation

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Introduction

Fluconazole is recommended for prophylaxis of invasive candidiasis in children with haematological malignancies and following allogeneic haematopoietic cell transplantation (HCT) [1]. There is robust pharmacokinetic data available for preterm and newborn infants to guide fluconazole dosing, but data for children and adolescents are limited. Furthermore, many paediatric cancer patients have subtherapeutic levels (< 11 mg/L), suggesting that current dosing may be inadequate also in allogeneic HCT recipient and that therapeutic drug monitoring would be needed [2].

Objective

The aim of this study was to build a population pharmacokinetic (popPK) model to evaluate the pharmacokinetic characteristics of oral fluconazole in immunocompromised children and adolescents following allogeneic HCT with the current prophylactic fluconazole dosing.

Patients & methods

In total, 199 samples from 36 children and adolescents (18 m / 18 f) after allogeneic HCT were analysed for their fluconazole concentration using a previously published validated HPLC-UV method [3]. The popPK model was developed using the software NONMEM version 7.4.3.

Results

The fluconazole concentration-time profiles were best described by a one-compartment model with first-order absorption. Clearance and volume of distribution were allometrically scaled. As a result of covariate screening, only serum creatinine and γ-glutamyl transferase were found as significant covariates for clearance. For the volume of distribution all covariates were ruled out.

Conclusion

Our model is highly effective in describing the special population of immunocompromised children after allogeneic HCT and provides initial evidence that serum creatinine levels must be considered when determining individual therapy.

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Poster Session 2

PP-2-01

In-vitro-Empfindlichkeitstestung von Candida-Spezies gegenüber klinisch relevanten Antimykotika bei Vulvovaginalkandidose

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Vulvovaginalkandidosen (VVC) gehören zu den häufigsten gynäkologischen Infektionen. Neben *Candida albicans* wird zunehmend über einen steigenden Anteil von Nicht-*albicans*-Spezies berichtet, die teilweise eine verminderte Empfindlichkeit gegenüber Azol-Antimykotika aufweisen. Gleichzeitig liegen aus dem deutschsprachigen Raum nur begrenzt aktuelle Daten zur Resistenzlage vaginaler *Candida*-Isolate vor.

Ziel der geplanten Studie ist die Untersuchung der in-vitro-Wirksamkeit von Nystatin sowie weiterer klinisch relevanter Antimykotika gegen vaginale *Candida*-Spezies bei Patientinnen mit akuter oder chronisch-rezidivierender VVC und deren klinische Bedeutung.

In einer multizentrischen, prospektiven Querschnittsstudie sollen vaginale Abstriche von erwachsenen Patientinnen mit leitliniengerecht diagnostizierter VVC gewonnen werden. Die Proben werden zentral mikrobiologisch aufgearbeitet. Die Identifizierung der Hefepilze erfolgt bis auf Artebene mittels MALDI-TOF-Massenspektrometrie. Die Bestimmung der minimalen Hemmkonzentrationen (MIC) von gängigen Antimykotika aus den Wirkstoffklassen der Polyene (Nystatin, Amphotericin B), Azole (Clotrimazol, Fluconazol, Voriconazol) sowie Echinocandine (Anidulafungin, Micafungin) wird anhand standardisierter Mikrodilutionsverfahren nach EUCAST durchgeführt. Ergänzend werden pseudonymisierte klinische Basisdaten, u.a. zu Begleiterkrankungen/-medikation erhoben.

Primärer Endpunkt ist die Beschreibung der MIC-Verteilung von Nystatin gegenüber unterschiedlichen *Candida*-Spezies. Sekundär sollen Empfindlichkeitsprofile weiterer Antimykotika sowie die Prävalenz einzelner *Candida*-Arten analysiert werden. Die Daten werden deskriptiv ausgewertet.

Die geplante Studie soll aktuelle Daten zur in-vitro-Empfindlichkeit vaginaler *Candida*-Isolate gegenüber Nystatin und weiterer Antimykotika liefern und über die Charakterisierung des aktuellen Erregerspektrums und der Resistenzsituation einen Beitrag zur evidenzbasierten Therapie der VVC leisten.

PP-2-02

Environmental Detection of Clade III *Candidozyma auris* in the Absence of Clinical Isolates

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Introduction

Candidozyma auris (*C. auris*), a WHO-designated critical-priority fungal pathogen, frequently causes healthcare-associated outbreaks and is often multidrug-resistant. Its prolonged surface survival and persistent patient colonization complicates prevention/treatment.

Patients & Methods

In May 2025, a single *C. auris* isolate was recovered from a used face mask collected via a blinded, anonymized environmental quality-control program in a dental clinic at the Medical University of Innsbruck. Identification used culture and MALDI-TOF MS. Clade assignment employed allele-specific PCR, *ERG11* sequencing, and whole-genome sequencing; antifungal susceptibility followed EUCAST broth microdilution. To contextualize this finding, all patient-related *Candida* detections processed at the Medical University of Innsbruck from 2017-2025 were retrospectively reviewed and categorized as invasive, non-invasive, or unknown.

Results

The *C. auris* isolate was assessed as clade III, carrying *ERG11* substitutions V125A/F126L, with high fluconazole MIC (256 mg/L) and low echinocandin MICs. Expanded phylogenomic analysis including approximately 5,000 *C. auris* genomes showed that the isolate clustered closely with genomes from the Valencia outbreak. No additional *C. auris* was found in environmental sampling.

Over nine years, 53,802 specimens (8,948 invasive, 41,709 non-invasive, 3,145 unknown samples) from 26,446 individuals (65.1% female) were analysed. *Candida albicans* predominated (54.7% in invasive, 57.4% in non-invasive, 56.9% in unknown samples), followed by *Nakaseomyces glabratus* (21.3% in invasive; 15.2% in non-invasive, 13.6% in unknown samples). *C. auris* was not detected in patient-related samples.

Conclusion

A single environmental detection of clade III *C. auris* was found, while comprehensive clinical surveillance identified no patient isolates. This supports no detected transmission and highlights structured environmental quality control as an early warning tool.

PP-2-03

Co-treatment of sertraline with amphotericin B or amorolfine change inhibitory concentration levels of antifungals and up regulates expression of MDR3 transporter in several *Trichophyton indotineae* isolates

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Many isolates of *Trichophyton indotineae*, belonging to the *T. mentagrophytes/ interdigitale* complex exhibit resistance against azoles as well as terbinafine[1]. Resistance mechanisms include amino acid exchanges based on point mutations in the squalene epoxidase *Erg1* or the sterol 14-α demethylase gene *Erg11B*[1, 2]. Another mechanism depends on amplification of *Erg11B* associated with mRNA overexpression[3, 4]. Additionally, efflux mechanisms mediated by transporters belonging multiple drug resistance (MDR) or major facilitator (MFS) subfamilies contribute to antifungal resistance[4-5]. In *T. rubrum* sertraline is able to down regulate the expression of MFS-like transporters as well as several ergosterol biosynthesis genes leading to ergosterol depletion[6].

MLN methods were adapted based on the CLSI protocol. The inhibitory properties of amorolfine or amphotericin B in combination with sertraline were analyzed and combined with expression data analysis[4]. Several *T. indotineae* isolates, previously characterized in a genomic study[3], were analyzed.

Sertraline was able to induce transporter MDR3 gene expression in all strains in a concentration-dependent manner without affecting fungal growth. Expression of ergosterol biosynthesis genes is more versatile, demonstrating up as well as down regulation in different isolate. The strain showing the greatest decrease of MIC values in co-treatment with sertraline showed down regulation of all analyzed ergosterol biosynthesis genes.

Increased resistance of fungi is a growing global health concern. It could be shown that sertraline exhibits considerable potential as an adjunct therapy for dermatomycoses.

1. Ebert et al. Mycoses (2020) 63: 717-28.

2. Burmester et al. Mycoses (2022) 67:97-102

3. Yamada et al. Antimicrob Ag Chemother (2023) 10.1128/aac.00933-23

4. Berstecher et al. J Fungi (2024) 10.3390/jof10110731

5. Monod et al. Antimicrob Ag Chemother (2019) 63, e00863-19

6. Galvao-Rocha et al. J Fungi (2023) 10.3390/jof9020275

PP-2-04

Activity of echinocandins including rezafungin against Candida auris biofilms

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Backround

In this study, we assessed the antibiofilm activity of three echinocandins—anidulafungin, micafungin, and the next-generation agent rezafungin—against C. auris biofilms.

Methods

Nine C. auris strains belonging to four different clades (India, South Africa, Venezuela, Middle East) were included. Broth microdilution testing following the EUCAST protocol was performed for all three antifungals to determine their minimum inhibitory concentrations (MICs). Both MIC and sub-MIC concentrations were applied to 24- and 48-hour-old biofilms. Following treatment for an additional 24, 48, and 72 hours, metabolic activity of biofilms was quantified using the XTT assay. This allowed assessment of the degree to which mature biofilms remained metabolically active after exposure to the different echinocandins.

Results

C. auris biofilms showed susceptibility to the tested agents in a strain- and concentration-dependent manner. After 48 hours of incubation with anidulafungin or micafungin at 1× MIC, metabolic activity was reduced by approximately 37% and 40%, respectively. In contrast, rezafungin produced only about a 10% reduction under the same conditions in 48-hour-old biofilms. Unlike anidulafungin and micafungin, rezafungin applied at concentrations below half the MIC did not significantly reduce metabolic activity. Extending incubation to 72 hours did not result in additional meaningful reductions for any of the three echinocandins compared with untreated controls.

Conclusion

Anidulafungin, micafungin, and rezafungin all inhibited mature C. auris biofilms, though with considerable variability between strains. Overall antibiofilm activity was highest for anidulafungin and micafungin, whereas rezafungin showed markedly weaker effects, especially at sub-MIC levels.

PP-2-05

Exploring Efflux Pump–Mediated Azole Resistance in *Aspergillus fumigatus*

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Introduction

Aspergillus fumigatus is a major fungal pathogen and poses a substantial clinical burden due to its high annual death toll. The management of *A. fumigatus*-caused aspergillosis is increasingly challenged by rising antifungal resistance, highlighting the need to better understand the underlying mechanisms of resistance. Unlike the well-studied *cyp51A* gene, other drivers of azole resistance like efflux remain largely understudied.

Objective

Investigate the role of both known and previously uncharacterised ABC-transporters in *A. fumigatus* azole resistance.

Methods

To elucidate the function of these ABC-transporters, *A. fumigatus* overexpression strains were generated for all putative transporters through protoplast-mediated CRISPR/Cas9 transformation. These respective

mutant strains were screened for altered azole resistance phenotypes through spot assays. Strains exhibiting altered phenotypes were further analysed to quantify the impact of ABC-transporter overexpression on azole susceptibility and sterol content, and to study the subcellular localisation of newly identified transporters.

Results

Using this approach, we identified 10 ABC-transporters – including Cdr1B and AtrF – that affected azole susceptibility upon overexpression. Interestingly, one uncharacterised transporter conferred pan-azole resistance when overexpressed.

Conclusion

Our findings demonstrate that previously undescribed ABC-transporters affect *A. fumigatus* azole susceptibility. These transporters confer either specificity for a particular azole or broader altered azole resistance. Although speculative, mutations leading to ABC-transporter overexpression may act independently or synergistically with *cyp51A*-associated mutations, potentially contributing to the emergence of unique azole resistance phenotypes in both clinical and environmental contexts.

PP-2-06

N-chlorotaurine limits the pro-inflammatory reaction of granulocytes and alveolar macrophages in response to *Aspergillus fumigatus*

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Introduction

N-chlorotaurine (NCT), a product of activated granulocytes and monocytes, can be applied as endogenous antiseptic for treatment of infections. It has also anti-inflammatory effects and is thought to be involved in the resolution of inflammatory response. NCT was recently demonstrated to have strong curative effects in a mouse model of fungal pneumonia.

Aim

The present study aimed to investigate the influence of NCT on the production of cytokines of granulocytes and alveolar macrophages to improve the understanding of its effects in pneumonia.

Materials & Methods

Murine alveolar macrophages were obtained from bronchoalveolar lavage, murine neutrophils were isolated from bone marrow. The cells were subsequently stimulated with lipopolysaccharide (LPS) as positive control or *Aspergillus fumigatus* spores. For comparison, *Staphylococcus aureus* or *Escherichia coli* were used. Interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α) were measured by ELISA.

Results

Both neutrophils and alveolar macrophages reacted on incubation with *Aspergillus fumigatus* spores with release of TNF-α. The kinetics were somewhat delayed compared to LPS, *Staphylococcus aureus* or *Escherichia coli*. Incubation of immune cells with NCT modified this inflammatory response: whereas 0.005% hardly reduced the cytokine secretion, a significant down-modulation could be achieved using 0.01% NCT. Higher NCT concentrations (0.05% NCT) even completely abolished the secretion of IL-6 and

TNF-α to that of unstimulated controls. Former experiments had proven that 1% NCT is well tolerated and can be used for therapeutic purposes, underlining the physiological relevance of the results.

Conclusions

NCT downregulates the pathogen-stimulated cytokine production of neutrophils and alveolar macrophages, thus limiting putatively harmful hyperinflammation. At clinically applied concentrations, this immunomodulatory activity may support the therapeutic potential of NCT in the treatment of pneumonia

PP-2-07

Antifungal Activity of Octenidine against Emerging Candida Species In Vitro

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Introduction

Infections caused by rare *Candida* species are increasingly reported in superficial and invasive settings, particularly in immunocompromised patients. The rapid emergence of antifungal resistance complicates treatment and highlights the need for adjunctive strategies for infection prevention and therapy. Effective topical antiseptics may help control fungal colonization and reduce infection risk. This study evaluated the *in vitro* efficacy of the widely used antiseptic octenidine (OCT) against a panel of less common but clinically relevant *Candida* species.

Methods

Antifungal activity of OCT (0.1%, 0.05%) and two commercial OCT-based products (octenisept®, octeniderm®) was assessed using quantitative suspension assays according to EN 13624:2013 under clean (0.3 g/L bovine serum albumin) and dirty conditions (3 g/L bovine serum albumin, 3 mL/L defibrinated sheep blood) with exposure times of 30, 60, 120 and 300 seconds. Tested species included *Candida albicans, Nakaseomyces glabratus* and less common isolates such as *Candidozyma auris*, *Pichia kudriavzevii, Candida tropicalis, C. dubliniensis, C. parapsilosis, C. orthopsilosis, C. metapsilosis, Meyerozyma guilliermondii* and *C. lusitaniae*.

Results

Even under dirty conditions, pure OCT as well as both ready-to-use OCT-containing formulations showed strong antifungal activity against all tested species within short contact times. Notably, the skin-antiseptic octeniderm® achieved complete growth inhibition within 30–60 seconds, even in the presence of high organic load.

Conclusion

The growing clinical relevance of less common *Candida* species, combined with increasing antifungal resistance, underscores the necessity for effective preventive and therapeutic strategies. These *in vitro* findings demonstrate that OCT provides rapid antifungal activity against a diverse range of clinically relevant yeasts, supporting its use in topical treatment and infection prevention measures in healthcare settings.

PP-2-08

PDR1 Gain-of-Function Mutations Drive Multidrug Efflux Pump Overexpression in Azole-Resistant Nakaseomyces glabratus: A Comparative Analysis of Targeted RNA Sequencing and RT-qPCR

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Background

Azole-resistant *Nakaseomyces glabratus* is of increasing clinical concern. Their prevalence is rising, and affected isolates frequently display cross-resistance spanning several to nearly all azole antifungal agents. A key resistance mechanism for azole resistance in *N. glabratus* is the overexpression of multidrug efflux pumps, which actively transport antifungal agents from the cell. This overexpression is frequently driven by gain-of-function mutations in the transcription factor Pdr1, which regulates the expression of the efflux pumps Cdr1, Cdr2, and Snq2.

Methods

Twenty-five azole-resistant *N. glabratus* clinical isolates harboring 29 distinct *PDR1* mutations and five azole-susceptible isolates without *PDR1* mutations were analyzed. Efflux pump gene expression (*CDR1*, *CDR2*, *SNQ2*) was quantified by RT-qPCR and targeted RNA sequencing to assess the comparability of both methods.

Results

Fourteen of 25 azole-resistant isolates exhibited ≥20-fold overexpression of *CDR1* relative to susceptible controls; four isolates demonstrated >100-fold upregulation. Previously described mutations, including D876Y and G346D, were identified in isolates with pronounced overexpression. Notably, the novel mutation F1084Y was associated with high *CDR1* upregulation of 1724-fold, representing the strongest effect observed in these isolates.

Conclusion

This study establishes a genotype–phenotype correlation between specific *PDR1* mutations and transcriptional upregulation of multidrug efflux pumps in azole-resistant *N. glabratus*. Beyond confirming the relevance of previously reported mutations, we identified novel gain-of-function variants. These findings reinforce efflux-mediated resistance as a predominant mechanism of azole resistance in *N. glabratus*.

PP-2-09

Genomic analysis of longitudinal *Coccidioides posadasii* isolates from relapsing disseminated coccidioidomycosis

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Introduction

Disseminated coccidioidomycosis is a rare manifestation of *Coccidioides* infection. Guidelines recommend fluconazole or itraconazole as primary antifungal therapy. Therapy changes are reported in up to 12%,

potentially due to side effects or lack of efficacy. In vitro resistance testing suggests elevated MICs for fluconazole or itraconazole in 37% and 1% of isolates, respectively.

Objectiv

To screen selected loci relevant to decreased antifungal susceptibility in serial isolates from a patient with two culture-positive relapses.

Methods

A patient developed travel-associated disseminated coccidioidomycosis (skin, lung) after travel to Arizona in 1994. Infection was documented by cultivation of *C. posadasii* from a skin lesion in 1998 (isolate 1). Itraconazole therapy improved cutaneous lesions. Culture-positive cutaneous relapses occurred in 2004 (isolate 2), treated with itraconazole, and 2012 (isolate 3), treated with posaconazole. No further relapse was documented at follow-up in 2015.

Isolates were grown from frozen stocks on potato dextrose agar under S3 conditions. DNA was extracted using the MasterPure Yeast DNA Purification Kit and submitted for sequencing. Short reads (Illumina MiSeq) were mapped to a reference sequence using CLC Genomics Workbench, resulting in approximately 50x coverage. Species (*PRA2*), mating type and *ERG11* loci were analysed.

Results

All three isolates were confirmed as *C. posadasii* and MAT1-1. Two *ERG11* loci were annotated in the reference (*ERG11_1*, *ERG11_2*) and detected in all isolates. No confirmed *ERG11* sequence changes were identified in the three isolates.

Conclusion

Serial isolates from relapsed coccidioidomycosis after oral azole therapy did not show a confirmed mutation in the azole target gene *ERG11*. Relapse may therefore involve other mechanisms, such as non-target-based tolerance, regulatory changes or insufficient itraconazole exposure for eradication. Further in silico and in vitro analysis are presented.

PP-2-10

Epidemiology of opportunistic and transmissible Candida species in Mwanza, Tanzania

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Background

Invasive candidiasis is estimated to affect > 1 Mio. patients annually with mortality up to 65%. Emerging transmissible species such as C. auris and C. parapsilosis may complicate clinical management, particularly in resource-limited settings. We assessed East-African Candida epidemiology, C. auris-selective agar under tropical conditions, antifungal resistance and molecular epidemiology.

Methods

We conducted a WHO-guided point prevalence survey at a tertiary hospital in Mwanza, Tanzania. Non-invasive swabs from ≥2 body sites and clinical data were collected. Species were identified by CHROMagar Candida Plus and MALDI-TOF MS. Colonization predictors were analyzed by logistic regression. Susceptibility was assessed by EUCAST broth microdilution and commercial assays. Relevant clusters were investigated by MLST and WGS-based SNP phylogeny.

Results

From 448 enrolled patients, 1082 swabs yielded 580 suspected Candida isolates, including 9 C. auris-like colonies; 562 yeast isolates were confirmed by MALDI-TOF MS. C. albicans predominated (39,7%), with C. parapsilosis as the leading non-albicans species (16,5%), particularly associated with neurosurgery/cardiac surgery and pediatric wards. Four C. parapsilosis isolates showed azole resistance and MLST indicated partial ward-associated clustering, consistent with hospital-associated lineages. C. lusitaniae accumulated on pediatric surgery/ICU wards with species-typical susceptibility patterns. SNP-based phylogeny showed proximity between a previous fatal pediatric sepsis strain and selected PPS isolates, suggesting possible persistence or repeated circulation of related C. lusitaniae lineages. None of the C. auris-like isolates were confirmed as C. auris.

Conclusion

This first systematic study of opportunistic Candida in Tanzania indicates possible nosocomial circulation of related lineages, highlighting the need for diagnostics, surveillance and infection prevention in resource-limited settings.

Figure 1

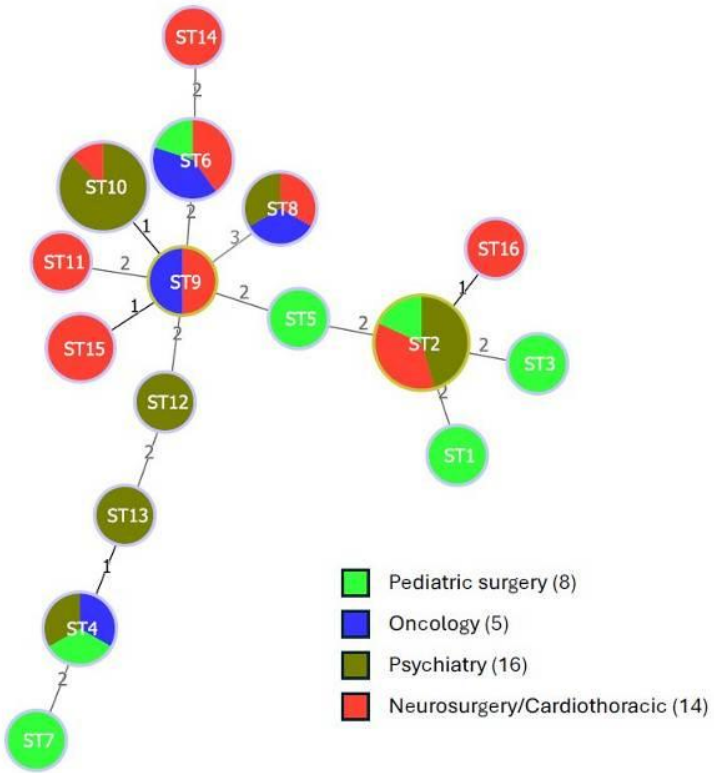
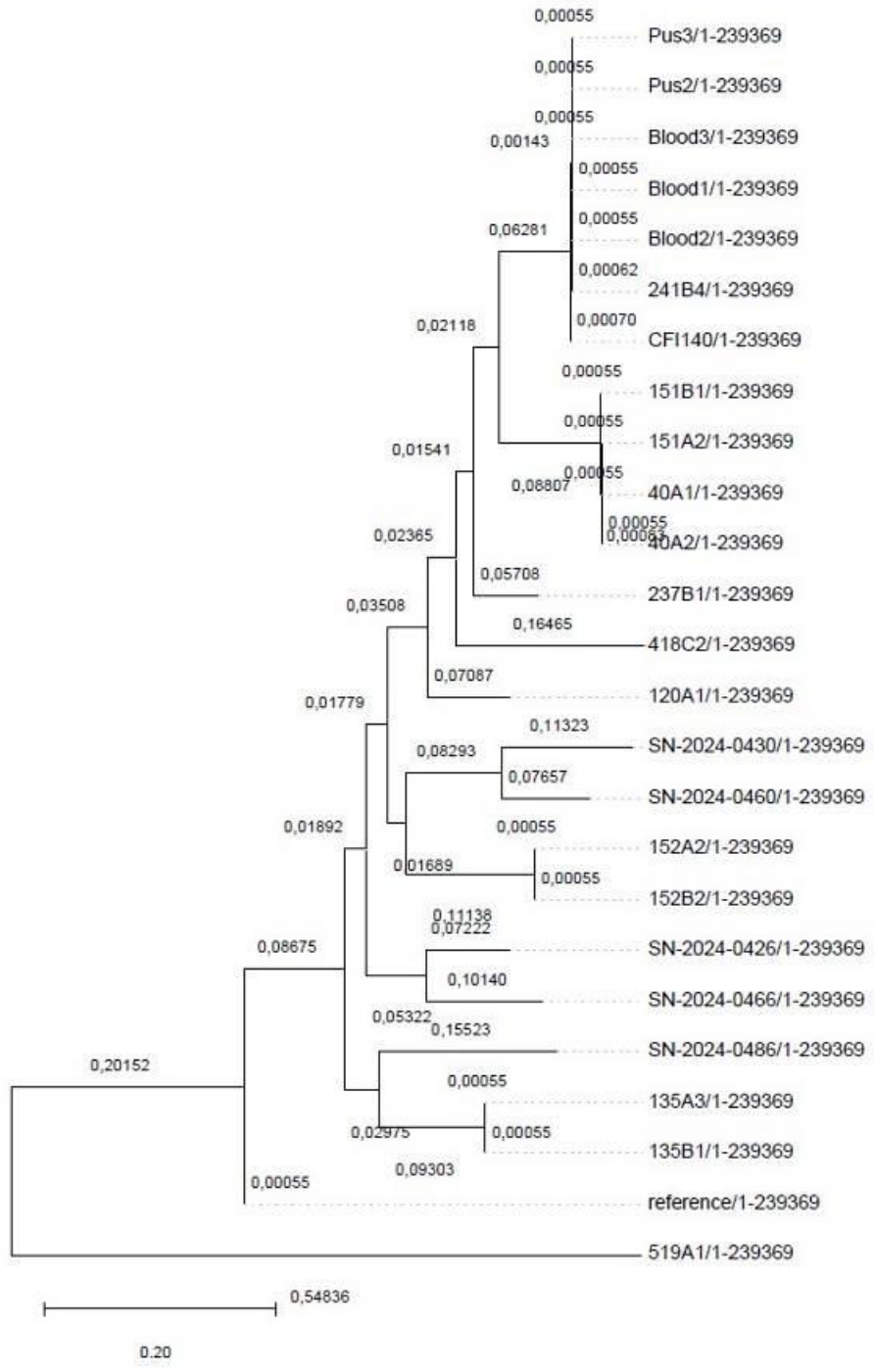


Figure 2



PP-2-11

Azole resistance of *Aspergillus fumigatus* in Germany and its molecular detection

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Aspergillus fumigatus is a ubiquitous fungus and opportunistic human pathogen, able to cause lethal infections. Azole antifungals targeting the lanosterol 14α-demethylase (*CYP51A*) are usually the drugs of choice. Therefore azole resistance, predominantly caused by mutations in the *cyp51A* gene, poses a serious risk to treatment success. Detection of azole resistance in *A. fumigatus* relies predominantly on

phenotypic antifungal susceptibility testing, however, cultivation of the pathogens is often not possible leaving only molecular methods. Commercial tests molecularly detect azole resistance from clinical samples by only targeting tandem repeats (TRs) without accounting for single point mutations. Therefore, the aim of our study was the development of a PCR based assay detecting all *cyp51A* mutations in DNA from clinical specimens. In order to know which gene fragments must be covered by the PCR, we analyzed *cyp51A* mutations of 218 resistant *A. fumigatus* strains received at the NRZMyk between 2014 and 2025.

In total, 21 different combinations of point mutations and TRs in the promotor region have been found. Most prevalent were *cyp51A* mutations combined with TRs that are considered to be environmentally evolved such as TR34/L98H (67.4%), TR46/Y121F/T289A (8.3%) and TR46/Y121F/T289/S363P/I364Y/G448S (8.3%). Point mutations emerging during azole usage in the patient (e.g. G54, M220) made up only 12%. The detected mutations cover all regions of *cyp51A*. Therefore, we developed a Nested PCR assay that amplifies the complete gene. However, the amplification rate of this assay was only high for samples with presumably high DNA content such as biopsy material. To increase the amplification rate also for DNA from paraffin-embedded tissues, sputum and bronchioalveolar lavage, we developed a second assay amplifying shorter fragments. Although the present assay depends on sufficient pathogen DNA, tests using clinical DNA extracts demonstrate an encouraging success rate.

PP-2-12

In Vitro Polyhexanide Exposure Induces Azole Resistance in Nakaseomyces glabratus via PMA1 Mutations

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Background

Fungal infections represent a major global health challenge, ranging from highly prevalent superficial infections to life-threatening invasive candidiasis, with fatality rates of 40-60%. Antifungal resistance in *Candida* species is an increasing concern, with azole resistance being of particular clinical relevance given the limited number of antifungal drug classes. In clinical settings, antiseptics represent an essential tool for preventing transmission of multidrug-resistant fungal strains especially in nosocomial environments. However, growing evidence suggests that antiseptic agents may exert selective pressure, potentially driving collateral antimicrobial resistance.

Methods

A high-throughput *in vitro* resistance evolution model was employed, exposing 96 replicates of *N. glabratus* and *C. albicans* to increasing polyhexanide (PHMB) concentrations to assess whether this antiseptic can induce selection pressure. EUCAST microdilution was performed on pre- and post-exposure isolates against eight antifungal and eight antiseptic agents. Whole genome sequencing (WGS) was used to screen for newly acquired mutations and identify potential resistance mechanisms.

Results

Serial PHMB exposure induced adaptive selection, with isolates adapting to grow at concentrations up to 1024 mg/L compared to an initial MIC of 4 mg/L. This phenotype appeared exposure-dependent and did not induce stable resistance to the antiseptic itself. However, *N. glabratus* isolates developed newly acquired resistance to all three tested azoles (fluconazole, voriconazole, and posaconazole) with 32-fold

MIC increases compared to pre-exposure values. WGS revealed newly acquired mutations in the *PMA1* gene, putatively leading to increased drug efflux.

Conclusion

To our knowledge, this is the first study demonstrating that PHMB can exert selective pressure *in vitro*, driving resistance to azole antifungals in *N. glabratus* through efflux mechanisms, warranting further investigation.

PP-2-14

IL-22 induced by *C. albicans* reduces the severity of invasive *S. aureus* pneumonia in mice

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Introduction

The commensal fungus *C. albicans* and the bacterium *S. aureus* frequently coexist in humans and can cause severe systemic infections in immunocompromised patients. Clinically, *S. aureus* commonly induces pneumonia and disseminates from the lung, whereas *C. albicans* almost never causes invasive pulmonary disease, even in mechanically ventilated patients with high fungal burdens.

Objectives

We aim to investigate the different behavior of *C. albicans* and *S. aureus* in the lung, and to assess how pulmonary pre-colonization with *C. albicans* influences subsequent *S. aureus* infection.

Methods

We established a lung pre-colonization/infection model using Balb/c mice. Mice were administered *C. albicans* intranasally at day 0 and infected intranasally with *S. aureus* on day 1. At 24, 48 and 96 h post *S. aureus* infection, lung, liver and kidney bacterial/fungal burdens as well as lung immune responses were analyzed.

Results

Following intranasal administration, pulmonary loads of both pathogens declined over time; however, only *S. aureus* disseminated to liver and kidney, closely mirroring the clinical situation. Pulmonary pre-colonization with *C. albicans* markedly altered the lung immune landscape and resulted in enhanced recruitment of neutrophils and $CD11b^+$ dendritic cells upon *S. aureus* infection. Cytokine profiling revealed a pronounced induction of IL-1β, IL-17, and IL-22 during fungal colonization followed by bacterial challenge. Importantly, *C. albicans* pre-colonization protected mice from lethal *S. aureus* lung infection. Neutralization of IL-22 abrogated this protective effect, identifying IL-22 as a critical mediator to *S. aureus* induced pneumonia. Early administration of recombinant IL-22 was sufficient to significantly enhance early survival during a lethal *S. aureus* pneumonia.

Conclusion

We established a physiologically relevant dual pathogen lung model and identified IL-22 as a key immunological switch determining the outcome of *S. aureus* lung infection.

PP-2-15

Decoding CXCL10: A potential regulator of macrophage responses to pulmonary infections

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Invasive fungal infections pose a major global health threat, particularly in immunocompromised individuals. Among these, invasive pulmonary aspergillosis caused by *Aspergillus fumigatus* (Af) is associated with high mortality, especially when diagnosis is delayed or missed. Despite its clinical relevance, the molecular mechanisms underlying Af pathogenesis and host immune responses remain incompletely understood.

Emerging evidence suggests that CXCL10 may play a key role in lung disease progression. Here, we investigate CXCL10 production by alveolar-like macrophages (ALMs) during early infection and explore its potential as a target for preemptive therapeutic intervention. We assessed ALM responses to *Af*, *Candida albicans* (Ca), and *Staphylococcus aureus* (Sa), demonstrating efficient phagocytosis of all three pathogens. Notably, bacterial infection induced stronger cytokine responses compared to fungal challenges. CXCR3 expression on ALMs was confirmed by flow cytometry, enabling functional studies of CXCL10 signaling.

CXCL10 treatment led to reduced surface expression of CD11c and ICAM1 after 24 hours, alongside enhanced TNF and IL-8 production following subsequent Af challenge. Transcriptomic profiling (NGS) will further reveal both pathogen-specific and shared response patterns, as well as CXCL10-induced shifts in gene expression. Collectively, our data indicate that CXCL10 modulates ALM phenotype and function and will be further studied regarding its influence on phagocytosis, antimicrobial activity, and migration. Ongoing studies targeting TNF, CXCL10, and CXCR3 aim to dissect the TNFα–CXCL10 axis, its role in shaping outcomes of pulmonary infections and the influence on other cells including chemotaxis and co-culture studies.

PP-2-16

Comparative Analysis of Macrophage Interactions with *Candida glabrata* and *Candida auris*

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Candida auris and *Candida glabrata* are recognized by the World Health Organization as priority human fungal pathogens. Both exhibit a remarkably reduced host immune activation during infection. *C. auris* persists on abiotic surfaces, where nutrient starvation increases its resilience. A key question is how environmental, or clinical stressors influence *C. auris* and *C. glabrata* interactions with macrophages.

This study comparatively analyses the interaction of *C. auris* and *C. glabrata* with human macrophages in detail, and investigates how stress pre-conditioning influences infection parameters.

Stress-primed *C. auris* and *C. glabrata* interactions were analyzed with human monocyte-derived macrophages (hMDMs). Fungal growth and stress-associated cell wall features were assessed using

microbiological methods, and host–pathogen interactions including phagocytosis, intracellular survival, macrophage responses and fungal escape were examined with infection biology techniques.

Our observations indicate that both species are efficiently phagocytosed by human macrophages. *C. auris* escaped faster while eliciting weak inflammatory signaling and preserving host cell viability. Initial analyses suggest that *C. auris* and *C. glabrata*, maintain stable interaction profiles after stress priming, without markedly altered macrophage responses.

Our findings reveal that stress-primed *C. auris* and *C. glabrata* are not affected in fungal fitness during macrophage interaction. This raises the question of how a robust host–pathogen interaction programme is sustained. These study will help us to identify stress-regulated genes and molecular pathways that sustain immune evasion.

PP-2-17

Monocyte-Mediated Immune Responses to Co-Infections with *Candida albicans* and *Staphylococcus aureus*

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Candida albicans and *Staphylococcus aureus* are common human commensals, but also opportunistic pathogens that can cause life-threatening systemic infections. Polymicrobial infections occur commonly but are under-researched and pose a particular challenge to innate immunity.

We investigate the responses to polymicrobial infections in human monocytes, central innate immune cells that help co-ordinate adaptive immune responses.

Human pan-monocytes were confronted in vitro to *C. albicans* and/or *S. aureus*, with and without opsonization. Flow cytometry resolved uptake kinetics and activation profiles across classical, intermediate, and non-classical monocytes, while live-cell fluorescence microscopy enabled real-time visualization of pathogen–host interaction dynamics. To dissect mechanistic determinants of phagocytosis, we employed *C. albicans* mannosylation-deficient mutants with defined alterations in cell-wall architecture.

Complement and SP-D increased pathogen uptake, with the strongest effects observed during co-infection. Classical monocytes exhibited the highest overall infection burden, whereas non-classical monocytes preferentially targeted *S. aureus*. Live *C. albicans* rapidly overgrew monocytes and triggered cell death within ~60–90 min, while yeast-locked and thimerosal-killed mutants induced substantially delayed cytotoxicity (≥8 h). Disrupted *Candida* mannosylation significantly reduced monocyte uptake and profoundly reshaped activation signatures.

Distinct subset-specific phagocytic dynamics and pathogen surface properties shape monocyte responses to fungal–bacterial co-infections. Ongoing work includes single-cell transcriptomics, extended co-culture (72 h) with T cells, and characterization of cell-death modalities to clarify impacts on adaptive priming and cytokine signatures.

PP-2-18

The commensal functions of the fungal peptide toxin candidalysin

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Several members of the human microbiome are opportunistic pathogens that can cause disease under certain predisposing conditions. While their virulence attributes are well studied in the context of disease, the evolution of these factors during their predominant commensal lifestyle remains largely unclear. *Candida albicans* can cause superficial and severe systemic infections. Recently it was demonstrated that hypha formation plays a crucial role in facilitating *C. albicans* gut colonization in hosts with either an undisturbed gut microbiota or carrying specific bacterial populations. In this niche, hypha-competent *C. albicans* outcompeted yeast-locked mutant cells. This phenotype was primarily attributed to the expression of *ECE1*, encoding the peptide toxin candidalysin (CaL). While it is well known that CaL directly inflicts damage to human cells, we aimed to investigate the mechanism of CaL-mediated antibacterial activity.

We found that while bacterial cell membranes are lysed by the toxin, cell wall components and structures provide protection. With comparative genomics we were able to identify orthologs of CaL with strong antibacterial activity in non-pathogenic *Candida* species, suggesting a toxin-carrying ancestor that evolved long before humans emerged. Furthermore, we found that the combination of CaL production with filamentation is essential for the peptides" commensal function, possibly by an indirect mechanism with CaL-mediated secretion of host-derived inflammatory mediators, which provides a competitive advantage for *C. albicans* in the presence of bacteria.

Our results present an explanation for the evolutionary conservation of these essential and multifunctional fungal factors in *C. albicans.* They likely evolved to improve fungal fitness in polymicrobial environments through inter-kingdom competition and make *C. albicans* both a successful commensal and pathogen.

PP-2-19

Role of Chitin Binding Proteins in Immune Regulation of Human Keratinocytes Responding to Fungal Infection

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Fungal infections represent an escalating global health concern, affecting millions of people every year while current treatment options remain limited. For the development of effective therapies, a comprehensive understanding of pathogenesis and dynamics of fungal infections is essential.

Activation of the human host response against fungi relies on the initial recognition of the fungal pathogen. Chitin, a major structural component of the fungal cell wall, is recognized by various host chitin-binding proteins, including chitinase-3-like protein 1 (CHI3L1) and LysM domain-containing protein 3 (LysMD3). However, despite their ability to bind chitin, their functional contributions to host defense during fungal pathogenesis remain insufficiently understood.

Here, we analyzed the effect of CHI3L1 on proliferation, hyphal formation and virulence of *Candida albicans*. We showed that during *C. albicans* infections of human keratinocytes, CHI3L1 is secreted and binds the fungal cell wall, in particular chitin and beta-glucan. We demonstrated that this binding decreased *C. albicans* growth and changed the expression of genes relevant in hyphae formation. Furthermore, CHI3L1 overexpressing three-dimensional reconstructed human epidermis (RHE) showed significantly greater stability against fungal infections than skin models with lower CHI3L1 levels. In addition, fewer *C. albicans* cells were observed in these models suggesting an antifungal and host protecting effect of CHI3L1. Further, we found that LysMD3 accumulates in the stratum corneum at sites of fungal invasion. Moreover, keratinocytes lacking LysMD3 had a reduced inflammatory response towards *C. albicans*.

Our data suggest an important role of CHI3L1 and LysMD3 in human defense against fungal pathogens highlighting their potential as antifungal therapeutics. Further investigations are required to elucidate their molecular mechanisms and pathophysiological relevance in the context of fungal skin infections.

PP-2-20

Dual effect of 5-Fluorouracil against Pancreatic Ductal Adenocarcinoma (PDAC) and against the tumor-promoting fungus *Malassezia globosa*

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Introduction

Malassezia globosa is hypothesized to trigger progression of Pancreatic Ductal Adenocarcinoma (PDAC) by inducing a chronic complement-mediated inflammation. Since cytostatic drugs are routinely given to affected patients, different drugs were compared regarding their cross-efficacy to *Malassezia* viability.

Aims

(1) to compare the efficacy of cytostatics to interfere with viability of *Malassezia* as single or combination therapy; (2) to monitor whether cytostatics modulate the fungal interaction with complement.

Materials & Methods

Malassezia was incubated with cytostatics, fungal proliferation was quantified by plating. Complement deposition on fungal surface was analysed by FACS.

Results

Cultivation of *Malassezia* with 5-fluorouracil (5-FU) resulted in significant reduction of fungal viability. This effect was also visible in pancreas homogenate to simulate PDAC environment. Even low 5-FU concentrations were effective against *Malassezia*. No adaptation of the fungus to 5-FU was observed when evaluating its long-term effect for 3 weeks as standard therapy duration. Anoxia that is typical for PDAC tissue modulated the 5-FU effect on *Malassezia*. Combination of 5-FU with oxaliplatin and irinotecan did not further enhance its inhibitory effect. Gemcitabine or cisplatin did not exert any effect on *Malassezia* proliferation. The cytostatics did not affect the interaction with the complement system as shown by the level of complement deposition on the fungal surface.

Conclusions

Proliferation of *Malassezia* as pro-carcinogenic trigger can be reduced by optimized choice of the cytostatics used for chemotherapy. 5-FU not only targets the viability of tumor cells, but also downmodulates the fungal proliferation, also in nutrient and oxygen conditions that are typical for PDAC. The interaction between fungus and the complement system is not altered, indicating that no additional inflammation is triggered by application of 5-FU.

PP-2-21

Host Adaptation by Reduced Biofilm Formation Drives Outbreak Persistence of a Major High Priority Human Fungal Pathogen

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Question

Outbreaks caused by invasive fungal pathogens pose a major global health threat. In recent years, multinational outbreaks of fluconazole-resistant (FLCR) *Candida parapsilosis* are associated with high mortality and are difficult to control. However, the microbial determinants underlying their persistence and global spread remain unclear.

Methods

We analyzed an international collection of *C. parapsilosis* bloodstream isolates using an integrated multi-omics and functional approach, including whole-genome sequencing, transcriptomics, and host–pathogen interaction models.

Results

FLCR isolates consistently exhibited a low-biofilm-producing (LBP) phenotype. Comparative genomics showed that LBP isolates emerged independently across multiple lineages, indicating convergent evolution. Transcriptomic analyses revealed metabolic and regulatory rewiring, including altered central carbon metabolism under biofilm-inducing conditions. Integration of in vitro and ex vivo assays (Fig.1) showed that LBP isolates display enhanced tolerance to environmental and host-imposed stresses and survive better

during interactions with macrophages and neutrophils. Mechanistically, these isolates exhibit increased masking of cell wall antigens, resulting in reduced immune recognition, decreased phagocytosis, and enhanced resistance to immune-mediated killing (Fig.2). In a murine infection model, LBP isolates show increased fungal burdens in immune cell–rich organs.

Conclusions

These findings challenge the prevailing view that robust biofilm formation is the principal driver of outbreak persistence. Instead, we identify biofilm attenuation as an adaptive tradeoff that promotes immune evasion, host-associated fitness, and long-term survival. This work reframes our understanding of *C. parapsilosis* outbreak evolution by shifting attention from environmental persistence toward host-driven selective pressures and non-environmental reservoirs as key determinants of global outbreak success.

Figure 1

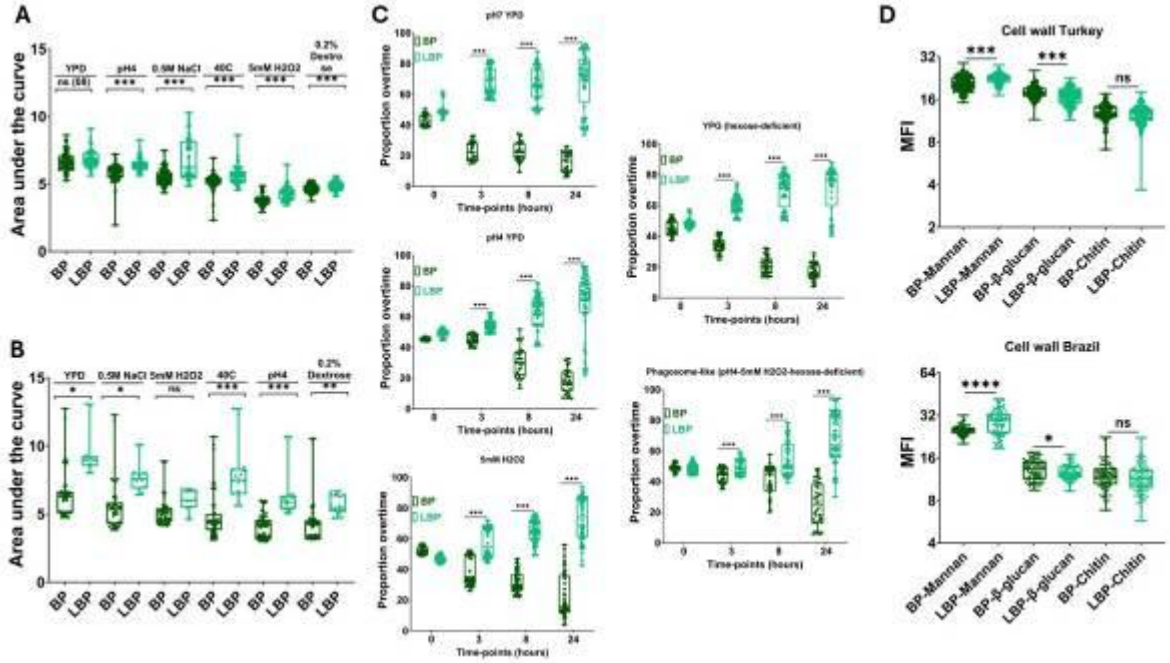
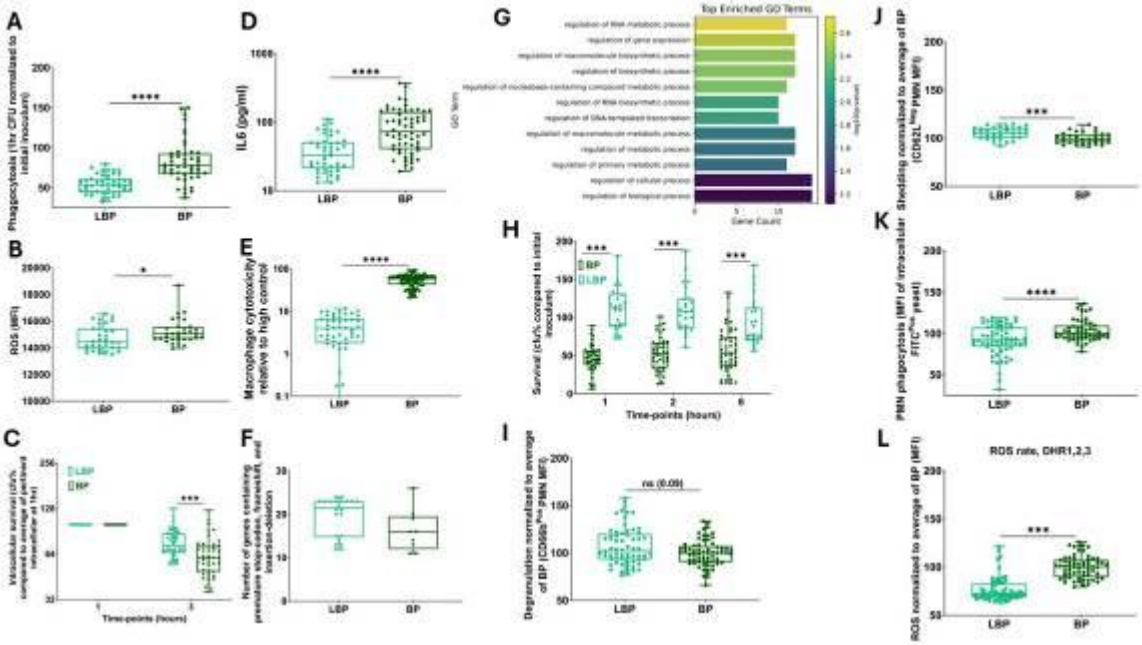


Figure 2



PP-2-22

Interaction of *Malassezia* with pancreatic enzymes in pancreatic cancer: potential role in fungal persistence and inflammatory activation

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Introduction

Pancreatic ductal adenocarcinoma (PDAC) is among the deadliest malignancies, and recent evidence has implicated the yeast *Malassezia globosa* as a potential contributor to its development. To exert this pro-carcinogenic effect fungal survival and proliferation in the pancreatic environment are essential.

Objective

To investigate the effect of pancreatic enzymes on *M. globosa* viability, lipid content, and its ability to trigger innate inflammatory activation.

Materials & Methods

M. globosa was incubated with pancreatic enzymes, including murine pancreatic homogenate, human pancreatic juice, pancreatin, lipase, and trypsin. Lipid content was assessed by FACS following incubation with lipolytic enzymes. Fungal viability was evaluated after exposure to all tested enzymes using a RealTime-Glo™ assay. C3 fragment deposition (C3c) was analyzed by FACS after incubation with normal human serum (NHS). C3a, C5a and TNF-α levels were quantified by ELISA.

Results

Pancreatic enzymes with lipolytic activity induced a marked reduction in lipid content. Despite these structural changes, fungal viability was not impaired but instead increased; similarly, trypsin had no effect on fungal viability. In addition, *Malassezia* pretreatment with pancreatic enzymes did not modify the fungal capacity to activate complement as shown by generation of significant levels of C3a and C5a in NHS. Moreover, the opsonisation on the fungal surface by C3c was not diminished. The cell-mediated immunity towards the fungus was also assessed. The presence of pancreatic enzymes did not interfere with the *Malassezia*-induced peripheral blood mononuclear cells (PBMCs) activation, as reflected by TNF-α production and secretion.

Conclusion

Lipolytic pancreatic enzymes induce lipid remodeling in M. globosa, while viability and pro-inflammatory potential remain unaffected across all enzymes. This may promote a chronic pro-inflammatory microenvironment relevant to PDAC.

PP-2-24

Repurposing a Human Cytochrome P450 Activity Assay for High-Throughput Screening of Fungal CYP51 Inhibitors

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Background

Fungal infections and crop diseases are increasing clinical and agricultural concerns, while antifungal discovery remains limited. Azoles inhibit fungal CYP51, a cytochrome P450 enzyme essential for ergosterol biosynthesis; however, resistance and off-target inhibition of mammalian CYPs can limit their utility. Scalable, mechanism-based assays are therefore needed to assess fungal CYP inhibition alongside mammalian CYP activity during early-stage antifungal screening.

Objective

Repurpose a commercially available Vivid™ CYP450 Screening Kit for functional detection of fungal CYP activity and assessment of azole-mediated inhibition in heterologous yeast membrane preparations.

Methods

Saccharomyces cerevisiae strains expressing fungal CYPs with their corresponding cytochrome P450 reductases were cultured, including *Aspergillus fumigatus* CYP51A and *Rhizopus arrhizus* CYP51F1. Crude membrane fractions were prepared by mechanical disruption followed by differential centrifugation. CYP activity was quantified using BOMCC as a fluorogenic substrate and an NADPH-regeneration system to support catalytic turnover. Human CYP3A4 Baculosomes was included as mammalian CYP-positive control.

Results

The adapted kit generated reproducible fluorescence signals from crude membranes expressing *A. fumigatus* CYP51A and *R. arrhizus* CYP51F1, demonstrating functional detection of fungal CYP activity using a repurposed mammalian CYP assay format. Human CYP3A4 positive control confirmed assay performance. The assay distinguished between azole compounds according to their relative inhibitory effects on the fungal CYPs tested, consistent with differences in CYP–azole interaction strength and species-specific azole susceptibility.

Discussion

This study establishes proof-of-concept that a commercially available human CYP450 fluorescence screening kit can be repurposed for functional screening of fungal CYP enzymes. The platform enables detection of fungal CYP activity in crude yeast membrane preparations and may support early-stage antifungal discovery by prioritising compounds with stronger fungal CYP inhibition and reduced mammalian CYP liability.

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ISBN: 978-3-948023-63-8