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ABSTRACTS

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Content

Keynote lecture

Keynote lecture I

KL-I

Invasive Fungal Infections: From Local Epidemiology to Global Strategies

A. Chakrabarti[1]
[1] Director, Doodhadhari Burfani Hospital and Research Institute, Haridwar

Since 1980s invasive fungal infections (IFIs) are an increasing global burden due to rise in number of AIDS and other immunosuppressed patients, transplantations, and use of immunosuppressive drug. Additionally, the change in three determinants of epidemiology in recent years – more fungi adapting higher temperature, non-neutropenic hosts becoming susceptible for IFIs, and environmental change bringing human and fungi closer, have contributed in the rise in number of cases[1,2]. It is estimated that annually more than 6.5 million people suffer from IFIs and 3.5 million die from this disease globally[2]. This has emphasized the need for improvement of local surveillance of IFIs, as epidemiology vary considerably across the continents regarding susceptible population, risk factors and spectrum of etiological agents. The epidemiological studies help in strategy planning. But, the nationwide epidemiological studies are few due to continuous neglect to this field. The neglect is higher in low and middle income countries (LMICs) due to limited awareness, expertise, and laboratories. However, sporadic studies reported high burden of IFIs is LMICs due to tropical environment where fungi thrive easily, compromise in healthcare due over-capacity patient load in hospitals, misuse and abuse of antibiotics and steroids. The recent global outbreaks due to antifungal resistant *Candida auris* and COVID-19 associated mucormycosis have caused panic in population at large[3, 4]. Considering the huge challenge from IFIs, World Health Organization (WHO) in 2022 developed the first fungal priority pathogens list to help research efforts towards managing fungal infections[5]. But, the access to fungal diagnostics is unevenly distributed, especially in LMICs, which is a major hurdle in implementation any control program including stewardship. Emergence of antifungal resistance in another major challenge especially when antifungal drugs are limited. Even the non-availability and non-affordability of those limited antifungal agents is a major issue in LMIC.

In this scenario, we need global concerted strategies to overcome the challenge in managing IFIs. The strategies should include a) education and training to develop more experts in this field, b) mapping of IFIs across the world, c) advocacy in each country for availability of essential diagnostics and antifungal medicine list approved by WHO at affordable price, d) promoting research for point of care diagnostics and development of new antifungal agents, e) implementation of one health program for antifungal resistance and distinct antifungal stewardship program, f) development of global guidelines for managing IFIs, and g) providing more fund for innovative research especially those disproportionately affect the LMIC's poor population . The international societies should play important role in those global strategies**.** ISHAM, ECMM, and GAFFI are already working together with many regional societies. Together they played a crucial role in expanding essential diagnostic and antifungal drug lists of WHO, networking and forming working groups, running e-training course modules, and developing global guidelines. However, there is a long way to go before the formidable challenge of fungal infections can be finally overcome.

References

1. Giannella M, *et al*. Clin Microbiol Infect 2025; 31: 29-36
2. Denning DW. Lancet Infect Dis 2024; 24: e428
3. Chakrabarti and Sood. J Med Microb 2021; 70: 001318

4. Muthu V, *et al*. Emerg Infect Dis 2023; 29: 8
5. https://www.who.int/publications/i/item/9789240060241

Keynote lecture II

KL-II

Treatment decision-making in Candidemia: The Science and The Art

A. Lopes Colombo[1]
[1] *Federal University of São Paulo, São Paulo*

Clinical practice guidelines intend to synthesize all practical recommendations to optimize patient care based on the best scientific evidence available. However, the inconvenient truth is that only a small subset of what is done in medicine has been tested in appropriate, well-designed studies. Consequently, recommendations of Guidelines are often insufficient to optimize patient care in a substantial number of clinical scenarios.
Just as an example, Fanaroff et al (JAMA,2019) reviewed the levels of recommendations supporting 51 guidelines organized by the American College of Cardiology, American Heart Association and European Society of Cardiology. After reviewing a total of 51 guidelines organized by all 3 mentioned societies, the authors found that only 14% of a total of 6329 recommendations were based on data generated by randomized clinical trials. These findings can substantiate our concept that evidence is essential but not sufficient to fully support the process of decision-making in several clinical scenarios we face in real life.
Along with my lecture, I will present scientific evidence available and research gaps in the clinical management of invasive candidiasis, with focus on 3 very relevant scenarios: intra-abdominal candidiasis, *Candida* endocarditis, and *Candida* prosthetic joint infections.

Talks

Session 1 - Host cell interaction and immune response

S1-01

Macrophages plasticity, trained immunity and their implications in fungal infection.

S. K. Biswas[1,2]
[1] *Ignaz Semmelweis Institute, Interuniversity Institute for Infection Research, and*
.[2]Clinical Division of Infectious Diseases, Medical University of Graz, Auenbruggerplatz 15, A-8036 Graz, Austria.

Monocytes/macrophages are the first line of immune defense against microbes and cancer. However, a dysregulation of these cells can lead to pathological consequences ranging from overt inflammation, chronic inflammation to immunosuppression. The mechanism(s) that drive monocytes/macrophages to an immunosuppressive state that facilitates fungal infection is still not clear. Moreover, whether different clinical conditions like cancer, sepsis or diabetes drive immunosuppression in macrophages through distinct or similar mechanisms is also not known. Interestingly fungi or fungal products can induce long-term changes (innate immune memory or trained immunity) in macrophages to enhance their inflammatory activation. However, to what extent trained immunity can contribute to a re-programming of macrophages to either drive pathogenesis or as a therapy to revamp macrophage functions is an important topic in the field. In my talk, I will discuss some of these issues.

S1-02

Comparison of the human fungal pathogenic fungi *Aspergillus fumigatus* and *Lichtheimia corymbifera* regarding the interaction with macrophages

F. Schmidt[1,2], R. Zaher[1,2,3], I. Heineking[1,2,3], T. Heinekamp[1,2], A. A. Brakhage[1,2]
[1]*Friedrich-Schiller-Universität Jena, Fakultät für Biowissenschaften, Institut für Mikrobiologie, Lehrstuhl für Mikrobiologie und Molekularbiologie, Jena, Germany*
[2]*Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie, Hans-Knöll Institut (Leibniz-HKI), Jena, Germany*
[3]*Jena School for Microbial Communication (JSMC), Jena, Germany*

Introduction

Human pathogenic fungi are a common cause of life-threatening complications for a constantly growing risk group of immunocompromised patients after stem cell or organ transplantation, chemotherapy or also viral infections like influenza. The understanding of the interaction of these fungi with the host immune system enables the development of new therapeutic or diagnostic strategies. Our research focuses on two pathogenic fungi, both characterized by a saprophytic lifestyle – *Aspergillus fumigatus*, as one of the major airborne fungal pathogens as well as *Lichtheimia corymbifera*, a member of the Mucorales order. Both human pathogenic fungi are able to cause severe infections like invasive aspergillosis or mucormycosis. Further, *Lichtheimia corymbifera* is known as a breakthrough infection especially following invasive aspergillosis or COVID-19.

Aim

This project aims to elucidate and compare the interactions of *Aspergillus fumigatus* and *L. corymbifera* spores with the innate immune system of the host, in particular macrophages.

Methods and results

To analyze the host-pathogen interaction, we concentrate on the uptake and intracellular phagosome maturation. We used different fluorescent staining methods or immunofluorescent protocols to elucidate the recruitment of protein complexes like vATPase or measure intraphagosomal ROS or Calcium. Furthermore we isolated spore-containing-phagolysosomes and stained for several markers and checked their co-localization or analyzed samples by western blots.

Conclusion

Elucidation of the interaction of spores of Aspergillus fumigatus or *Lichtheimia corymbifera* with macrophages enables the development of new therapeutic strategies. Especially the increase of azol-resistent *Aspergillus* isolates shows the need of innovative approaches. Furthermore the comparison of both human pathogenic fungi could help to get more insights into the understanding of breakthrough infections by *Lichtheimia corymbifera*.

S1-03

Using human airway and alveolar organoid-derived monolayers to quantify parameters of early cryptococcal infections

S. Reusch[1], E. Korsch[1], J. Ibrahim-Bacha[1], C. Schwister[1], A. Aebischer[1], C. Klotz[1], V. Rickerts[1]
[1]Robert Koch-Institut, Department of Infectious Diseases, Unit 16 Mycotic and Parasitic Agents and Mycobacteria, Berlin, Germany

Introduction

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 the pathomechanisms from pulmonary uptake to dissemination, complementary models are required.

Methods

We cocultured cryptococcal reference strains (C. gattii VGII/R265 as a primary lung pathogen; C. neoformans VNI/H99 as the main genotype associated with CNS infections in immunocompromised) 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 quantify 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 in 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.

Discussion

Studying interactions of cryptococci with primary human cells of the respiratory tissue is feasible with Cryptococcus and suggests different fungal-host interactions of C. gattii and C. neoformans due to specific tissue reaction in proximal versus distal tissues. Future studies will be used to characterize immunologic response and analysis of fungal subpopulations.

S1-04

Comparative analysis of the role of reactive oxygen intermediate deficiency in host responses to *Candida albicans* and *Aspergillus fumigatus*

A. Shehata[1], K. Hünniger-Ast[2], F. Schmidt[3], O. Kniemeyer[3], T. Fontaine[4], V. Aimanianda[4], A. A. Brakhage[3], O. Kurzai[2]
[1]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Fungal Septomics, Jena, Germany
[2]Universitätsklinikum Würzburg, Institut für Hygiene und medizinische Mikrobiologie,

Würzburg, Germany
[3]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Jena, Germany
[4]Institut Pasteur – Université de Paris, Paris, France

Chronic Granulomatous Disease (CGD) is a genetic immunodeficiency caused by mutations in genes encoding components of the NADPH oxidase in phagocytic cells, impairing antimicrobial activity. *Ex vivo* whole-blood samples from CGD patients showed immune dysregulation triggered by *A. fumigatus*, but not *C. albicans*. The upregulation of genes encoding cytokines and chemokines suggested a monocyte-dependent effect. To overcome the limitations of patient samples, CGD was mimicked in primary monocytes using GSK2795039, a NADPH oxidase inhibitor. GSK inhibited reactive oxygen species (ROS) production in monocytes and led to significantly increased pro-inflammatory cytokines (e.g. IL-1β) and chemokines (e.g. GRO-β) after *A. fumigatus* exposure, but not *C. albicans* or *C. glabrata*. This pathogen-specific immune response was independent of fungal morphology, viability, or opsonization. Additionally, *Staphylococcus aureus*, another common CGD pathogen, triggered increased IL-1β secretion in GSK-treated monocytes. To identify the factors driving this dysregulated monocyte activation, GSK-treated monocytes were incubated with purified *A. fumigatus* cell wall components. β-1,3-glucan, α-1,3-glucan, and galactosaminogalactan (GAG) induced dysregulation, with GAG specifically enhancing inflammasome-dependent IL-1β secretion. These findings were confirmed using *A. fumigatus* cell wall mutants. Blocking the NLRP3 inflammasome and Caspase-1 reduced IL-1β secretion. However, the upstream signaling pathways involved in this dysregulated activation are still under investigation. Given defective autophagy in CGD phagocytes and its role in inflammasome regulation, we are exploring whether autophagic dysfunction contributes to IL-1β hypersecretion in GSK-treated monocytes.

In conclusion, *A. fumigatus* induces cytokine dysregulation in GSK-treated monocytes, primarily through GAG in the fungal cell wall. Ongoing work aims to uncover the pathways triggered during this dysregulated monocyte activation

S1-05

New perspectives on antifungal immunotherapy

S. Wurster[1]
[1]The University of Texas MD Anderson Cancer Center, Houston, TX

Translation of adjunct antifungal immunotherapy has been hampered by the artificiality of preclinical research, difficulties to perform clinical trials in highly heterogenous and increasingly complex immunocompromised patient populations, poorly defined endpoints and response criteria, and toxicity concerns. In my presentation, I will address some of the key conceptual challenges that have been contributing to the persistent bench-to-bedside disconnect of antifungal immunotherapy. I will further discuss potential future advances such localized (e.g., inhaled) delivery of immunomodulators. Lastly, I will briefly show some of our latest preclinical work to demonstrate how we seek to incorporate important clinical variables (e.g., active leukemia) and study early deployment of multimodal therapy in murine models of invasive mold infections.

Session 2 - Innovative antifungal therapies and drug development

S2-02

Resistance challenges in emerging fungi and therapeutic innovation in high-burden settings

S. Rudramurthy[1]
[1]Department of Medical Microbiology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Fungal infections are an escalating global health concern, particularly in vulnerable populations and intensive care unit (ICU) settings. The challenge is intensified by emerging antifungal resistance and limited treatment options, especially in low- and middle-income countries, where these diseases have a high burden. In 2022, the World Health Organisation (WHO) released the Fungal Priority Pathogen List (FPPL), classifying pathogens into critical, high, and medium priority groups. Among the most concerning are azole-resistant Aspergillus fumigatus, azole-resistant Candida parapsilosis, multidrug-resistant Nakaseomyces glabratus, and Candidozyma auris.

The COVID-19 pandemic coincided with an epidemic of COVID-associated mucormycosis—an inherently antifungal-resistant and often fatal infection. Additional challenges include intrinsic resistance in some Candida species, terbinafine-resistant Trichophyton indotineae, and emerging mechanisms such as efflux pump–mediated azole resistance in Aspergillus flavus.

Although novel antifungal agents are in development, their clinical deployment remains years away. Meanwhile, agricultural fungicides with similar modes of action to medical azoles contribute to cross-resistance in critical pathogens like A. fumigatus.

Addressing this growing threat requires a multifaceted global approach: accelerating the development of innovative therapeutics, ensuring equitable access, enhancing surveillance, and implementing antifungal stewardship to preserve the efficacy of current drugs.

S2-03

Non-fumigatus aspergillus species in clinical practice: Diagnostic and therapeutic implications

A. Seyedmousavi[1]
[1] Microbiology Service, Department of Laboratory Medicine, Clinical Center, National Institutes of Health, Bethesda, MD, USA

Aspergillus infection poses a major clinical challenge, particularly in immunocompromised individuals, with invasive diseases associated with high mortality. While *Aspergillus fumigatus* remains the predominant species causing human infections, recent studies highlight the growing clinical significance of lesser-known and cryptic *Aspergillus* species, which often exhibit reduced susceptibility to standard antifungal therapies. we analyzed 196 clinical *Aspergillus* isolates from 107 patients treated at the NIH Clinical Center between 2019 and 2022. A total of 38 *Aspergillus* species across 11 taxonomic sections were identified, with non-*fumigatus* and cryptic species accounting for 77.1% of all isolates. The most frequently recovered species were *A. fumigatus* sensu stricto (22.9%), *A. sydowii* (8.7%), *A. calidoustus* (7.1%), *A. nidulans* (6.6%), *A. tanneri* (6.1%), and *A. terreus* (5.6%). Species level identification was achieved in 43% of isolates using MALDI-TOF MS. In contrast, PCR sequencing confirmed species identity in over 88% of isolates by targeting the internal transcribed spacer (ITS) region of rDNA, 81% using the β-tubulin gene, and 68.7% using the calmodulin gene. The most common underlying clinical conditions among patients were bronchiectasis (35%), chronic granulomatous disease (CGD) (22%), and pulmonary non-tuberculous mycobacterial infection (17%). Out of 107 patients, 8 died (8/107, 7.5%); six of these deaths occurred in patients with CGD and two in patients with RAG1 deficiency. Antifungal susceptibility testing showed that olorofim had the lowest minimal inhibitory concentrations across species. In contrast, the activity of triazoles and amphotericin B was

variable, particularly against *A. tanneri*, *A. calidoustus*, and *A. sydowii*. This study presents one of the largest species-level datasets of *Aspergillus* isolates to date, underscoring the diversity, pathogenic potential and resistance profiles of non-*fumigatus* species. Accurate species identification is essential to guide appropriate antifungal therapy and improve clinical outcomes.

S2-04

Establishment of an advanced cell culture model for investigation of antifungal drug delivery applications

D. N. Cömert[1], S. Dietz[1], A. Meyer[1], T. Orasch[1]
[1]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Transfer Group Antiinfectives, Jena, Germany

Introduction

Invasive Aspergillosis (IA) continues to pose a threat to humans. Despite current treatment methods, IA related mortality remains unacceptably high up to 95% depending on the patient cohort. This emphasizes the importance of developing novel and effective treatment methods. Drug delivery systems like nanoparticles could overcome pharmacological issues of conventional antifungals, but their special behavior requires advanced in vitro methods mimicking the in vivo situation for evaluation of their effectiveness. For inhalation, submerged cell culture has not provided a realistic pulmonary physiological environment. By contrast, Air-Liquid-Interface (ALI) cultures offer an alternative approach mimicking the lung milieu for drug delivery testing.

Objectives

The aim of the study is to develop and optimize a complex in vitro cell model to mimic lung conditions for testing of novel antifungal formulations.

Materials and Methods

A549 human alveolar epithelial cells were seeded into ALI inserts and were exposed to air for 4 days. Subsequent, differentiated BLaER1 macrophages were added to the ALI culture. This co-culture was infected with fluorescent *A. fumigatus* conidia and treated at different timepoints with different antifungal formulations. The model and treatment effectiveness were evaluated by fluorescent microscopy.

Results: Alveolar type I and type II epithelial cells were confirmed with cell type specific markers AQP-5 and SP-C, respectively, while differentiated macrophages were confirmed for CD68 expression by fluorescent microscopy. Infection with *A. fumigatus* conidia revealed functionality of the model, e.g. phagocytosis by macrophages. The best infection dose was established.

Conclusion

Functional ALI cell co-culture was established for investigating antifungal drug delivery systems, which contributes to the development of novel approaches to fight IA.

S2-05

A new approach to tackle infectious diseases of *Aspergillus* species using programmable cytotoxic nucleases

R. Heger[1], C. Zurek[2], T. Fauth[1], P. Scholz[1]
[1]Akribion Therapeutics GmbH, Zwingenberg, Germany
[2]BRAIN Biotech AG, Zwingenberg, Germany

Worldwide, nearly 2 million new cases of chronic pulmonary aspergillosis (CPA), a lung disease caused by a persistent infection with *Aspergilli*, arise each year, often as a consequence of tuberculosis. Current treatment relies primarily on surgery and/or antifungal medication, which often involves lifelong antifungal therapy with a high probability of developing resistance. In a metagenomics screening to discover novel CRISPR nucleases, we revealed a new family of Cas nuclease, called G-daseE (GdE), which induces collateral DNA and RNA degradation upon guide RNA-mediated recognition of a target RNA. Here we show that this RNA-inducible nuclease activity can be applied for selective elimination of fungal cells. *Aspergillus niger* was transformed via PEG-mediated protoplast transformation using a single-plasmid system containing the expression cassette for the cytotoxic GdE and the gRNA transcription cassette. Functionality of the GdE system was then determined by targeting different user-defined mRNA targets such as amylases and proteases, and measuring colony growth. To leverage our system for the simultaneous combat of multiple CPA-relevant *Aspergillus* strains, we designed gRNAs targeting a conserved site of ribosomal RNA found in various *Aspergilli*. Strikingly, we observed complete clone reduction in *Aspergillus*, whereas cell viability assays in human tissue culture showed inactivity of GdE in human cells due to the lack of the conserved fungal rRNA target site. Since, the cell wall of fungal cells represents a major obstacle for therapeutic drug delivery, more clinically relevant delivery methods such as cationic lipid formulations and nanoparticles are currently being evaluated. In summary, we showed that GdE can be programmed to induce selective cell elimination upon recognition of *Aspergilli*-conserved rRNAs, thereby expanding the molecular toolbox for the treatment of CPA and other infectious diseases caused by fungi.

S2-07

A novel complement-based antifungal therapy targeting clinically relevant molds

V. Harpf[1,2,3], C. Speth[1], G. Rambach[1], V. Fleischer[1], M. O. Skjødt[4], R. Würzner[1], P. Garred[3], A. Rosbjerg[3]
[1]Medizinische Universität Innsbruck, Institute of Hygiene and Microbiology, Innsbruck, Austria
[2]University of Copenhagen, Department of Veterinary and Animal Sciences, Copenhagen, Denmark
[3]Rigshospitalet, Department of Clinical Immunology Section 7631, Copenhagen, Denmark
[4]University of Copenhagen, Department of Immunology and Microbiology, Copenhagen, Denmark

Introduction

Complement (C) is a primary line of defense against fungi and bridges innate and adaptive immunity. We demonstrated that the complement serine protease MASP-1 binds to *Aspergillus fumigatus*, thereby activating C and triggering phagocytosis. To combat rising cases of invasive fungal infections and antifungal resistance, we designed a peptibody – a novel antifungal comprised of a human IgG1 Fc region, a hinge region, and a MASP-1-

derived peptide instead of the Fab region. Modes of action of this novel treatment include Fc opsonization, C opsonization and C activation thereby increasing fungal clearance.

Objectives

(i) Proof the interaction between the peptibody and C1q, a complement pattern recognition protein; (ii) Determine the binding specificity of the peptibody to different clinically relevant fungi.

Methods

Heat-aggregated peptibody was immobilized on ELISA plates and incubated with C1q. Bound C1q was measured using an ELISA plate reader. Heat-aggregated Fc fragments and human IgG (hIgG) were used as positive controls and BSA as negative control.

Furthermore, different clinically relevant fungi (*L. corymbifera*, *M. circinelloides*, *R. arrhizus, A. flavus*, *A. fumigatus*, *A. niger*, *A. terreus*) were opsonized with the peptibody and bound peptibody was determined by flow cytometry. Fc fragments were utilized as a negative control.

Results

The heat-aggregated peptibody bound significantly more C1q than either hIgG or Fc fragments.

While the Fc fragments bound C1q but none of the tested fungi, the peptibody exhibited a broad binding specificity. Besides *A. fumigatus*, the peptibody was detected on *M. circinelloides* and *R. arrhizus* and all of the tested *Aspergillus* species, but not *L. corymbifera*.

Conclusion

In conclusion, the study shows the interaction between the pattern recognition protein C1q and the peptibody proofing one of the modes of action, and a broad binding specificity of this new antifungal drug candidate.

Session 3 - Pediatric fungal infection

S3-01

Update on new antifungal drugs in paediatrics

Z. D. Pana[1]
[1]Medical School UNIC, Cyprus

Invasive fungal infections (IFIs) remain a significant cause of morbidity and mortality in pediatric populations, particularly among immunocompromised children. While recent international guidelines (e.g., ECIL8, ECMM) have advanced the management of IFIs in children, most novel agents remain unapproved or off-label for pediatric use due to insufficient pediatric-specific clinical trial data. The heterogeneity of pediatric patients—encompassing distinct pharmacodynamics, immune responses, and comorbidities—necessitates tailored studies to ensure safe and effective antifungal treatment in this vulnerable group. This presentation provides an evidence-based overview of emerging antifungals highlighting their mechanisms of action, current regulatory status, and existing pediatric data. Particular emphasis will be given to isavuconazole use in children, with a summary of evidence from both regulatory trials and published clinical studies evaluating its pharmacokinetics, safety, and clinical efficacy. Given the global rise in antifungal resistance, including in pediatric populations, the need for pediatric-specific data on these new agents is urgent. Without robust pediatric trials and pharmacologic data, there is a risk of suboptimal treatment and antifungal resistance development. Bridging this evidence gap is critical for informed, equitable, and effective antifungal stewardship in children.

S3-02

Yeast in Pediatric Leukemia

Andreas H. Groll[1], Simone Cesaro[2], Konrad Bochennek[3], Julia Alten[4], Andishe Attarbaschi[5], Draga Barbaric6, Nicole Bodmer[7], Valentino Conter[8], Sarah Elitzur[9] Anja Möricke[4], Martin Schrappe[4], Jan Stary[10], Ester Zapotocka[11], Martin Zimmermann[12], Thomas Lehrnbecher[3]
[1]Infectious Disease Research Program, Department of Pediatric Hematology and Oncology and Center for Bone Marrow Transplantation, University Children's Hospital Münster, Münster, Germany
[2]Paediatric Haematology Oncology, Department of Mother and Child, Azienda Ospedaliera Universitaria Integrata, Verona, Italy
[3]Divison of Pediatric Hematology and Oncology, Department Hospital of Pediatrics, Johann Wolfgang Goethe-University, Frankfurt, Germany
[4]Pediatrics, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany
[5]St. Anna Kinderspital and Children's Cancer Research Institute, Vienna, Austria
[6]Sydney Children's Hospital, Randwick, New South Wales, Australia
[7]University Children's Hospital Zurich, Zurich, Switzerland
[8]Clinica Pediatrica and Centro Ricerca Tettamanti, Università di Milano-Bicocca, Fondazione MBBM/S.Gerardo Hospital, Monza, Italy
[9]Pediatric Hematology-Oncology, Schneider Children's Medical Center, Petah Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Israel
[10]Czech Working Group for Pediatric Hematology, Prague, Czech Republic
[11]Department of Pediatric Hematology/Oncology, University Hospital Motol, 2nd Faculty of Medicine, Charles University, Prague Czech Republic
[12]Department of Pediatric Hematology/Oncology, Hannover Medical School, Hannover, Germany

Invasive infections by opportunistic yeast remain important causes of morbidity and mortality in children and adolescents with acute lymphoblastic leukemia (ALL). However, detailed, multinational epidemiological data on incidence, presentation and outcome of invasive yeast infections in pediatric patients with ALL are scarce. We therefore analyzed prospectively captured severe adverse event (SAE) reports of proven/probable invasive yeast infection of children enrolled in the international, multi-center clinical trial AIEOP-BFM ALL 2009 using the updated 2020 EORTC/MSG consensus definitions of invasive fungal diseases (IFDs). Among 6136 children and adolescents (median age 5.2 years) enrolled into AIEOP-BFM ALL 2009, a total of 68 proven/probable invasive yeast infections were reported in 68 patients (incidence; 1.1%, median age 4.6 years; relative proportion among IFDs: 29.2%). Most infections occurred during induction chemotherapy (protocol I; 77.0%), followed by re-intensification- (protocol II/III; 13.3%, respectively), and high risk cycles [HR I, II or III; 5.9%). There were 58 episodes of proven and 10 episodes of probable invasive yeast infections. Proven infections were due to *Candida albicans* (18), *non-albicans Candida* spp. (27), unspecified *Candida* (9), and rare yeast (4) and involved the bloodstream (51.8%), the bloodstream plus various deep tissue sites (29.3%), and deep tissues without documented fungemia (18.9%); the Central Nervous System (CNS) was affected in 12.1% of cases. Probable infections were due *Candida-* (9) and *Malassezia* (1) spp. and involved the liver plus spleen and kidney (7), the liver (3) and the lung (1). Overall mortality at 12 weeks post diagnosis was 5.9% and similar at one year; all deaths occurred within 6 weeks post diagnosis. Taken together, this uniquely systematic data provides important information on the epidemiology of invasive yeast infections in pediatric ALL patients with full access to state-of-the-art medical care and will hopefully help to refine prophylaxis, diagnosis and management in this high-risk setting.

S3-04

Yeast infections in neonates

S. Butzer
[1]*Universitätsklinikum Köln (AöR), Klinik und Poliklinik für Kinder- und Jugendmedizin, Abteilung für Kinderonkologie und -hämatologe, Abteilung für Pädiatrische Infektiologie, Cologne, Germany*

Invasive fungal infections remain a significant cause of morbidity and mortality in neonates, particularly in very low birth weight infants. *Candida spp.* account for most cases globally, but concerns are rising about emerging rare molds and antifungal resistance. The immature immune system, use of broad-spectrum antibiotics, indwelling catheters, pre- and postnatal corticosteroids, and prolonged hospitalization all contribute to the high vulnerability of this population.
Diagnosis is often delayed due to nonspecific signs and overlaps with other conditions such as sepsis or necrotizing enterocolitis. Conventional blood cultures have low sensitivity, and newer diagnostics—such as fungal biomarkers or molecular assays—are promising but not yet validated for neonates. Histopathology and culture confirmation are frequently delayed, especially in rare but lethal infections like mucormycosis.
Therapeutic options remain limited. Few antifungals are approved for neonates, and pharmacokinetic variability complicates dosing. Drug toxicity, resistance, and limited access to second-line agents further challenge management. Combined medical and surgical approaches are often needed in invasive disease, yet mortality remains high.
The lack of large-scale studies, limited diagnostics, and underreporting of cases hinder prevention and treatment strategies. As survival improves in extremely preterm infants, clinicians face increasing numbers of rare and difficult-to-treat mycoses. Strengthened infection surveillance, adoption of rapid diagnostics, and stewardship to minimize unnecessary antibiotics and steroids are urgently needed. Multidisciplinary collaboration among neonatologists, microbiologists, and infectious disease specialists will be key to improving care and reducing the burden of neonatal fungal infections.

Session 4 - Advances in fungal diagnostics

S4-01

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

K. Bihlmaier[1], L. Vonbrunn[1], R. Strauß[2], K. Macha[3], R. Schneider[4], L. Herbst[1], C. Willam[1], M. Schiffer[1], C. Bogdan[5], J. Held[5]
[1]Uniklinik Erlangen, Medizinische Klinik 4, Erlangen, Germany
[2]Uniklinik Erlangen, Medizinische Klinik 1, Erlangen, Germany
[3]Uniklinik Erlangen, Neurologische Klinik, Erlangen, Germany
[4]Uniklinik Erlangen, Medizinische Klinik 2, Erlangen, Germany
[5]Uniklinik Erlangen, Mikrobiologisches Institut, Erlangen, Germany

Introduction

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 increasing evidence that a considerable number of false-positive BALF GM tests lead to misdiagnosis and antifungal overtreatment.

Objective

To examine if aspiration is causing false-positive BALF GM tests.

Methods

All adult, non-surgical ICU patients who underwent a BAL with testing for GM (Platelia Aspergillus Ag Assay, BioRad), mycological culture, and *Aspergillus* PCR (AsperGenious, PathoNostics) from 11/2020 until 03/2025 were retrospectively included. Additional data were collected to classify the patients for IPA following the FUNDICU and the EORTC/MSGERC 2020 criteria, respectively. The likelihood of previous aspiration was assessed on the basis of 18 risk factors for aspiration (e.g. resuscitation or dysphagia).

Results

356 BALF specimens from 180 ICU patients were included in this study. A positive BALF GM (ODI≥0.5) was determined in 69 (19.4%) BALF specimens of 51 (28.3%) patients. In this group, 21 (30.4%) BALF specimens of 17 (33.3%) patients were also positive for *Aspergillus* PCR and/or *Aspergillus* culture (true-positive GM group). The remaining 48 (69.6%) BALF specimens of 34 (66.7%) patients were GM-positive only (GM-only group). The frequency of patients with previous aspiration was significantly higher in the GM-only group (35/48; 72.9%) compared to the true-positive GM group (5/20; 25.0%, $p<0.001$).

Conclusion

Our results show that the majority of patients have only positive BALF GM values. These patients also have a greatly increased aspiration rate, suggesting a link between aspiration and false-positive GM levels. A weighted aspiration score could be used to identify patients with likely false-positive GM results and reduce misdiagnosis of IPA and antifungal overtreatment.

S4-02

Mucorales PCR testing in bronchoalveolar lavage fluid samples: a prospective cohort study

J. Prattes[1], K. Dichtl[1], S. Sedik[1], U. Glatz[1], M. Egger[1], A. Wölfler[1], P. Zajic[1], H. Kessler[1], M. Hönigl[1]
[1]Medical University Graz, Graz, Austria

Objectives

To assess the clinical value of MucorGenius® PCR in BALF-samples for detecting mucormycosis in at-risk patients.

Methods

BALF samples from patients considered to be at risk for IMIs and sent for microbiological work-up, were collected from 12/2014 until 01/2024 and stored at -80°C. BALF samples from patients exhibiting at least one of the following baseline characteristics at bronchoscopy were included in the study: intensive care unit (ICU) admission, EORTC/MSGERC or FUNDICU host factors, diabetes mellitus, polytrauma, severe burns, chronic lung disease, autoimmune disease, or immunodeficiency.

All patients were retrospectively categorized according to the EORTC/MSGERC or FUNDICU criteria. All included samples were tested for presence of Mucorales spp. DNA by using the MucorGenius® assay.

Results

A total of 1,407 BALF samples from 1,330 patients were analyzed. IMI diagnosis was routine-proven in 3 (aspergillosis = 2, mucormycosis = 1), probable in 25, and possible in 20 patients.

BALF-GM testing was done in 399 samples (28.3%), Aspergillus LFD in 95 (6.7%), Aspergillus PCR in 107 (7.6%), and culture in 1,397 (99.3%). CT scans were available for 758 BALFs (53.9%).

MucorGenius® testing gave a negative result in 1,366 (97.1%) BALFs, a positive result in 32 (2.3%) BALFs and was inhibited in nine samples (0.6%). This results in a specificity of 98.59% (95% CI 97.81 – 99.15). In only three BALF samples, Mucorales spp. could be detected by fungal culture. All three also turned out positive with the MucorGenius® PCR. In addition, one patient was diagnosed with proven mucormycosis post-mortem, where BALF culture remained negative 2 days before death, however, PCR was already positive indicating mucormycosis.

Conclusions

In conclusion, MucorGenius® PCR performed in BALF-samples obtained from patients at risk for IMIs turned out to be highly specific and may indicate mucormycosis before routine diagnostic tools (i.e. culture).

Figure 1

	Overall patients (n = 1,330)	Proven/Probable IMI - EORTC/MSGERC (n = 11)	Possible IMI - EORTC/MSGERC (n = 20)	Probable IPA - FUNDICU (n = 17)
Age, years	63 (53 - 73)	59 (49 – 63)	63 (47.5 - 66)	61 (54.5 – 69.5)
Females	468 (35.2)	6 (54.5)	6 (30)	5 (29.4)
Underlying conditions*				
Hematological malignancy	125 (9.4)	5 (45.5)	7 (35)	0
HSCT, allogeneic	34 (2.6)	1 (9.1)	3 (15)	0
HSCT, autologous	12 (0.9)	1 (9.1)	1 (5)	0
Neutropenia$	48 (3.6)	2 (18.2)	5 (25)	0
SOT recipients	41 (3.1)	1 (9.1)	4 (20)	0
Malignancy, non-hematological	324 (24.4)	1 (9.1)	0	3 (17.6)
Immunodeficiency#	52 (3.9)	2 (18.2)	5 (25)	0
Lung disease	428 (32.2)	1 (9.1)	5 (25)	8 (47.2)
HIV	5 (0.4)§	0§§	0§§§	1 (5.3)§§§§
ICU admission	702 (52.8)	6 (54.5)	13(65)	17 (100)
Viral induced ARDS&	79 (5.9)	2 (18.2)	2 (10)	7 (41.2)
Mechanical ventilation at bronchoscopy	618 (46.5)	4 (36.4)	9 (45)	15 (88.2)
Host factor present				
EORTC/MSGERC host factor	256 (19.6)	9 (81.8)[a]	20 (100)	0
FUNDICU host factor	664 (49.9)	6 (54.5)	4 (20)	17 (100)

Median (25th – 75th percentile) or absolute number (%) displayed if not indicated otherwise.
*More than one per patient possible
#Active autoimmune disease under treatment and primary immunodeficiency's included
$<500 neutrophils/mm³ neutrophils
§HIV PCR and/or screening with antigen and antibody testing available for 434 patients
§§HIV PCR and/or screening with antigen and antibody testing available for 5 patients
§§§HIV PCR and/or screening with antigen and antibody testing available for 15 patients
§§§§HIV PCR and/or screening with antigen and antibody testing available for 7 patients
&Influenza (n=27), SARS-CoV-2 (n=33), RSV (n=4), others (n=15)
[a]Two cases with proven IMI had no underlying EORTC/MSGERC risk factor
Abbreviations: ARDS = acute respiratory distress syndrome; EORTC/MSGERC = European Organization for Research and Treatment of Cancer and Mycoses Study Group Education and Research Consortium; FUNDICU = Invasive Fungal Diseases in Adult Patients in Intensive Care Unit consensus definitions; HIV = human immunodeficiency virus; HSCT = hematopoietic stem cell transplant; ICU = intensive care unit; SOT = solid organ transplant

S4-03

Sequential serum galactomannan as response marker for invasive aspergillosis - an exploratory study from the FungiScope© registry

C. Többen[1,2], O. A. Cornely[1,2,3], C. Joisten[1,2], J. A. Cozzi[4], B. Hoellinger[5], D. Yilmaz Karapinar[6], D. Richter[7], A. H. Groll[8], G. A. Méndez[9,10], J. D. Jenks[11,12], N. Erben[13], L. López Soria[14], P. Köhler[1,2,15], A. Apostolopoulou[16,17], D. Deeren[18], R. Draenert[19], I. Falces-Romero[20], J. Maquera-Afaray[21], L. Meintker[22], R. Kolamunnage-Dona[23], D. Seidel[1,2], J. Stemler[1,2,3]
[1]University Hospital Cologne, Department I of Internal Medicine, Excellence Center for Medical Mycology (ECMM), Köln, Germany
[2]University Hospital Cologne, Faculty of Medicine and University Hospital Cologne, Department I of Internal Medicine, Excellence Center for Medical Mycology (ECMM), Köln, Germany
[3]German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Köln, Germany
[4]Universidad Nacional de Rosario, Centro de Referencia de Micología, F.C.B.F-UNR,

Rosario, Argentina
[5]Strasbourg University Hospitals, Department of Infectious Diseases, Strasbourg, France
[6]Ege University Medical School, Children's Hospital, Department of Pediatric Hematology, Bornova, Turkey
[7]Heidelberg University Hospital, Anaesthesiology, Heidelberg, Germany
[8]Children's University Hospital Münster, Münster, Germany
[9]Infectious Diseases Service, Hospital Escuela de Agudos Dr. Ramón Madariaga, Posadas, Argentina
[10]Infectious Diseases Department, Facultad de Medicina Universidad Católica de las Misiones, Posadas, Argentina
[11]Durham County Department of Public Health, Durham, NC, United States
[12]Duke University, Division of Infectious Diseases, Department of Medicine, Durham, NC, United States
[13]Eskisehir Osmangazi University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Eskişehir, Turkey
[14]Hospital Universitario Cruces, Barakaldo, Spain
[15]University of Cologne, Faculty of Medicine and University Hospital Cologne, Department I of Internal Medicine, Division of Clinical Immunology, Köln, Germany
[16]Massachusetts General Hospital, Harvard Medical School, Division of Infectious Diseases, Boston, MA, United States
[17]Weill Cornell Medicine, Division of Infectious Diseases, New York, NY, United States
[18]AZ Delta hospital, Roeselare, Belgium
[19]LMU Klinikum, Stabsstelle Antibiotic Stewardship, Munich, Germany
[20]Hospital Universitario La Paz, Microbiology and Parasitology, Madrid, Spain
[21]Universidad Ricardo Palma, Instituto de Investigación en Ciencias Biomédicas, Lima, Peru
[22]Friedrich-Alexander Universität Erlangen-Nürnberg, Department of Internal Medicine 5, Hematology and Internal Oncology, Erlangen, Germany
[23]University of Liverpool, Department of Health Data Science, Liverpool, United Kingdom

Question

Invasive aspergillosis (IA) poses significant diagnostic and therapeutic challenges. While galactomannan index (GMI) is established as diagnostic tool, its utility in monitoring antifungal treatment (AFT) response and prognostic value remains debated. This study evaluates validity of GM as biomarker for AFT monitoring and its prognostic significance by correlating GMI with clinical response and survival in a heterogeneous patient population.

Methods

Patients with IA and at least two sequential serum GMI measurements during diagnosis, treatment, and follow-up were identified from the FungiScope® registry. Joint event-time longitudinal models between GMI and time to death, as well as GMI and time to drop-out were used to predict GMI for the analysis of GMI vs. survival and GMI vs. AFT response. Cox proportional hazards models and logistic regression models regressed survival on GMI changes at day 7 as primary predictor.

Results

Among 66 patients, lung was affected in all patients while eight patients also presented adjacent organ involvement or dissemination (Table 1). Day 7 GMI predictions correlated to observed values by 92% (survival analysis) and 88% (AFT response analysis). GMI decreased in both patients who died before 42 days and those who survived but started with and maintained higher in patients who died (Figure 1). Most patients with baseline GMI<1 were alive at day 42, while most deceased patients by day 42 had baseline GMI≥1.

Conclusions

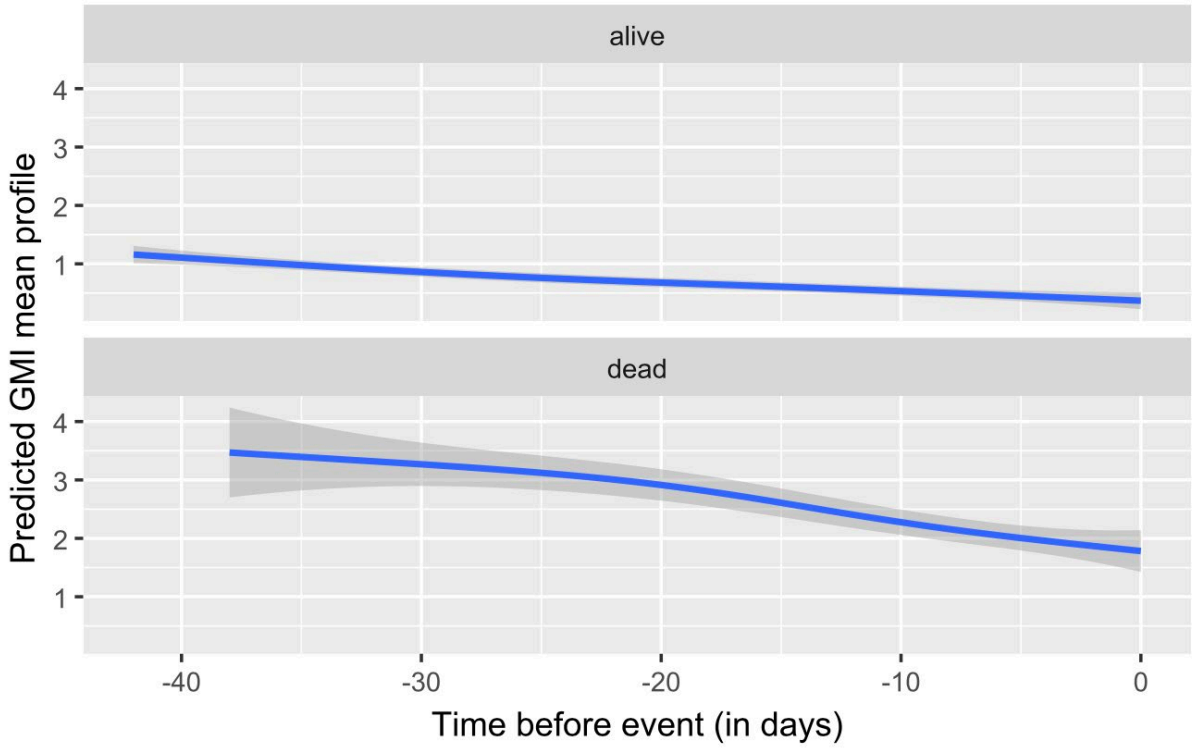
This study highlights the potential of serum GMI as non-invasive, predictive tool for estimating survival probability at onset of IA. Early changes in GMI correlate with survival – with similar although not statistically significant trends seen for AFT response. Early GMI increase could prompt timely adjustment of AFT and guide therapeutic interventions in real-time potentially improving clinical outcomes. GMI could serve as surrogate endpoint in clinical trials, facilitating development of new AFT strategies.

Figure 1

	n=66	%
Age		
1-6 years	8	12
7-11 years	2	3
12-16 years	2	3
17-29 years	9	14
30-49 years	12	18
50-69 years	27	41
70-89 years	6	9
Biological sex		
male	40	61
female	26	39
EORTC/MSG criteria		
Proven	10	15
Probable	51	77
Possible	4	6
Other[1]	1	2
Site(s) of infection		
Lung	58	88
Lung + paranasal sinuses	4	6
Lung + brain	2	3
Other[2]	2	3
Underlying conditions and host factors		
Hematological/Oncological disease[3]	51	77
Allogenic HSCT	9	14
Autologous HSCT	5	8
Solid organ transplantation[4]	13	20
Active acute GvHD	3	5
Diabetes mellitus	6	9
Neutropenia	38	58
Corticosteroids	45	68
Other[5]	65	98
Antifungal treatment day 0 – day 7[6]		
Antifungal prophylaxis[7]	18	27
Survival	27	41

[1]not classifiable under the revised 2019 EORTC/MSG criteria
[2]lung, mediastinum (n=1); lung, brain, mediastinum, ascending aorta (n=1)
[3]acute leukemia (n=27); aplastic anemia (n=4); lymphoma (n=9); myelodysplastic syndrome (n=1); multiple myeloma (n=3); fanconi anemia (n=1); solid tumor (n=5); monoclonal gammopathy (n=1)
[4]liver (n=2); heart (n=8); liver, heart (n=1); kidney, heart (n=1); kidney (n=1)
[5]Crohn's disease (n=1); autoimmune neutropenia (n=1); alcoholism (n=1); chronic cardiovascular disease (n=14); chronic liver disease (n=2); chronic pulmonary disease (n=6); chronic kidney disease or acute kidney injury (n=7); obesity (n=5); underweight (n=1); viral pneumonia within 90 days prior invasive fungal infection (n=7); treatment in ICU (n=20)
[6]azoles (n=38); polyenes (n=13); echinocandins (n=3); azoles + polyenes (n=6); azoles + echinocandins (n=1); azoles + polyenes + echinocandins (n=2); unknown (n=3)
[7]amphotericin B liposomal (n=3); caspofungin (n=2); fluconazole (n=3); micafungin (n=2); posaconazole (n=5); voriconazole (n=3)

Figure 2



S4-04

Diagnostic accuracy of PCR assays for Mucormycosis: A systematic review and meta-analysis

M. Lackner[1]
[1]Medizinische Universität Innsbruck, Institute of Hygiene and Microbiology, Innsbruck, Austria

Research Question

How accurate are polymerase chain reaction (PCR) assays in diagnosing mucormycosis across different specimen types?

Methods

A systematic search of PubMed, Embase, Global Health, and the Cochrane Library was conducted from inception to December 3, 2024. Studies using PCR-based methods on human specimens to diagnose mucormycosis were included. A bivariate meta-analysis assessed PCR performance using the 2020 European Organisation for Research and Treatment of Cancer–Mycoses Study Group Education and Research Consortium (EORTC-MSGERC) definitions for proven and probable invasive mould disease, modified to include all at-risk patients. The study protocol was registered in PROSPERO.

Results

From 4,855 articles, 30 studies met inclusion criteria, covering 5,920 PCR reactions on 5,147 specimens from 819 proven/probable mucormycosis cases and 4,266 non-cases. Sensitivity varied by specimen type ($p < 0.001$), while specificity was consistent ($p = 0.662$). Bronchoalveolar lavage fluid (BALF) had the highest sensitivity (97.5%, 95% CI: 83.7–

99.7%) and specificity (95.8%, 95% CI: 89.6–98.4%), with LR+ of 23.5 and LR− of 0.03. Tissue samples showed sensitivity of 86.4% (95% CI: 78.9–91.5%) and specificity of 90.6% (95% CI: 78.1–96.3%), with LR+ of 9.2 and LR− of 0.15. Blood samples had sensitivity of 81.6% (95% CI: 70.1–89.4%) and specificity of 95.5% (95% CI: 87.4–98.5%), with LR+ of 18.3 and LR− of 0.19. Formalin-fixed paraffin-embedded (FFPE) specimens had the lowest sensitivity (73.0%, 95% CI: 61.0–82.3%) but the highest specificity (96.4%, 95% CI: 87.5–99.0%), with LR+ of 20.2 and LR− of 0.28. Heterogeneity was mainly explained by specimen type, study design, and disease prevalence.

Conclusion

PCR demonstrates high diagnostic accuracy for mucormycosis, particularly in BALF, blood, and tissue specimens. These findings support incorporating PCR-based detection into future diagnostic guidelines for mucormycosis.

S4-05

CandEYE – Serial non-mydriatic fundoscopy in patients with candidemia

I. Reinhold[1], L. Altay[1], A. Lentzsch[1], J. Salmanton-García[1], E. Makcevic[1], C. Cursiefen[1], O. A. Cornely[1], R. Sprute[1]
[1]University Hospital Cologne, Köln, Germany

Objectives

The incidence of ocular candidiasis (OC) in candidemia ranges from 2–26% for chorioretinitis and <2% for endophthalmitis. OC influences treatment, including antifungal selection and potential surgery. Guidelines recommend fundoscopy for all candidemia patients, yet indirect fundoscopy may be limited by resource constraints. Non-mydriatic fundoscopy allows examination without dilating agents and can be performed by non-specialists. This study evaluates its feasibility for OC screening in candidemia, aiming also to define optimal timing and assess patient risk stratification based on findings.

Methods

The Optomed Aurora IQ handheld fundus camera enables imaging without pharmacologic pupil dilation (≥3.1 mm). Adult patients with candidemia at University Hospital of Cologne were assessed. Patients with interfering miosis were excluded. Serial exams every 48–72 hours were conducted by infectious disease physicians or medical students until antifungal therapy ended. Retinal images were reviewed via teleophthalmology by an ophthalmologist. If feasible, patients also underwent a day 7 mydriatic fundoscopy by an ophthalmologist.

Results

Between February and April 2025, 12 patients with candidemia were screened. Eight (67%) were included in serial exams. Exclusions were due to miosis (2), death (1), or transfer (1). Patient characteristics are shown in Table 1. The main limitation was lid closure from sedation or fatigue (3/8, 38%). No OC findings were observed. Ophthalmologist-performed mydriatic fundoscopy was done in 3 patients and showed no discrepancies compared to non-mydriatic exams.

Conclusions

Preliminary results show that non-mydriatic fundoscopy by non-specialists is feasible for

most candidemia patients. The limited availability of specialist exams emphasizes the need for alternative screening approaches. The study will continue for at least one year. Future work will explore AI-based image interpretation.

Figure 1

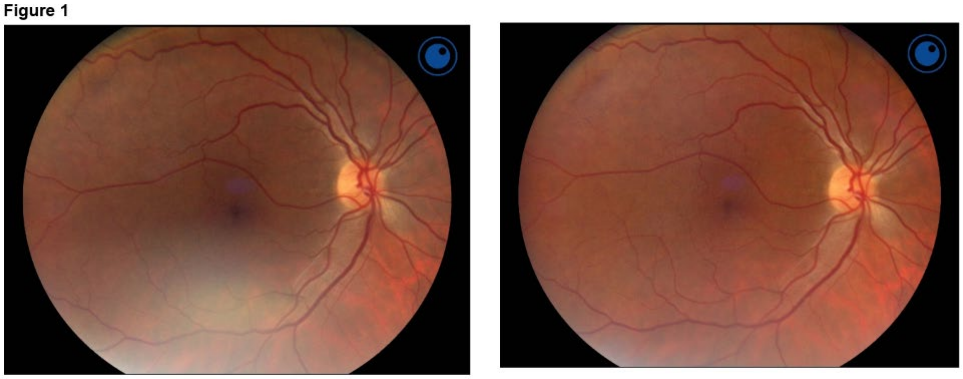
Table 1: Baseline characteristics of 12 patients with *Candida* spp. blood stream infection evaluated for non-mydriatic fundoscopy

n total =12		n	%	Mean	Min	Max
Age at diagnosis (years)				56	18	74
Gender	Female	3	25			
	Male	9	75			
Neutropenia <0.5 G/l	Yes	1	8			
	No	11	92			
Ward	ICU / IMC	6	50			
	General ward	6	50			
Candida species [1]	*C. albicans*	6	46			
	C. glabrata	3	23			
	C. dubliniensis	2	17			
	C. parapsilosis	2	17			
Duration of BC positivity (days)				3.9	2	10
Time between initial positive BC sampling and treatment initiation (days)				2.3	1	4

Abbreviations: BC: blood culture; ICU: intensive care unit; IMC: intermediate care unit
[1] one patient had two episodes of *Candida* spp. blood stream infections (*C. albicans and C. glabrata*)

Figure 2

Figure 1



Example of a retinal image obtained in the same patient by non-mydriatic fundoscopy at day 4 (left) and day 7 (right) after onset of candidemia

S4-06

Development of a point-of-care DNA extraction for the detection of fungal DNA from diverse sample types such as hair, nails, skin or liquids

J. Graf[1], A. Wende[1]
[1]Xpedite Diagnostics GmbH, Hallbergmoos, Germany

Traditional DNA extraction from clinical and environmental samples, e.g. skin, nail, hair, environmental swabs or liquids typically requires laborious multi-step protocols involving long incubations and extensive purification. These methods often yield low DNA quantities, especially when fungal biomass is limited, posing challenges for accurate detection. This study aimed at developing a rapid and simplified DNA extraction protocol suitable for a range of fungal detection applications, e.g. systemic, respiratory or superficial fungal diseases, without compromising the sensitivity or specificity of downstream molecular assays. A key goal was to enable decentralized diagnostics.

Based on our cell capturing and reverse purification technology, we developed a refined protocol for detection of DNA from fungal species from skin, hair, nail, environmental swabs and liquids. The improvements comprise the following key steps: (a) enrichment of fungal cells and spores from liquid samples, (b) rapid lysis, and (c) one-step inhibitor removal by reverse purification rendering the extracted DNA applicable to various molecular methods.

The finalized protocol requires minimal hands-on time and reduces total DNA extraction from tough-to-lyse fungal to under 30 minutes. The core innovation lies in the ability to process larger sample volumes while maintaining high recovery rates for a broad range of fungal species allowing for earlier detection and faster response to potential health threats. Results demonstrate that the protocol performs equivalently to conventional silica membrane-based kits, while being significantly faster and easier to use.

This rapid extraction protocol facilitates timely and reliable fungal detection directly at sampling sites or in small laboratories. It is highly efficient and simple making it a valuable tool for broader fungal surveillance, clinical diagnostics, and outbreak response, thereby allowing earlier intervention and improved patient outcomes.

S4-07 | PII-11

ImmunoPET and LSFM-based imaging for early diagnosis of invasive Aspergillosis using Fc-modified anti-*Aspergillus fumigatus* antibodies

S. Tonneau[1], L. Allerchen[2]
[1]*University Tübingen, Werner Siemens Imaging Center, Tübingen, Germany*
[2]*Universität Essen-Duisburg, Institute for Experimental Immunology and Imaging, Essen, Germany*

Aspergillus fumigatus is an airborne mold that can cause invasive aspergillosis (IA) in immunocompromised patients, including those with cancer, transplant recipients, and individuals with severe viral infections such as COVID-19. Recent studies also show vulnerability in immunocompetent individuals. IA is associated with mortality rates over 40% [1], largely due to diagnostic delays and the non-specific nature of clinical symptoms. Current diagnostics rely on invasive procedures like biopsies or BAL, and imaging techniques like CT and MRI, which lack sensitivity and specificity for early detection [1,2]. Molecular imaging using immunoPET, which combines PET with radiolabeled antibodies, offers high sensitivity and target specificity. Our research builds on prior work using the JF5 monoclonal antibody [3], which binds a secreted antigen unique to *A. fumigatus* during active hyphal growth [1,4,5]. While effective in identifying fungal lesions, the original tracer suffers from prolonged circulation time due to the IgG1 Fc domain, causing high background signal and limiting early detection. To address this, we are developing Fc-modified JF5 variants with reduced binding to the neonatal Fc receptor (FcRn) to accelerate clearance and enhance contrast [6]. These variants are radiolabeled with copper-64 and tested in murine pulmonary IA models using PET/MR imaging, with LSFM for microscopic validation [1]. We hypothesize that tracer uptake correlates with fungal antigen expression and decreases with effective antifungal therapy, making it a candidate biomarker for treatment monitoring. Comparison with unmodified tracers and analysis under antifungal or antibacterial therapy will help define clinical utility.

References

1. Henneberg et al., *Nat Commun*, 2021.
2. Beziere et al., *Theranostics*, 2019.
3. Thornton, *Clin Vaccine Immunol*, 2008.

4. Rolle et al., *PNAS*, 2016.
5. Davies et al., *Theranostics*, 2017. [6] Pyzik et al., *Front Immunol*, 2019.

Figure 1

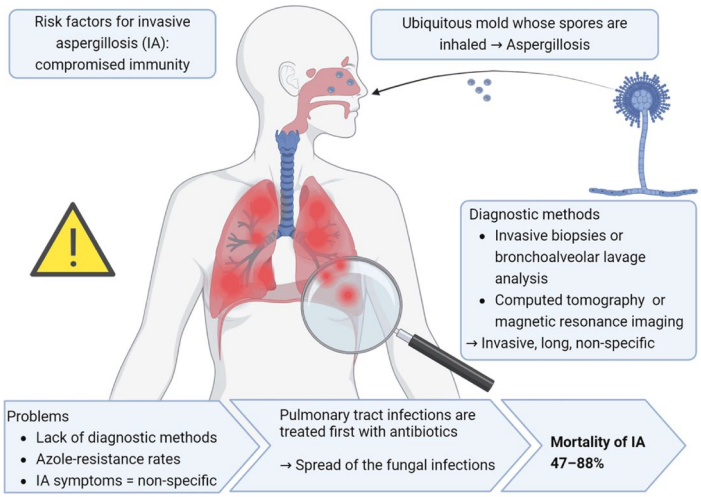
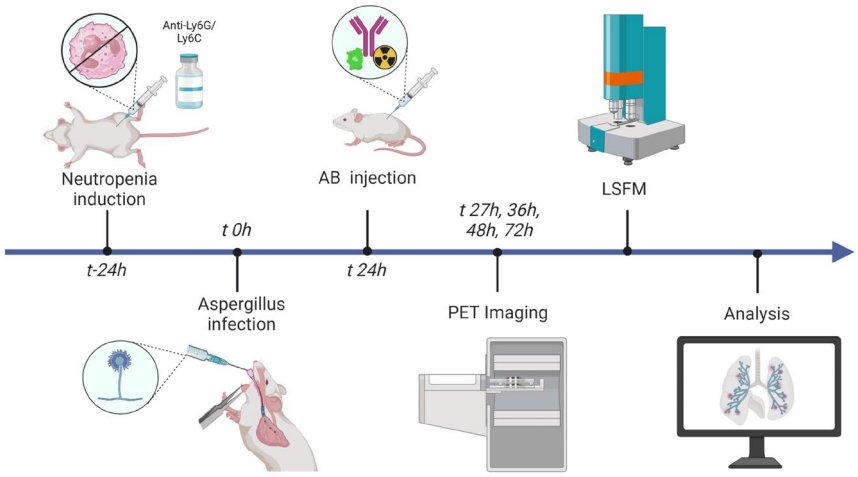


Figure 2



S4-08 | PII-14

Image processing algorithms to differentiate the extent of *in vitro* infections with *Tricho Phyton rubrum* on bovine hoof sheets

U. Bock[1], D. Neumann[2]
[1]*Bock Project Management, Tawern, Germany*
[2]*Scientific Consilience GmbH, Kleinblittersdorf, Germany*

Introduction

Autonomous and simple documentation of nail color by digital imaging may simplify early detection of onychomycosis [1-2]. Furthermore, the spread of the infection, its increase in severity and the effect of (topical) antifungal therapy can be easily monitored.

Objectives

Bovine hoof sheets (BHS, 400 µm thickness, 16 mm diameter) have proven to be a suitable model to study infection with *T. rubrum* [3-4]. BHS have been applied in multiple topical lacquer [3] and semisolid developments [4] including nail infections with different dermatophytes [5]. BHS with varying degrees of *T. rubrum* infections were examined versus non-infected BHS by digital imaging with differently colored backgrounds.

Materials & Methods

Twelve non-infected and nineteen *T. rubrum* infected BHS were scanned on ten different background colors (BG) to account for interindividual differences. Using only averaged color information, classification was performed using clustering and supervised learning methods. The performance of the latter was assessed by repeated cross-validation.

Results

Using all data points and assuming only two clusters, clustering resulted in a sensitivity of only 65% due to the BG variation. A supervised learning method gave an average sensitivity of 99%.

Conclusion

The fast and cost-effective microscopic examination of nail material by an expert result in up to 15% false-negatives [6]. Our results underline the high potential of learning methods for early disease detection. Improving the image processing algorithm and increasing the available training data may allow for establishing a fast and highly sensitive method for early infection detection.

References

1. Baran *et al.,* J. Drugs Dermatol., 2004;
2. Bulinska *et al.,* J. Fungi, 2024;
3. Bonetti *et al.,* Int. J. Pharm., 2021;
4. Kappes *et al.,* Pharmaceutics, 2021:
5. Temporiti *et al.,* J. Fungi, 2022;
6. Brillowska-Dabrowska *et al.,* J. Clin. Microbiol., 2007

S4-09

Improving *Talaromyces marneffei* diagnostics via a mitochondrial-targeting qPCR and isothermal reaction-based lateral flow assay (LAMP-LFA)

W. van de Sande[1], R. Mohd-Tap[2], J. G. Pereira Brunelli[3], J. Houbraken[4], F. Hagen[1,5,6]
[1]*Westerdijk Fungal Biodiversity Institute, Medical Microbiology, Utrecht, Netherlands*
[2]*Institute for Medical Research, Mycology Section, Selangor, Malaysia*
[3]*Ministerio de Salud Pública y Bienestar Social, Centro de Especialidades Dermatologicas, Asuncion, Paraguay*
[4]*Westerdijk Fungal Biodiversity Institute, Food and Indoor Fungi, Utrecht, Netherlands*
[5]*University Medical Center Utrecht, Medical Microbiology, Utrecht, Netherlands*
[6]*University of Amsterdam, Institute for Biodiversity and Ecosystem Dynamics, Amsterdam, Netherlands*

Introduction

Talaromyces marneffei is an opportunistic fungal pathogen that primarily affects immunocompromised individuals, and is endemic in Southeast Asia. Despite its clinical significance, talaromycosis remains an underdiagnosed and neglected tropical disease, largely due to limited diagnostic infrastructure and low clinical awareness.

Objectives

To help improve the diagnosis, this study aims to develop new molecular diagnostic assays. A qPCR assay was designed for areas with access to more advanced equipment, while a loop-mediated isothermal amplification (LAMP) assay was developed for low-resource settings.

Materials & Methods

We evaluated published qPCR assays, targeting single-copy genes or multi-copy ribosomal DNA loci, for their specificity for *T. marneffei* using 34 *T. marneffei* strains and a panel of other (*Talaromyces*) species. To determine the limit of detection a gBlock of the target gene was used. For the LAMP assay, the in-house *Talaromyces* strain sequence data was used to develop an assay. The strain set was used to assess specificity and sensitivity. The qPCR was transformed into a LAMP and LAMP-LFA assay.

Results

The qPCR showed the highest sensitivity compared to the existing qPCRs. The assay exhibited no cross-reactivity with any of the 93 tested non-*T. marneffei* pathogens and were positive for all 34 *T. marneffei* strains. Similarly, this was observed for the LAMP and LAMP-LFA assay.

Conclusions

The novel mitochondrial-targeting qPCR assay to detect *T. marneffei* shows high specificity and sensitivity and can detect low fungal burden in clinical samples. Compared to conventional diagnostic methods (culturing), this qPCR is faster and more robust. For low-resource areas LAMP-LFA is a technique with high specificity and sensitivity for the detection of *T. marneffei*. Due to its simplicity, speed and low cost, the technique represents a promising alternative to current techniques.

Session 5 - Dermatophytes and mucocutaneous infections

S5-01

Rare keratinophilic fungi - potentially harmful and on the brink of pathogenicity?

J. Brasch[1]
[1]*Klinik für Dermatologie, Venerologie und Allergologie, UKSH, Campus Kiel*

Human beings are coated with keratin. 54 type 1 and type 2 α-keratins are the main components of human stratum corneum, hair, and nails. These keratins are crucially important for the integrity and proper function of our outermost defence barrier against environmental hazards such as microorganisms. Therefore, fungi that have the capability to degrade keratins are potentially harmful and of outstanding medical interest. E.g., pathogenic

dermatophytes all have keratinolytic abilities by means of which they can induce superficial dermatomycoses.

It is interesting therefore, that in recent years occasionally geophilic dermatophyte species were unexpectedly isolated from various lesions of human skin and nails although these fungi have not been classified as pathogens for humans up to now. The spectrum of such findings was broadened by newly detected *Onygenales* species. Furthermore, some keratinolytic fungi unrelated to genera of dermatophytes were detected on human skin with various anomalies. Examples of such observations will be presented.

Obviously, the range of fungi that are able to degrade keratin and can at least temporarily colonize skin under favourable conditions is broader than has been assumed so far. Clinicians should be aware that such fungi might catch their chance for a permanent colonization under supportive circumstances that in a next step might even transform into true infection. Therefore, mycological diagnostics in dermatology should not be restricted to the detection of well-known tinea causing dermatophytes but should aim to identify all suspect fungal isolates. The challenge for clinicians will then be to assess the pathogenic relevance of unexpected species. Such a sentinel surveillance will help to early identify those unforeseen agents that are on the brink of pathogenicity.

S5-02

Azole-resistant *Trichophyton rubrum* isolates exhibit *Erg11B* Gly443Cys substitutions comparable to *T. indotineae* mutants but no genomic amplification of *Erg11B*

A. Burmester[1], L. Kraußе[1], J. Tittelbach[1], P. Nenoff[2], M. Fabri[1], C. Wiegand[1]
[1]*Universitätsklinikum Jena, Klinik für Hautkrankheiten, Jena, Germany*
[2]*Labopart-medical laboratories, Mölbis, Germany*

Itraconazole-resistant *Trichophyton indotineae* isolates[1] of the *T. mentagrophytes/ interdigitale* complex feature amino acid subsitutions in the sterol 14-α demethylase gene *Erg11B*[2], as well as two distinct types of *Erg11B* gene amplifications[3]. Recently, *T. rubrum* isolates were obtained from a patient who failed therapy with itraconazole, voriconazole and terbinafine[4].

To better understand resistance development, azole-resistant phenotypes and genotypes of *T. rubrum* were compared with those of *T. indotineae*. MLN methods were adapted according to the EUCASTE.Def11.0[5] and comparable protocols for itraconazole susceptibility testing. *T. indotineae* strains were classified according to type I or type II amplification patterns as previously described[3]. The recently analyzed *T. indotineae* isolate UKJ 476/21, which shows overexpression of *Erg11B*[6], could be classified as type II amplification of *Erg11B*. The *T. rubrum Erg1* Ile479Thr mutant strain also harbored a Gly443Cys amino acid substitution in *Erg11B*. Replacement of RPMI1640 for azole resistance testing with Sabouraud-glucose broth improved discrimination between resistant and sensitive isolates. Resistant *T. rubrum* strains maintained single copies of both *Erg11B* and *Erg11A*, confirming that *Erg11B* amplification remains, to date, restricted to *T. indotineae*.

Comparable mutations of *Erg1* and *Erg11B* have been detected in itraconazole-resistant strains of both *T. rubrum* and *T. indotineae*. This suggests that similar selective pressure, likely driven by prolonged antifungal therapy, have led to convergent resistance development in these species.

References

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. Nenoff et al. Dermatologie (2023) 10.1007/s00105-023-05232-4
5. Arendrup et al. Clin Microbiol Infect (2021) 27:55-60.
6. Berstecher et al. J Fungi (2024) 10.3390/jof10110731

S5-03

Isolation of *Histoplasma capsulatum* from wild and domestic animals in Germany

J. Gerkrath[1], I. Mc Cormick Smith[1], T. Störiko[2], M. Suntz[3], U. Mayer[4], A. Klatt[1], W. Tobias[1], S. H. Tausch[2], V. Rickerts[1]
[1]Robert Koch-Institut, FG16, Berlin, Germany
[2]Robert Koch-Institut, MF1, Berlin, Germany
[3]Chemisches und Veterinäruntersuchungsamt, Tiergesundheit Pathologie, Histologie, Forensik, Freiburg i. Br., Germany
[4]IDEXX Laboratories, Kornwestheim, Germany

Histoplasmosis is a systemic fungal infection caused by the thermally dimorphic fungus *H. capsulatum*. Human Histoplasmosis is a major public health threat in parts of North-, Latin- and South America, Asia and Africa but occurs worldwide. Infections in Europe appear to be mostly imported in human cases. We have previously demonstrated histoplasmosis in wild and domestic animals by PCR from pathology blocks but failed to cultivate the fungus from animals. Here, we rport on the succesful isolation of *H. capsulatum* from tissues of a badger and a cat (positive by microscopy and Histoplasma PCR).

Tissue samples were cultivated on fungal media including Mycosel and Brain Heart Infusion Agar with blood for up to 6 weeks. Genomic DNA was extracted from suggestive isolates for ITS sequencing, MLST analysis and Illumina whole genome sequencing. The MycoSNP-nf pipeline was used to construct a whole genome variant-based phylogeny of animal isolates and isolates from human histoplasmosis cases imported to Germany from Asia as well as a variety of *Histoplasma* strains retrieved from the Sequence Read Archive.

Growth of suggestive fungal colonies was observed after 17 - 35 days cultivation at 26°C. Concatenated MLST-sequences clustered with the so-called Eurasian clade. In the whole genome-based phylogeny, animal isolates clustered with clinical isolates imported from Asian countries within a cluster of South American strains. Subcultures demonstrated growth on mycosel, brain-heart infusion with blood and potato dextrose agar.

We cultivated *Histoplasma capsulatum* from superficial infections of a cat and a badger from Germany. Phenotypic characterization of the isolates and detection of environmental niches are mandatory for risk assessment. We recommend molecular typing of *Histoplasma* isolates to increase knowledge on the molecular epidemiology of histoplasmosis in Europe.

S5-04

Dynamic gene expression and functional networks underlying spore germination in *Microsporum*

X. Zhou[1], P. Feng[2], S. de Hoog[1]
[1]Radboud University Medical Center, Nijmegen, Netherlands
[2]Sun Yat-sen University, Guangzhou, China

Introduction

Microsporum canis is a zoophilic dermatophyte that causes highly transmissible infections in animals and humans. Spore germination represents a critical phase in host invasion, but the underlying regulatory mechanisms remain poorly characterised.

Objectives

To uncover dynamic gene expression profiles, regulatory networks, and metabolic transitions driving spore germination in *M. canis*.

Materials & Methods

Transcriptomic sequencing was conducted on three developmental stages: mycelium, dormant spores (0h), and germinating spores (4h). Differential expression, GO/KEGG enrichment, gene clustering, and alternative splicing were analysed. Protein-protein interaction (PPI) networks were constructed. Twelve genes were validated via qPCR across five time points (0–8h).

Results

Transcriptomic profiling revealed 593 DEGs between Spore 0h and 4h. Germination was characterized by upregulation of genes involved in DNA replication (*POL1*, *MCM*), oxidative phosphorylation (ATP synthase, cytochrome complex), and ribosome biosynthesis, alongside downregulation of *PEX* family genes and fatty acid β-oxidation, indicating a shift from lipid to mitochondrial metabolism. Eight gene expression clusters revealed temporally regulated transcriptional modules (Fig1). Exon skipping and mutually exclusive exon splicing events targeted genes in methylation, energy metabolism, and cytoskeletal reorganization. PPI analysis identified *SLP1*, *MEC1*, and *UBI4* as key regulators linked to Ras/cAMP-PKA and MAPK signaling (Fig2). Unlike *Aspergillus*, *M. canis* displayed low HSP90 expression and a putative ribosome storage strategy.

Conclusion

This study presents the first systems-level insight into *M. canis* spore germination, revealing conserved and species-specific regulatory mechanisms. These findings offer a molecular basis for early-stage antifungal intervention.

Figure 1

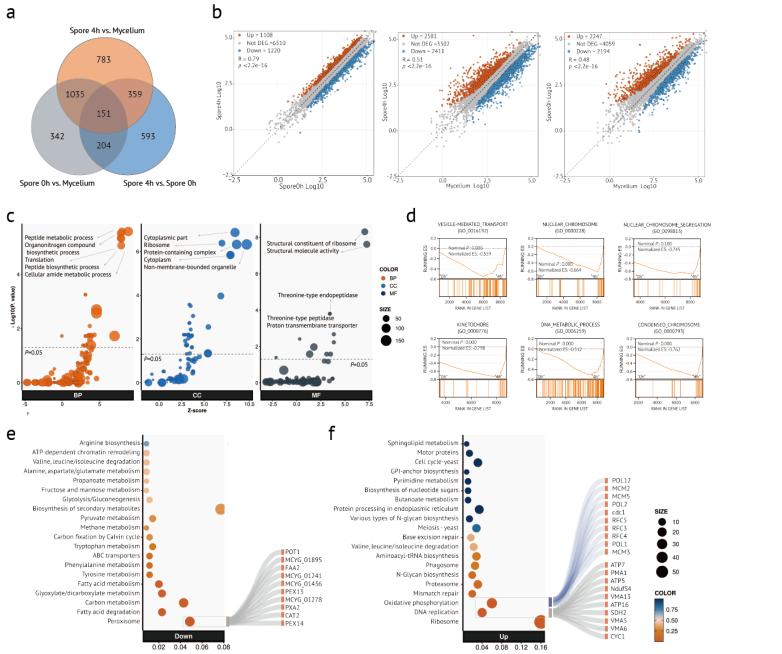
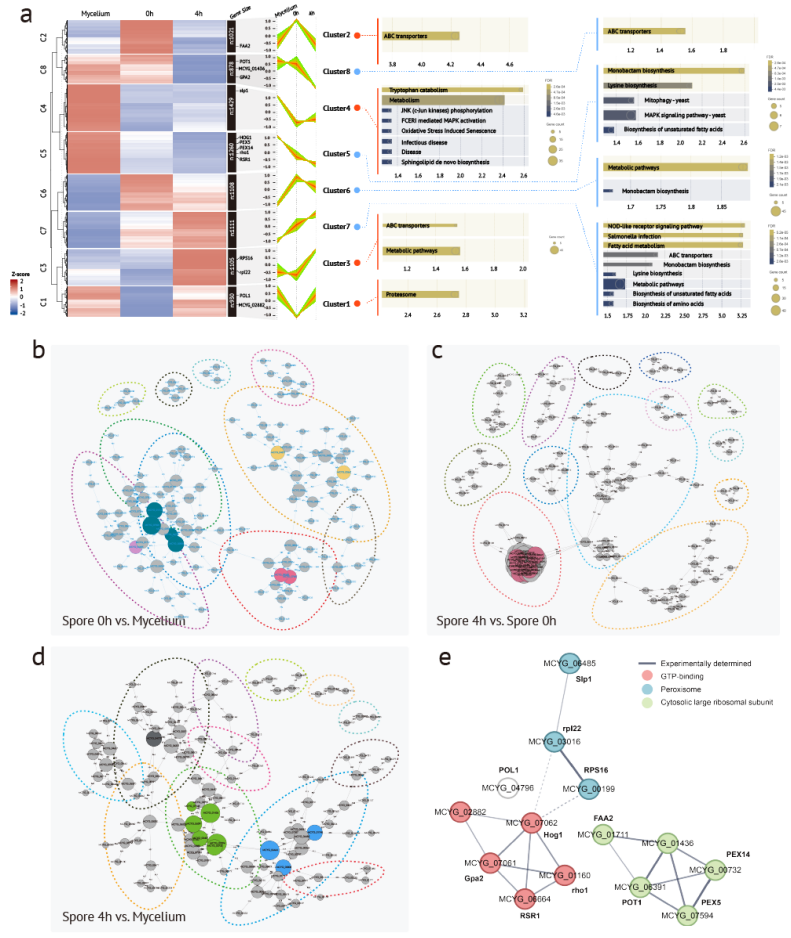


Figure 2



S5-05

Novel, fast and cost-effective real-time PCR based method for the differential diagnosis of Dermatophytes in veterinary medicine

V. Garg[1], R. Söller[2], A. Wende[3], J. Graf[3], Y. Gräser[1]
[1]Charité - Universitätsmedizin Berlin, Berlin, Germany
[2]Anchor Diagnostic, Hamburg, Germany
[3]Xpedite Diagnostics GmbH, Hallbergmoos, Germany

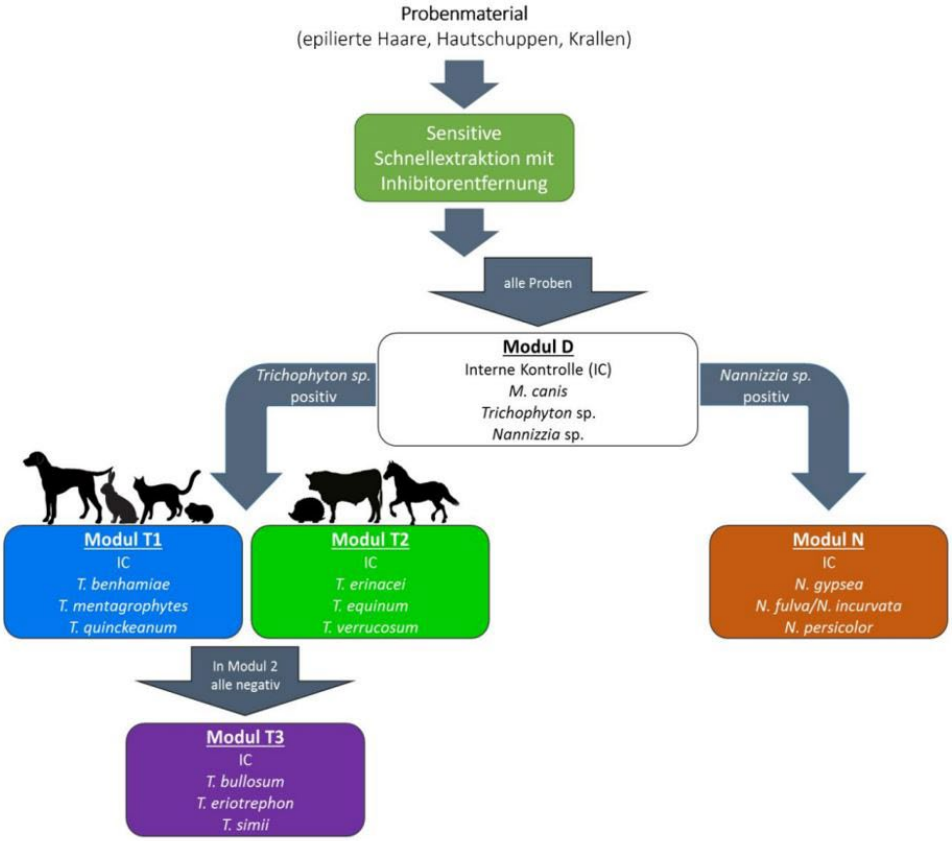
Diagnosing dermatophyte infections in animals remains a persistent hurdle in veterinary practice, largely due to the limitations of traditional testing methods, which often fail to deliver accurate or reliable results. To overcome these challenges, we aim to develop a cutting-edge molecular diagnostic approach using quantitative PCR (qPCR) technology, designed specifically to detect and identify animal-infecting dermatophytes with high precision.

This research centers on developing qPCR primers tailored to specifically identify a subset of dermatophyte species—particularly those that are zoophilic. By carefully designing and rigorously validating these primers, our goal is to establish a reliable qPCR-based assay that can sensitively and accurately detect dermatophyte DNA in clinical specimens. Such a diagnostic advancement has the potential to transform the way dermatophytosis is diagnosed in animals, paving the way for earlier intervention and more precise treatment options.

This project is being carried out in collaboration with two key partners. Dr. Andy Wende from Xpedite Diagnostics who is leading the development of a rapid DNA extraction protocol tailored for veterinary samples, while Dr. Rainer Söller of Anchor Diagnostics who is focusing on refining and optimizing the multiplex PCR components of the assay.

Our qPCR-based diagnostic system will be developed through five integrated modules, each targeting a critical stage of the workflow—ranging from sample collection and DNA extraction to primer refinement, assay construction, and final validation. This modular approach allows for a thorough and systematic development process, ensuring that each component of the diagnostic tool is carefully optimized and effectively implemented.To date, we have successfully completed the first module of the project.The results from singleplex qPCR assays demonstrate high specificity and sensitivity across these targets. Multiplexing of these oligonucleotides is currently underway

Figure 1



S5-06

Molecular epidemiology of the "forgotten" dermatophyte *Microsporum ferrugineum* in Germany – now also detected as a double infection with *Trichophyton tonsurans* in wrestlers

S. Uhrlaß[1], C. Baldauf[2], O. Hirschsteiner[2], K. Dumann[3], D. Koch[1], H. Muetze[1], C. Krueger[1], U. Paasch[3], P. Nenoff[1]
[1]*labopart - Medizinische Laboratorien, Rötha OT Mölbis, Germany*
[2]*Salus Health Centre Dermatology Clinic, Bad Reichenhall, Germany*
[3]*Paasch Dermatologists, Taucha, Germany*

Introduction

In Germany, *Microsporum (M.) ferrugineum* has hardly ever been isolated in the last 50 years.

Objective

Since 2016, individual strains of the anthropophilic dermatophyte have been repeatedly detected. In addition, there have been localised outbreaks of dermatophytosis caused by *M. ferrugineum*. Since 2023, the number of infections caused by *M. ferrugineum* has been rising again.

Methods

M. ferrugineum isolates from routine diagnostics were morphologically characterised. All isolates were identified by molecular biology using PCR and sequencing of the ITS region and/or the t*ef*-1α gene. In the event of a double infection with *Trichophyton (T.) tonsurans*, only *T. tonsurans* is culturally detectable due to the faster growth of *T. tonsurans*. However, both dermatophytes can be detected using molecular methods.

Results

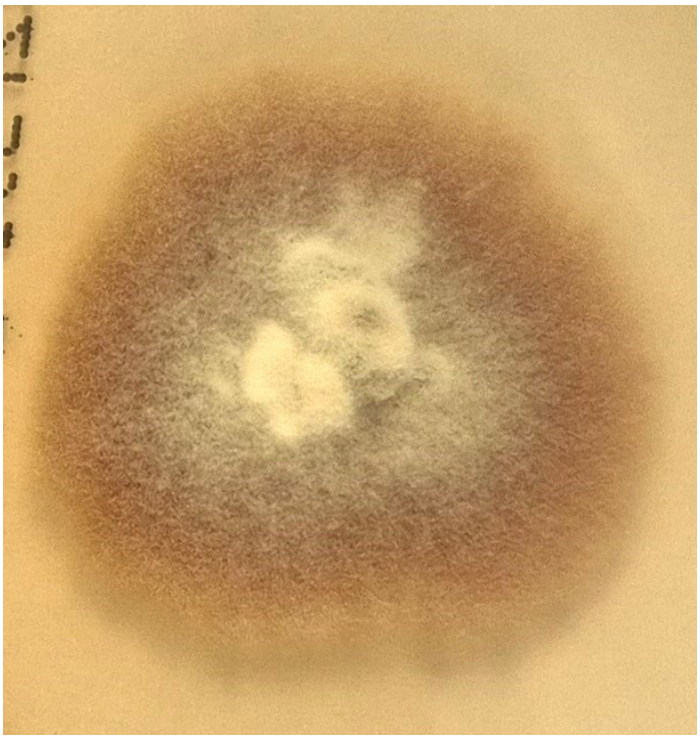
From 2016 to March 2025, *M. ferrugineum* was isolated from a total of 46 patients. The patients came from Germany. Tinea mainly affected children and adolescents. Forty (87%) were male and 3 (7%) were female. Possible sources of infection include sports such as wrestling, judo and boxing. This was consistent with the fact that 19 (41%) of the 46 patients were wrestlers or had contact with wrestlers. Some of those affected had a migrant background. What is new is that three wrestlers aged between 8 and 13 with tinea capitis developed double infections with *M. ferrugineum* and *Trichophyton tonsurans*, as detected by Microarray (Euroimmun®) and RT-PCR DermaGenius® 3.0 (PathoNostics) plus sequencing.

Conclusion

Currently, dermatophytoses, mostly tinea capitis, caused by *M. ferrugineum* are once again to be expected, especially in ring sports athletes. Double infections with *M. ferrugineum* and *Trichophyton tonsurans* are possible. The identification of *M. ferrugineum* is a major challenge because *M. ferrugineum* isolates can grow differently morphologically. The differentiation of *M. ferrugineum* should always be confirmed by molecular identification.

Figure 1

Figure 2



Session 6 - Host cell interaction and immune response

S6-01

Dysregulated inflammatory responses of (recurrent) vulvovaginal candidiasis

M. Gresnigt[1],
[1] Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Jena, Germany

Vulvovaginal candidiasis (VVC) is a common infection of the vaginal mucosa that affects the quality of life of millions of women. This is particularly true for those experiencing recurrent vulvovaginal candidiasis (RVVC). The pathogenesis of (R)VVC is underpinned by a complex interplay between fungal pathogenicity mechanisms and host responses. A characteristic feature of the disease is that, in cases where it is caused by C. albicans, neutrophils wreak havoc on the vulvovaginal mucosa rather than clearing the infection efficiently.

Although (R)VVC is often categorised as one disease, it is important to note that infections caused by non-albicans Candida species do not exhibit an inflammatory pathogenesis. Furthermore, the intrinsic differences in the host responses of women who develop recurrent infections compared to those who do not are not fully characterised.
Guided by patient sampling, our aim is to uncover the pathways that drive VVC pathogenesis and that could serve as future diagnostic or therapeutic targets.

S6-02

Role of Chitin sensing in the immune regulation of human Keratinocytes responding to fungal infections

C. Imelmann[1], T. Obser[1], J. B. Staudenmeyer[1], S. Vidal-y-Sy[1], C. Gorzelanny[1]

[1]*Universitätsklinikum Hamburg-Eppendorf, Dermatologie, Hamburg, Germany*

The polysaccharid chitin is an integral component of the fungal cell wall. Chitin has been identified as a pathogen-associated molecular pattern (PAMP) and is associated with an inflammatory response by the innate immune system. The human skin is frequently colonized by different fungi such as *Candida albicans* or *Trichophyton rubrum.* Previous studies suggest that human keratinocytes express the putative chitin receptors TLR2 and LYSMD3. However, whether fungal chitin can be recognized by keratinocytes to contribute to the immune response is unknown.

In this study, three-dimensional reconstructed human epidermis (RHE) was infected with *C. albicans*, and the immune response of keratinocytes was investigated. Expression levels of TLR2, LYSMD3 and the pro-inflammatory cytokines interleukin-8 (IL-8) and IL-6 were measured by quantitative real-time PCR (qPCR) and ELISA. Genetically modified knockout cells provided insights into the specific function of TLR2 and LYSMD3 in chitin recognition and immune regulation.

We demonstrated that *C. albicans* invasion into the epidermis is time-dependent, with structural damage to the tissue 48 h post infection. The increased expression of IL-8 and IL-6 6 h post-infection indicated an inflammatory activation prior to tissue destruction. At the same time, the TLR2 expression was elevated. While the expression of IL-6 and IL-8 continued to increase as the infection progresses, TLR2 was downregulated. In contrast, the expression of LYSMD3 was not influenced by the invasion of *C. albicans*. Knockout of LYSMD3 but not of TLR2 reduced the inflammatory response towards *C. albicans* and chitin-containing cell wall extracts.

Our data suggest a complex interplay between chitin recognition and immune regulation in response to fungal skin infections. Further investigations are necessary to better understand the acting molecular mechanisms and the pathophysiological relevance of chitin in the context of fungal skin infections.

S6-03

Role of mitochondrial dynamics in fungal pathogen-driven host defense

I. Heineking[1,2], A. A. Brakhage[1], F. Schmidt[1], L. Jia[2]
[1]*Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Molekulare und Angewandte Mikrobiologie, Jena, Germany*
[2]*Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Phagosome Biology and Engineering, Jena, Germany*

Introduction

After phagocytosis, phagosomes undergo maturation which is characterised by the assembly of vATPase and Nox2 complexes on the phagosomal membrane, resulting in the accumulation of H+ and reactive oxygen species (ROS) within the phagosomal lumen, aiding pathogen killing. These processes rely on ATP and NADPH, which could be supplied by mitochondria. While the direct interaction of phagosomes/lysosomes with mitochondria following bacterial infections has received much attention, less is known for fungal infections.

Objective

To orchestrate host defence, mitochondria are able to regulate immune signalling, metabolic adaptation, apoptosis, ROS production, mitochondrial dynamics, and autophagy. Our aim is

to elucidate the role of mitochondrial recruitment to phagosomes containing fungal pathogens.

Materials/Methods

We infected several cell lines as well as primary cells with conidia of *Aspergillus fumigatus* (wild-type and *pksP*) or *Lichtheimia corymbifera*. The recruitment of mitochondria to phagosomes was accessed by using transmission electron microscopy (TEM), immunofluorescence, Western blotting and proteomics methods.

Results

TEM images revealed close proximity of mitochondria to phagosomes containing *Aspergillus fumigatus* or *Lichtheimia corymbifera* conidia. This mitochondrial association was also observed by immunofluorescence at various time points post-infection. Furthermore, proteomic analysis of isolated phagolysosomes containing *A. fumigatus* conidia identified mitochondrial proteins, supporting the involvement of mitochondria in phagosome-associated processes.

Conclusion

Mitochondria are recruited to phagosomes containing fungal pathogens. With upcoming experiments, we aim to further characterise the role of mitochondria-phagosome interaction in defense against fungal infections.

S6-04

***Candida albicans*-epithelial interactions at the CNS barriers**

S. Schmidt[1], C. Schwerk[2], H. Schroten[2], H. Ishikawa[3], B. Häupl[4], T. Lehrnbecher[1], H. Rudolph[1]
[1]University Hospital Frankfurt, Goethe University, Department of Pediatrics, Division of Hematology, Oncology and Hemostaseology, Frankfurt a. M., Germany
[2]University Children's Hospital Mannheim, Pediatric Infectious Diseases, Mannheim, Germany
[3]University of Tsukuba, Laboratory of Regenerative Medicine, Department of Neurosurgery, Tsukuba, Japan
[4]University Hospital Frankfurt, Goethe University, Department of Medicine II, Hematology/Oncology, Frankfurt a. M., Germany

Background

Despite the availability of potent antifungal compounds, invasive fungal disease poses significant morbidity and mortality in immunocompromised patients. *Candida albicans* is one of the leading pathogens in this setting and may affect the central nervous system (CNS), which is an extremely severe form of the infection. As the exact pathogenesis of *Candida* CNS infection is not clear, we investigated the mechanisms and effects of *C. albicans* infection of the Blood-Cerebrospinal Fluid Barrier, which might be helpful for early diagnosis, prevention and treatment.

Methods

We used a human *in vitro* HIBCPP-cell based model of the Blood-Cerebrospinal Fluid Barrier (BCSFB) and investigated the mechanism of *C. albicans* translocation into the CNS with a special focus on the epithelial response of HIBCPP-cells to *C. albicans* translocation applying

MACE-sequencing and proteomics. Barrier integrity was monitored via measurement of transepithelial resistance and paracellular permeability.

Results

Although *C. albicans* impairs barrier integrity and exhibit cell damage at higher concentrations, it can cross BCSFB in a stealthy manner without affecting barrier integrity at low concentrations. Gene expression profiles determined by MACE-Sequencing revealed distinct regulation of specific genes depending on the dose of infection with *C. albicans*. Interestingly, two major integrin ligands involved in immune cell migration, namely CXCR4 and ICAM1, are upregulated following *C. albicans* infection. The roles of these molecules in NK cell migration across the infected BCSFB are the focus of ongoing investigations.

Conclusion

Although *C. albicans* is capable of transcellular translocation into the CNS in the absence of local inflammation, distinct gene regulation is induced in a dose dependent manner. These findings may lead to the identification of targets for the prevention of CNS invasion of *C. albicans* as well as of potential biomarkers for early diagnosis of CNS infection.

S6-05

Role of neutrophil-derived extracellular vesicles in supporting *Candida albicans* escape from immune phagocytosis

J. Patitz[1], N. Nieuwenhuizen[1], T. Krüger[2], A. Solomatina[2], Y. Bachelot[2], A. K. Zimmermann[2], M. Blango[2], O. Kniemeyer[2], A. A. Brakhage[2], M. T. Figge[2], O. Kurzai[1], K. Hünniger-Ast[1]
[1]Universitätsklinikum Würzburg, Institut für Hygiene und medizinische Mikrobiologie, Würzburg, Germany
[2]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Jena, Germany

C. albicans is a common commensal fungus but can cause life-threatening invasive infections in immunocompromised individuals and is a leading cause of hospital-acquired sepsis. Neutrophils, the most abundant circulating leukocytes, provide a rapid innate immune response against *C. albicans*. In an *ex vivo* whole-blood model, a subset of fungal cells escaped phagocytosis and killing. Imaging and flow cytometry revealed that extracellular *C. albicans* cells displayed the neutrophil marker CD66b on their surface, suggesting interaction with neutrophil-derived components. This study investigates whether neutrophil-derived extracellular vesicles (EVs) contribute to *C. albicans* immune evasion.

Using an *in vitro* infection model with isolated human neutrophils, we observed that neutrophil markers (e.g. CD66b) and Annexin V appeared on the surface of extracellular *C. albicans* after 60 min, suggesting that neutrophil-derived EVs may bind to fungal cells and mediate the deposition of neutrophil proteins. To test this directly, opsonized *C. albicans* cells were incubated with isolated EVs from *C. albicans*-challenged neutrophils, resulting in a significant increase in surface expression of neutrophil markers relative to fungal cells incubated in medium without EVs. Notably, EV association with *C. albicans* required initial opsonization with C3b/iC3b, as non-opsonized fungal cells showed significantly reduced binding. This interaction did not affect fungal viability, since hyphal growth was comparable between EV-treated and untreated control cells. Importantly, pre-incubation of *C. albicans* with EVs prior to confrontation with neutrophils or whole blood resulted in a higher proportion of extracellular fungal cells than infection with untreated *C. albicans*, indicating reduced phagocytic uptake.

Taken together, these results reveal a previously unknown role for neutrophil-derived EVs in promoting immune evasion of *C. albicans* cells by altering their susceptibility to phagocytosis.

S6-06

Immunology of *Malassezia* in Pancreatic Cancer: role of complement and fungal surface modifications by pancreatic enzymes

D. Aly[1], G. Rambach[1], N. Parth[2], M. Neurauter[3], M. Maglione[4], C. Speth[1]
[1]*Medizinische Universität Innsbruck, Institute of Hygiene and Microbiology, Innsbruck, Austria*
[2]*Medizinische Universität Innsbruck, University Hospital for Internal Medicine V, Innsbruck, Austria*
[3]*Medizinische Universität Innsbruck, Institute of Hygiene and Microbiology, Innsbruck, Austria*
[4]*Medizinische Universität Innsbruck, Department of Visceral, Transplant, and Thoracic Surgery, Innsbruck, Austria*

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is among the deadliest cancers; recently, a central role of the yeast *Malassezia globosa* has been identified for PDAC development.

Aims

(i) to study how *Malassezia*-triggered pro-carcinogenic inflammation involves activation of complement and neutrophils; (ii) to investigate the effect of pancreatic enzymes on *Malassezia* surface lipid content, viability, complement opsonization, neutrophil interaction.

Materials and Methods

M. globosa was incubated with pathway-specific sera followed by quantification of complement deposition by FACS. Neutrophil–*Malassezia* interaction was assessed by FACS. Pancreatic environment was simulated by fungal incubation with murine pancreatic homogenate (PH), pancreatin or purified lipase.

Results

Malassezia triggered complement deposition on its surface, but to a lower extent than other fungi. Whereas lectin pathway was described in literature to be most relevant, experiments with EDTA/EGTA and depleted sera implied that mainly classical and alternative pathway trigger *Malassezia* opsonization. Viability of the fungus was not reduced by incubation with normal human serum as complement source, presumably due to the thickness of the cell wall.

Simulation of pancreatic conditions were performed by incubating the fungus with PH, pancreatin or lipase; a significant decrease in lipid content was observed that might also affect its interaction with complement or neutrophils. Also anaerobic conditions that are typical for PDAC lowered the fungal lipid content.

Conclusions

Our complement studies imply that *M. globosa* delays or even escapes complement recognition, a prerequisite for its chronic pancreatic colonization. Complement pathway

studies revealed that anti-MASP antibodies targeting only the lectin pathway might be less effective in PDAC therapy than e.g. complement inhibitors like compstatin. Moreover, the fungal surface is greatly altered under simulated PDAC conditions.

Session 7 - Innovative antifungal therapies and drug development

S7-01

Transforming mycology: How AI enhances fungal disease management

D.R. Giacobbe[1]
[1] University of Genoa, Department of Health Sciences, Genoa, Italy

Artificial intelligence is increasingly being explored as a promising tool to support the diagnosis and management of invasive fungal diseases. Applications of machine learning and natural language processing, particularly via large language models, range from early risk prediction and diagnostic assistance to support in initiating and adjusting antifungal therapy. These technologies bring opportunities for more timely and individualized care, but also raise challenges that impact clinical reasoning and antifungal stewardship.

S7-04

Toward Shorter Therapy for Candidemia in Adults: Defining Uncomplicated Candidemia

I. Reinhold[1], S. Picardi[2], B. Liss[3], D. Seidel[1], J. Stemler[1], P. Köhler[1], T. Rügamer[1], R. Sprute[1], O. A. Cornely[1]
[1]University Hospital Cologne, Köln, Germany
[2]Heidelberg University Hospital, Anaesthesiology, Heidelberg, Germany
[3]Helios University Hospital Wuppertal, Hematology, Oncology, Infectious Disease and Palliative Care, Wuppertal, Germany

Objectives

The success of candidemia treatment depends on patient baseline characteristics, as well as clinical and microbiological findings. While few patient populations with candidaemia are considered at risk for complications, such as neutropenic patients, further stratification criteria distinguishing uncomplicated from complicated disease remain undefined. This literature review aimed to propose criteria for defining uncomplicated candidemia.

Methods

A systematic review was performed including literature from 1999 to 2025 to analyse outcome data of different studies and identify criteria associated with favourable or unfavourable outcome. Host factors, source control, time to antifungal treatment initiation, mycological and clinical treatment response, and microbiological findings were assessed.

Results

Uncomplicated candidemia was defined as *Candida* blood stream infection with clearance of blood cultures within five days of adequate antifungal treatment. This includes candidemia with controlled source and requires both mycological and clinical response to treatment within 120 hours. Patients with relevant immunosuppression, i.e. neutropenia, ongoing prolonged use of glucocorticosteroids, haematological malignancy without remission,

allogeneic haematopoietic stem cell transplantation or acute graft versus host disease grade III or IV, active intravenous drug use, extra-abdominal organ involvement or candidemia with echinocandin-resistant *Candida* species or recurrent candidemia were considered complicated candidemia (Fig.1). Certain criteria were further distinguished as time-dependent criteria (Fig. 2), while other criteria assesed did not enter definition (Fig. 1).

Conclusions

To validate and potentially adapt the proposed definition for uncomplicated candidemia for clinical trial use, it must first be applied to large cohorts. Based on this definition, shorter, individualized treatment durations could be considered for selected patient populations.

Figure 1

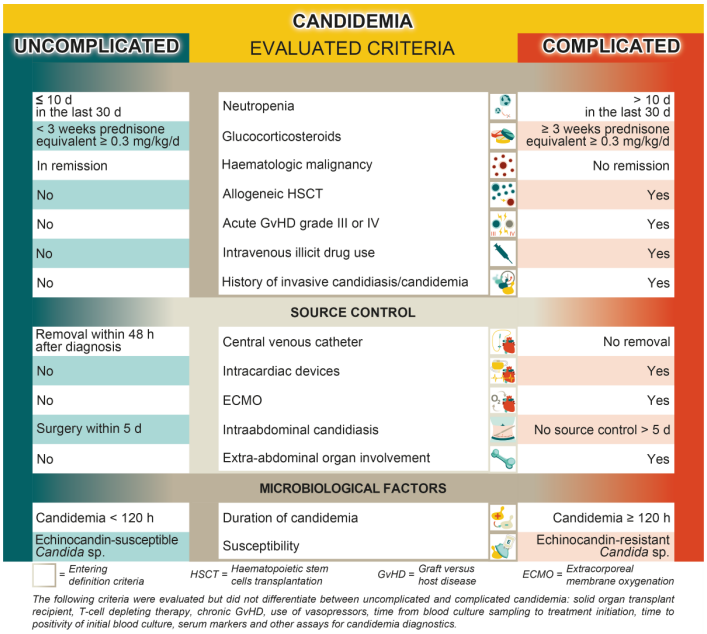
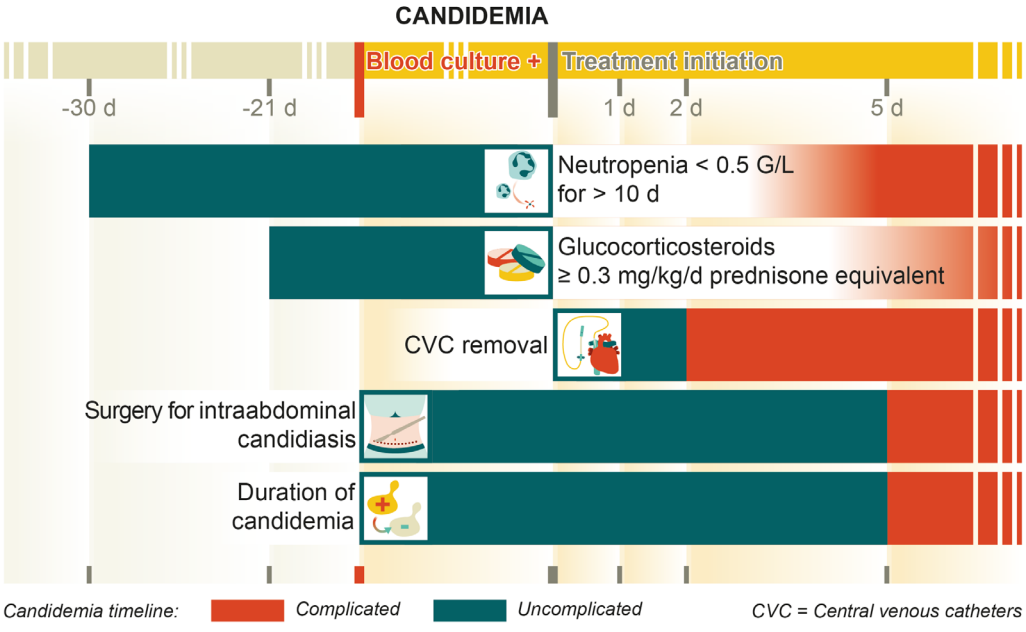


Figure 2



S7-05

Macromolecular prodrugs to treat intracellular persisting fungal pathogens

T. Orasch[1], J. Alex[1,2], K. Gonzalez[1,2], G. Gangapurwala[2], A. Vollrath[2], M. Händel[1], N. Roesner[2], Z. Cseresnyés[1], M. Rosin[1], C. Weber[2], S. Hoeppener[2], T. Heinekamp[1], C. Guerrero-Sánchez[2], M. T. Figge[1,2], U. S. Schubert[2], A. A. Brakhage[1,2]
[1]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Jena, Germany
[2]Friedrich-Schiller-Universität, Jena, Germany

Introduction

Conidia of *Aspergillus fumigatus* can avoid their elimination inside phagolysosomes (PLs) of alveolar macrophages and cause invasive aspergillosis in immunocompromised patients. The treatment of intracellular persisting pathogens is challenging, because the utilized drugs have to cross two membranes, the cytoplasmic and the PL membrane. Drug delivery systems bear the potential to reach intracellular persisting microorganisms and, by applying macromolecular prodrugs (MPDs), can lead to high local concentrations of the drug specifically in the PL.

Objectives

The study was aiming to elucidate whether nanoparticles (NPs) can target intracellular persistent pathogens.

Methods

Dye-labeled NPs with a size large enough for phagocytosis by macrophages were formulated. Internalization of NPs into RAW 264.7 macrophages was analyzed by imaging flow cytometry and intracellular localization was confirmed by fluorescence microscopy and TEM. MPDs were consisting of an antifungal, a linker specifically cleaved in PLs and a polymer. Drug release from MPDs was quantified by LC-MS analysis

Results

Macrophages internalized NPs efficiently and addition of NPs to prior infected macrophages confirmed co-localization of NPs and conidia in the same PL due to fusion of separate PLs. The number of phagolysosomes containing both conidia and PPs increased at elevated NP concentrations or after addition of the fusion enhancer Vacuolin-1. Dye-labeled MPD also showed co-localization with conidia in PLs and drug release was specifically executed by an enzyme present in the PL.

Conclusion

Fusion of conidia- and NP-containing PLs was proposed as putative mechanism for NPs reaching intracellular conidia and fusion rate could be increased by certain methods. Furthermore, smart prodrugs were employed to release the drug only in the PL. These results represent the requisite for the development of advanced delivery systems reaching intracellular persistent pathogens.

Session 8 - Emerging fungal threats and fungal outbreaks

S8-01

The invisible threat: Strategies for monitoring environmental fungal load in healthcare settings

J.-P. Gangneux[1]
[1]Rennes University, Rennes Teaching Hospital, Rennes, France

Fungal infections are a public health issue in hospitals. Aspergillosis is the most significant opportunistic disease in immunocompromised patients: this fungal infection is caused primarily by Aspergillus fumigatus. Less frequent but similarly severe infections can be caused by other fungi, including Rhizopus, Mucor, Absidia, Fusarium and rare fungi. Exposure to these environmental fungi occurs through inhalation of air or aerosolized droplets of water, or more rarely by ingestion. Despite improvements in diagnosis and treatment, invasive fungal infections are often fatal with a mortality rate remaining around 50% for invasive aspergillosis.

Hospital acquisition prevention of fungal infections in high-risk patients can rely both on chemoprophylaxis and on preventive measures. Preventive measures are, therefore, taken in operating rooms and in high-risk units. In particular, high efficiency particulate air (HEPA) filtration systems and rooms with laminar airflow are useful in hematology wards to minimize ambient fungal spore concentrations. Therefore, an environmental surveillance program is often implemented in hospitals in order to assess the efficacy of these preventive measures. However, there is no consensus on when, where and how monitoring of hospital indoor air quality should be undertaken. In this work, we performed a survey in order to have a picture of the practices in different settings in Europe with the ambition to reach consensus and standardize this practice.

S8-02

Optimizing surveillance and management of pulmonary aspergillosis in solid organ transplant recipients

L. N. Walti[1]
[1]Inselspital Bern, Infectious Diseases, Bern, Switzerland

Pulmonary Aspergillosis is the most frequent mold infection after solid organ transplantation. Epidemiology varies according to organ transplant. This talk will review current prevention and management strategies as well as knowledge gaps in pulmonary aspergillosis in SOT recipients. With an emphasis on lung transplant recipients, the SOT recipients most affected by pulmonary aspergillosis.

S8-03

Public health mycology – where next

D. Denning[1]
[1] FRCP FRCPath FIDSA FMedSci, Professor of Infectious Diseases in Global Health, Manchester Fungal Infection Group, The University of Manchester, Manchester, United Kingdom

Fungal diseases affect billions annually. Skin diseases attract huge attention from the public, but less from public health authorities. Tinea capitis probably affects about 200 million children globally. With nearly 300 million cases of onychomycosis globally, about 10 million cases of onychomycosis are attributable to Aspergillus spp. Mucosal candidiasis is common. Between 50-75% of women develop vulvovaginal candidiasis at least once in their lives. Recurrent VVC (rVVC), defined as four or more episodes of confirmed VVC within 12 months, probably affects ~138 million annually and 372 million through their lifetime. The incidence of serious fungal diseases found about 6.5 million annually across the world, with ~3.8 million deaths of which ~2.6 million are directly attributable to that disease. The largest number of cases were invasive aspergillosis, followed by chronic pulmonary aspergillosis and invasive candidiasis. Allergic bronchopulmonary aspergillosis (ABPA) in asthma and severe asthma with fungal sensitization (SAFS) complicate asthma, itself affecting ~300 million annually. Mycetoma, chromoblastomycosis and sporotrichosis are considered Neglected Tropical Diseases by the WHO and probably affect 100,000s annually.

Recent global health advocacy efforts have raised the profile of fungal diseases. Engagement with the WHO, CDC, Africa CDC, PAHO and other key agencies have placed fungal disease on the R&D agenda, but not yet on most donor's agendas for LMICs. Diagnostics for aspergillosis and histoplasmosis are infrequently done in Africa and many parts of SE Asia. Fungal stains on tissue are often not done or done days later. Antifungal susceptibility testing is not done in many parts of the world to aid clinical decision-making. Data on DALYs and YLL are missing for many diseases and countries. So the questions that facing public health to improve care and clinical outcomes include:

- How can the best economic case be made for fungal diagnostics and treatment?
- Clinical awareness is key, but is it enough and if it is, how can changes in routine clinical practice be implemented in a cost-effective manner?
- Disease surveillance requires accurate diagnosis – for which fungal diseases is this most easily implemented and how?
- Is a global system of environmental surveillance for antifungal resistance in Aspergillus required?
- Who will coordinate and display these information in near real time?

S8-04

Differential susceptibility of five *Candida auris* clades against surface disinfection

A. Lang[1], H. Gabriel[2], T. L. Meister[3], J. Meis[4], E. Steinmann[5], F. H. H. Brill[2], J. Steinmann[1]
[1]Paracelsus Medical University, Klinikum Nürnberg, Institute of Clinical Microbiology, Infectious Diseases and Infection Control, Nürnberg, Germany
[2]Dr. Brill + Partner GmbH, Institute of Hygiene and Microbiology, Hamburg, Germany
[3]Universitätsklinikum Hamburg-Eppendorf, Institut für Infektionsforschung und Impfstoffentwicklung, Hamburg, Germany
[4]Radboudumc-CWZ Center of Expertise for Mycology, Nijmegen, Netherlands
[5]Ruhr-Universität Bochum, Abteilung für Molekulare & Medizinische Virologie, Bochum, Germany

Candida auris is an globally emerging multidrug-resistant fungal pathogen that causes nosocomial outbreaks in healthcare facilities. In this study, we conducted standardized tests (EN 13624 and EN 16615) in order to evaluate the susceptibility of five different *C. auris* clade strains to commonly used disinfecting agents and commercially available ready-to-use disinfecting wipes. *Candida albicans* ATCC 10231 strain, often used as a surrogate for determining yeasticidal activity of disinfecting agents, was included as a control.

Suspension tests under EN 13624 guidelines revealed that ethanol-based disinfectants at 40% concentration effectively achieved a 4log10-fold reduction for all *Candida* strains.

Quaternary ammonium compound (QAC)-based disinfectants showed considerable inter-species and inter-clade variation. When tested under the EN 16615 four-field method, ethanol-based commercial disinfectant wipes achieved a 4log10-fold reduction for *C. auris* clades I, II, III and V, whereas *C. albicans* ATCC strain and *C. auris* clade IV strain did not reach the required reduction factor. The QAC-based product showed uniform efficacy across all strains. Propanol + QAC-based disinfectant achieved effective inactivation of *C. auris* strains, but not the *C. albicans* ATCC strain. Hydrogen peroxide-based wipes failed to reach the necessary reduction factor across all tested strains under dirty conditions.

These results emphasize the variability in the disinfecting efficacy of commercially available products between *C. auris* clades. Based on the obtained data, *C. albicans* may not serve as a universally reliable indicator for evaluating yeasticidal efficacy against the diverse clades of *C. auris*. The finding that hydrogen peroxide-based disinfectant wipes showed reduced yeasticidal effect against *C. auris* warrants further investigations to obtain more data on inter-clade susceptibility differences.

S8-05

Candida auris in Austria: Repeated introductions from abroad based on epidemiological and phylogenetic data

K. Spettel[1,2], F. Lötsch[1], R. Kriz[2], M. Loy[1], B. Willinger[1]
[1]*Medizinische Universität Wien, Klinisches Institut für Labormedizin, Abteilung für klinische Mikrobiologie, Wien, Austria*
[2]*FH Campus Wien, Biomedizinische Analytik, Wien, Austria*

Introduction

Candida auris has emerged as a major public health concern worldwide due to its ability to cause hospital-associated outbreaks. Its frequent resistance to multiple antifungal drugs and increased tolerance to disinfectants complicate both treatment and containment efforts. In Austria, *C. auris* was first identified in 2018, with multiple strains reported since. This study presents an updated analysis of the epidemiological situation in Austria.

Methods

Antifungal susceptibility testing was performed using broth microdilution in accordance with EUCAST guidelines, including the novel antifungal agent manogepix. Whole genome sequencing (WGS) was used to explore phylogenetic relationships. Epidemiological data, including travel history and clinical features, were analyzed to identify possible routes of transmission.

Results

A total of 14 *C. auris* cases have been reported in Austria, with most linked to travel abroad or hospital stays in other countries. The travel destinations included Greece (6 cases), Spain (1), Romania (1), India (1), and South Africa (1), with two additional cases associated with travel history in both Turkey and India. Apart from one persistent case of otitis, all cases were colonizations without evidence of invasive infection. WGS classified the isolates into Clade I (South Asian clade) and Clade III (South African clade). The observed genetic variability suggests multiple separate introductions into Austria rather than transmission in Austria.

Discussion

Genomic data indicate that the majority of *C. auris* cases in Austria are linked to introductions from abroad, particularly associated with international travel and prior hospitalization in foreign healthcare systems. These findings highlight the necessity of screening patients transferred from foreign healthcare facilities.

S8-06

Current trends on antifungal prophylaxis in solid organ transplantation

J. Salmanton-García[1,2,3,4,5,6], A. Giacinta[7], M. Giannella[8], A. Vena[9], P. Muñoz[10], O. A. Cornely[1,2,3,4,5,6,11], M. Valerio[12]
[1]University of Cologne, Faculty of Medicine and University Hospital Cologne, Köln, Germany
[2]University of Cologne, Institute of Translational Research, Köln, Germany
[3]University of Cologne, Cologne Excellence Cluster On Cellular Stress Responses in Aging-Associated Diseases (CECAD), Köln, Germany
[4]University of Cologne, Department I of Internal Medicine, Köln, Germany
[5]University of Cologne, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD) and Excellence Center for Medical Mycology (ECMM), University of Cologne, Köln, Germany
[6]German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Köln, Germany
[7]Hospital General Universitario Gregorio Marañón, Department of Clinical Microbiology and Infectious Diseases, Madrid, Spain
[8]IRCCS-Sant'Orsola Polyclinic, Department of Clinical Microbiology and Infectious Diseases, Bologna, Italy
[9]University of Genoa, Department of Health Sciences (DISSAL), Genoa, Italy
[10]Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain
[11]University of Cologne, Clinical Trials Centre Cologne (ZKS Köln), Köln, Germany
[12]Complutense University of Madrid, Madrid, Spain

Introduction

Invasive fungal infections (IFI) pose significant risks to solid organ transplant recipients, especially within 180 days post-transplant. European and US guidelines remain limited, with prophylaxis shifting from universal strategies due to risks like rare fungal infections, adverse effects, drug interactions, and costs. This study examines current antifungal (AF) prophylaxis practices in transplant institutions to inform guideline development.

Methods

From May 2023 to May 2024, tertiary care institutions completed an online questionnaire on AF prophylaxis after solid organ transplantation. Data included transplant volumes, IFI incidence by pathogen, and prophylactic strategies, including triggers, preferred AF agents, and duration.

Results

We analyzed 64 responses from 32 countries, primarily in Europe. Kidney transplants were most common, followed by liver transplants, often in multi-organ procedures. Air quality measures, including HEPA filtration and air sampling, varied, with lung and heart transplant units adopting them more frequently. AF prophylaxis was consistently used in lung transplants and frequently in liver, bowel, and heart transplants, triggered by factors like reintervention, retransplantation, or Candida spp. colonization. Preferred AF agents varied by organ type, commonly including liposomal amphotericin B, caspofungin, and fluconazole.

Breakthrough IFI incidence varied significantly by organ type and pathogen, with most institutions reporting dedicated infectious disease teams.

Conclusion

This survey provides a comprehensive overview of AF prophylaxis practices in solid organ transplantation. Standardized, evidence-based guidelines are essential to address variability and optimize IFI management post-transplant.

Session 9 - Fungal pathogenesis, biofilms and mycotoxins

S9-01

Investigation of Aspergillus fumigatus small RNA biogenesis uncovers evidence of double-stranded RNA-dependent growth arrest

X. Pan[1], A. Kelani[1], M. Blango[1]
[1]*Hans-Knöll-Institut, Jena, Germany*

Aspergillus fumigatus, a dangerous human fungal pathogen, produces a limited repertoire of small RNAs, consisting in large part of tRNA-derived RNAs (tDRs). Using advanced small RNA-seq and tDR-seq, we improved our understanding of small RNAs in conidia and mycelium of *A. fumigatus* and revealed morphotype-specific tDR enrichment (e.g., Asp(GTC)5"tRH in conidia vs. His(GTG)-5"tRH in hyphae). Inducing canonical RNA interference (RNAi) via inverted-repeat transgene overexpression yielded predominantly 20-nt, 5"-uridine-rich small RNAs dependent on argonaute and dicer-like proteins. Surprisingly, dsRNA overexpression also impaired growth in both wild-type and RNAi-deficient strains, with a strain lacking the two *A. fumigatus* RNA-dependent RNA polymerase orthologs particularly sensitive. We propose that dsRNA accumulation, as during a mycoviral infection, inhibits growth in *A. fumigatus* similar to a cell-cycle checkpoint. Ultimately, our work has provided an improved description of small RNA biogenesis in *A. fumigatus* and uncovered a novel link between dsRNA metabolism and fungal growth in this filamentous fungus.

S9-02

Presence of endosymbiont bacteria in clinical strains of *Rhizopus microsporus*

A. Uribe Munoz[1], G. Walther[2], R. Martin[1], O. Kurzai[1,2]
[1]*Julius-Maximilians-Universität Würzburg, Institute of Hygiene and Microbiology, Würzburg, Germany*
[2]*Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), National Reference Center for Invasive Fungal Infections, Jena, Germany*

Introduction

Mucormycosis is a deadly invasive fungal disease caused mostly by *Rhizopus* spp. Since the discovery of endosymbiont bacteria in *R. microsporus* by Partida-Martinez in 2008 there has not been consensus over their prevalence in clinical specimens.

Objectives

To determine the prevalence of endosymbiont bacteria in an extensive collection of clinical strains of *R. microsporus* and to investigate if clinical procedures affect the presence of endosymbionts in the fungus.

Materials and methods

We screened 96 clinical strains of *R. microsporus* (94/96 from Germany), retrieved from the National Reference Center for Invasive Fungal Infections, the Jena Microbial Resource Collection and the Institute of Hygiene and Microbiology in Wuerzburg for the presence of endosymbiont bacteria using a 16s rRNA PCR. Positive results were sequenced and identified to the species level.

The positive strains together with two environmental strains (CBS 699.68 and CBS 700.68) which are known to harbor bacterial endosymbionts were subjected to a series of subcultures in different culture media for fungi including Malt Extract, Yeast Peptone Dextrose, Potato Dextrose and Sabouraud with and without streptomycin and penicillin supplement and then submitted to an endosymbiont extraction process.

Results

From 96 screened isolates, only three were positive in the PCR screening. The detected bacteria were identified as *Mycetohabitans rhizoxinica and M. endofungorum.*

We managed to extract living endosymbionts from all tested strains after 3 to 4 subcultures in the aforementioned media. Most of the endosymbionts could not be preserved outside the host for more than 1 subculture.

Conclusion

Our results indicate that the presence of bacterial endosymbionts in clinical isolates of *R. microsporus* in Germany is low, and the process of fungal isolation and culturing in clinical settings itself did not affect the bacterial endosymbionts.

S9-03

***Candida albicans* strain diversity: Impact on colonisation and host responses**

S. Chakraborti[1], K. A. Merga[1], I. D. Jacobsen[1]
[1]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Jena, Germany

Systemic candidiasis in humans usually originates from strains that have long-term colonized mucosal surfaces – especially the gut – prior to the onset of infection. Likewise, mucosal candidiasis is caused by strains that colonize the oral or vaginal cavity, often for years without causing problems. While research has long focused on the pathogenesis of candidiasis, recent studies began to explore the consequences of colonization beyond infection risk.

It is becoming increasingly evident that *Candida albicans* colonization profoundly influences the host"s immune system, including responses to subsequent candidiasis. It is also well established that *C. albicans* strains can differ significantly in their ability to colonize mucosal surfaces, virulence, and outcome of interaction with immune cells. However, if strain variability also impacts colonization-induced protection from systemic candidiasis is largely unknown.

We used strain 101 as a prototype "commensal" isolate characterized by low cytotoxicity and the ability to establish prolonged mucosal colonization, and compared it to the highly invasive thoroughly studied strain SC5314. *C. albicans* 101 colonized the murine gut at a higher level in the presence of intact microbiota, but was outcompeted by SC5314 in this setting. Despite

higher intestinal fungal load, colonization with *C. albicans* 101 provided less protection against subsequent systemic challenge. We excluded a reduced Th17 response to 101 colonization as the underlying mechanism, but found differences in IgG induction and higher induction of tolerogenic cytokines as possible causes of reduced protection.

Thus, strain-to-strain variation affects colonization-induced immune responses, with consequences for the susceptibility to systemic candidiasis.

S9-04

Virulence of *Aspergillus* section *Flavi* using the *Galleria mellonella* model

S. Zhou[1,2], S. O. Abd Algaffar[3], M. A. I. Ismail[4], H. van der Lee[1], Y. Kang[2], S. de Hoog[1,5], S. A. Ahmed[1,5,6]
[1]*Radboud University Medical Center, Center for Expertise in Mycology, Nijmegen, Netherlands*
[2]*Guizhou Medical University, Key Laboratory of Environmental Pollution Monitoring and Disease Control, Ministry of Education of Guizhou, Key Laboratory of Microbiology and Parasitology of Education Department of Guizhou, School of Basic Medical Science, Guiyang, China*
[3]*University of Science and Technology, Faculty of Pharmacy, Omdurman, Sudan*
[4]*University of Khartoum, Khartoum, Sudan*
[5]*Foundation Atlas of Clinical Fungi, Hilversum, Netherlands*
[6]*Kuwait University, Department of Microbiology, Faculty of Medicine, Kuwait, Kuwait*

Background

Aspergillus section *Flavi* encompasses multiple species, with *A. flavus* being significant for human health because of its dual role as a major producer of aflatoxins and as an opportunist. However, the mechanisms underlying its virulence remain incompletely understood.

Objectives

This study evaluates the pathogenic potential of *A. flavus* and its relatives using the *Galleria mellonella* infection model.

Methods

Twenty-six *A. flavus* isolates (clinical and environmental) and 17 relatives/ domesticated species were tested in *G. mellonella*, with larval survival monitored over seven days. Histology, direct microscopy, and culture were used to validate the infection. Growth kinetics, and spore sizes were measured to evaluate correlations with pathogenicity.

Results

All *A. flavus* isolates demonstrated high virulence, causing 90%, and 100% mortality of *G. mellonella* larvae within three and seven days, respectively, with no significant differences between sources. Aflatoxin-producers exhibited higher virulence, resulting in 100% mortality of *Galleria* larvae within five days (p<0.005). Related species exhibited lower virulence, larval mortalities ranging from 20 to 70% within three days, ranked as *A. flavus* >*A. pseudonomiae* >*A. parasiticus* >*A. nomiae* >*A. tamarii* >*A. pseudocaelatus*. Growth kinetics and spore size were correlated with virulence, as rapid growth and smaller spores were associated with increased pathogenicity.

Conclusions

Aspergillus flavus exhibits higher virulence than its relatives, with growth rate, and spore size influencing pathogenicity. The *G. mellonella* model proves effective for comparative virulence studies. These findings highlight the potential health risks of *A. flavus*, including its domesticated relatives used in food fermentations, necessitating further investigations into their pathogenic potential.

S9-05

Unraveling the pathogenicity of the *Candida parapsilosis* species complex through comparative pan-genomic analysis

Y. Tang[1,2], Y. Ning[3,4], G. Butler[5], L. Zhang[3,4], A. E. Barber[1], B. Zhai[2]
[1]*Friedrich-Schiller-Universität, Mikrobiologie, Jena, Germany*
[2]*Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Institute of Symbiotic Biology, Shenzhen, China*
[3]*Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Department of Laboratory Medicine, State Key Laboratory of Complex Severe and Rare Diseases, Beijing, China*
[4]*Beijing Key Laboratory for Mechanisms Research and Precision Diagnosis of Invasive Fungal Diseases, Beijing, China*
[5]*University College Dublin, School of Biomolecular and Biomedical Science, Conway Institute, Dublin, Ireland*

Introduction

Invasive fungal infections pose a life-threatening risk to millions of individuals annually. The *Candida parapsilosis* species complex (CPSC) comprises three species-*C. parapsilosis* (Cpara), *C. orthopsilosis* (Cortho), and *C. metapsilosis* (Cmeta)-that collectively represent a major cause of human fungal disease. Despite their close genetic relatedness, Cpara alone accounts for over 90% of infections within this complex.

Objectives

We aim to elucidate the genomic basis underlying CPSC's distinct patterns of clinical prevalence.

Materials & Methods

We analyzed 1,051 genomes of CPSC clinical isolates collected across three continents using comparative genomics approaches.

Results

Gene accumulation curves reached saturation with increasing numbers of genomes sampled, suggesting closed pangenomes in CPSC members. Cpara possesses the largest core genome, while Cmeta exhibits the largest accessory genome. This is consistent with previous studies showing that Cpara's genome is the least variable, as indicated by its high homozygosity. We next predicted transposable elements (TEs) and found that most predicted TEs were short and fragmented, with only a few exceeding 1,000 bp in length, indicating that TEs are unlikely to be major contributors to the genomic differences among the three species. Although previous studies have described Cpara as largely clonal, with evidence of recombination limited to lineages within Cortho and Cmeta, our population structure analysis showed admixture signals within Cpara as well. Reticulate branching was

observed in the neighbor-net trees of each species, further suggesting the occurrence of recombination in Cpara. However, this recombination did not lead to substantial genomic variation among individual Cpara isolates.

Conclusion: Our findings suggest that genomic streamlining may facilitate Cpara's successful adaptation to clinical settings, potentially explaining its higher prevalence compared to its two sister species.

S9-06

Detection of the yeast *Malassezia* in pancreatic cancer tissue correlates with grading and staging of the tumor

C. Speth[1], R. Bellotti[2], G. Thurner[3], G. Schäfer[3], G. Ranches[3], T. Nemeth[4], L. Balogh[4], G. Rambach[1], M. Maglione[2]
[1]Medizinische Universität Innsbruck, Institute of Hygiene and Microbiology, Innsbruck, Austria
[2]Medizinische Universität Innsbruck, Department of Visceral, Transplant, and Thoracic Surgery, Innsbruck, Austria
[3]Medizinische Universität Innsbruck, Institute of Pathology, Neuropathology and Molecular Pathology, Innsbruck, Austria
[4]Semmelweis University, Department of Rheumatology and Clinical Immunology/Department of Internal Medicine and Oncology, Budapest, Hungary

Introduction

Malassezia might contribute to pancreatic ductal adenocarcinoma (PDAC) by triggering a chronic inflammation. However, the precise mechanisms remain unclear and no analysis exists for *Malassezia* presence in different tumor grades and stages.

Aims

(1) To quantify the presence of *Malassezia* in different pancreatic tissue samples; (2) to study whether neutrophils in the tumor microenvironment contribute to *Malassezia*-triggered inflammation.

Materials and Methods

Presence of *Malassezia* in paraffin-embedded pancreatic tissue samples was analysed by TaqMan PCR. Neutrophils were tested for *Malassezia*-induced activation by radical oxygen species release.

Results

A cohort of 137 pancreatic tissue samples derived from patients with either benign lesions, chronic pancreatitis, premalignant cysts (IPMN/MCN/PanIN) or PDAC were analysed for *Malassezia* presence. *Malassezia* levels were highest in PDAC samples, followed by the premalignant lesions. Tissue with chronic pancreatitis or benign lesions contained significantly lower amounts of fungal DNA.

A classification of PDAC samples according to tumor grading revealed that the *Malassezia* amounts are higher in early than in late grading, where cancer cell abnormality is increased. Similarly, classification according to tumor staging showed a higher *Malassezia* signal when size and spreading of the tumor is still limited.

Despite the unique surface of *Malassezia*, neutrophils react on fungal presence with significant release of reactive oxygen species. Compared to e.g. *Candida*, neutrophil activation occurred with a delayed time kinetic and to a lower extent.

Conclusion

The elevated level of *Malassezia* in the PDAC tissue, particularly in early grading and staging categories, supports the hypothesis of *Malassezia* as tumor-promoting factor. *Malassezia* can contribute to tumor progression by triggering a neutrophil-mediated inflammation; the limited extent could favor *Malassezia* survival in the tumor microenvironment.

S9-07

Experimental platforms of medical device-related biofilms and anti-biofilm strategies

J. Steinmann[1]
[1] *Paracelsus Medical University, Institute of Clinical Microbiology, Nuremberg, Germany*

Biofilm formation by fungi increases virulence and resistance against antifungals. Together with the human immune response, biofilm formation is one important factor of invasive fungal infection development. In the presentation, two human-like biofilm models, precision cut lung slices (PCLS) and biofilm co-culture model, will be introduced to test the antibiofilm activity of antifungals against A. fumigatus. In both assays, metabolic active A. fumigatus biofilms were examined at different biofilm developmental stages using an XTT assay. A decrease in metabolic activity of the fungal biofilms was detected for each of the tested agents in both assays. Significant antibiofilm effects exist against early-stage biofilm in the co-culture model. In the PCLS assay, amphotericin B showed the strongest inhibition after 24 h. In conclusion, the applied PCLS ex vivo model could study the property and activity of certain antifungal compounds against Aspergillus biofilm. With its close resemblance to human conditions, the PCLS model has the potential of improving the current understanding of biofilm treatments in laboratory settings.

Session 10 - Host cell interaction and immune respons

S10-01

Immune response of mucormycosis and perspective for future vaccines.

A. Ribeiro dos Santos[1]
[1] *Federal University of São Paulo, São Paulo*

Immune response of mucormycosis and perspective for future vaccines.
Mucormycosis is a serious and devastating invasive fungal infection, and has emerged as a global public health threat during the COVID-19 pandemic. Infection occurs via diverse routes, such as inhalation, percutaneous, or ingestion of spores. Mucormycosis can have a wide variety of manifestations, with rhinocerebral and pulmonary diseases being the most common, with a mortality rate that varies from 46% to 70%, and is up to 90% upon dissemination. The acute incidence and rapid progression associated with the reduced susceptibility and intrinsic resistance of the Mucorales to antifungals underscore the challenges of current treatments, emphasizing the pressing need for innovative approaches, including immunotherapies and vaccines. The first step in the direction of immunotherapies approaches is to understand an effective immune response against the Mucorales. In this talk, I will present results of previous studies using immunocompetent experimental models of mucormycosis to characterize an effective immune response against *Rhizopus oryzae-induced* pulmonary or disseminated mucormycosis. The second part of this discussion will focus on the current literature regarding the challenges and potential solutions in vaccine

development for fungal diseases, with a specific emphasis on the progress made towards creating a vaccine for mucormycosis.

S10-02

Anakinra silences the immune chaos that drives influenza-associated pulmonary aspergillosis

L. Seldeslachts[1], S. Kraisin[2], I. Dewi[3], S. Feys[4], F. Staels[4], M. Gkountzinopoulou[5], C. Jacobs[4], B. Tielemans[6], E. Vanhoffelen[6], A. Reséndiz-Sharpe[6], L. De Herdt[6], O. Kwan[4], N. Vandamme[7], J. Roels[7], J. Neumann[4], T. Prezzemolo[4], B. Malengier-Devlies[8], M. Stroobants[4], A. Carvalho[9], P. Matthys[4], L. Naesens[4], K. Lagrou[4], M. Khan[10], P. Mombaerts[10], E. Verbeken[6], K. Martinod[2], J. Wauters[4], F. van de Veerdonk[3], G. Vande Velde[6], S. Humblet-Baron[4]
[1]KU Leuven, Department of Microbiology, Immunology and Transplantation & Department of Imaging & Pathology, Leuven, Belgium
[2]KU Leuven, Department of Cardiovascular Sciences, Leuven, Belgium
[3]Radboud University Medical Center, Department of Internal Medicine, Nijmegen, Netherlands
[4]KU Leuven, Department of Microbiology, Immunology and Transplantation, Leuven, Belgium
[5]Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology, Heraklion, Greece
[6]KU Leuven, Department of Imaging & Pathology, Leuven, Belgium
[7]VIB, VIB Single Cell Core, Leuven, Belgium
[8]University of Edinburgh, Centre for Reproductive Health and Centre for Inflammation Research, Edinburgh, United Kingdom
[9]University of Minho, Life and Health Sciences Research Institute (ICVS), Braga, Portugal
[10]Max Planck Research Unit for Neurogenetics, Frankfurt a. M., Germany

Influenza-associated pulmonary aspergillosis (IAPA) is a severe fungal infection in critically ill patients with influenza. Despite the use of antiviral and antifungal therapies, the survival rate for IAPA patients remains only 50%. To date, insights into how influenza alters the fungal host immune response remain scarce, thereby limiting the development of new treatments. Using a unique combination of a clinically relevant mouse model of IAPA and patient samples, we aimed to investigate how influenza predisposes to the development of invasive pulmonary aspergillosis (IPA).

Immunocompetent mice were challenged with an intranasal instillation of influenza or sham on day 0, followed by an orotracheal inoculation with *Aspergillus* or sham 4 days later. Anakinra was administered daily starting from day 0 or day 4. Lung lesions and fungal burden were longitudinally monitored via micro-CT and bioluminescence imaging. At days 4 and 7, we performed immunophenotyping, single-cell RNA-seq, spatial transcriptomics, RNAscope, and histopathology.

We identified IL-1 inflammation, neutrophil activation, and NET release as crucial features in the pathogenesis of IAPA. This inflammation led to an immunological imbalance, marked by defective neutrophil effector functions such as NADPH activation and ROS production, thereby creating a highly permissive environment for *Aspergillus*. Supporting these findings, IAPA patient samples showed deficient NADPH oxidase activity—essential for ROS production. Blocking the IL-1 receptor with anakinra from day 4 significantly reduced inflammation, restored neutrophil effector function, and rescued influenza-infected mice from IPA**.** Notably, anakinra administered from day 0 did not yield beneficial effects, underscoring the importance of timing**.**

Our findings underscore the crucial role of IL-1 inflammation in the immunological chaos that drives IAPA and suggest timely anakinra as a promising immunomodulatory therapy for IAPA.

S10-03

Characterization of programmed cell death in *Aspergillus fumigatus* conidia to enable the design of a 'live/dead' reporter strain

M. Händel[1,2], K. Gonzalez Rojas[1], M. Kawashima[1,2], T. Krüger[1], S. Schäuble[3], T. Heinekamp[1], A. A. Brakhage[1,2]
[1]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Molekulare und Angewandte Mikrobiologie, Jena, Germany
[2]Friedrich-Schiller-Universität, Mikrobiologie, Jena, Germany
[3]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Microbiome Dynamics, Jena, Germany

Aspergillus fumigatus is a filamentous fungus that can cause severe infections in immunocompromised individuals by invading the lungs via outgrowth of inhaled conidia. Alveolar macrophages belong to the first line of defence. They phagocytose and intracellularly process conidia to clear them from the airways. However, *A. fumigatus* can evade this immune response to some extent, that makes antifungal treatment essential. Current antifungal drugs often cause adverse side effects, highlighting the need for new therapeutic approaches. To distinguish between viable and dead conidia *in situ* remains challenging, as both show minimal morphological or metabolic differences in the first hours. A reporter strain expressing a fluorescently tagged cell death-associated protein could allow visualization of conidial death via fluorescence microscopy.

To identify candidate proteins, we investigated programmed cell death (PCD) in *A. fumigatus* conidia. An *in vitro* cell death assay was developed using different cell death inducers, concentrations of compounds, duration of treatment, and culture conditions. Among the tested treatments, H_2O_2 in nutrient-rich medium was most effective in killing resting conidia, outperforming amphotericin B and voriconazole. Based on these findings, optimal conditions for proteomic analysis were established. Comparative proteomics of resting, swollen, and dying conidia revealed eleven proteins with differential abundance during PCD. Reporter strains were generated expressing either the green fluorescent protein or mScarlet3 fused to the selected PCD-associated proteins.

The successful generation of fluorescent reporter strains paves the way for real-time monitoring of fungal cell death, particularly during host-pathogen interactions. Such a tool holds potential for advancing our understanding of fungal pathogenesis and improving the evaluation of antifungal treatments.

S10-05

Active Immunization against mucormycosis, first preclinical evidence

K. Dallmeier[1]
[1] *KU Leuven Department of Microbiology, Immunology & Transplantation, Laboratory of Molecular Vaccinology & Vaccine Discovery (MVVD), B-3000 Leuven, Belgium*

The increasing incidence of mycoses, including hard-to-treat or drug-resistant invasive fungal disease (IFD), poses a growing public health issue. Prophylactic immunization may offer a solution, however, in contrast to many viral and bacterial infections, efforts developing vaccines for the prevention of fungal infections have failed and until today there is not a

single prophylactic antifungal vaccine available. Besides scarce knowledge on protective antigens, vaccine development is further hampered by a fundamental lack in knowledge on adaptive immunity to fungi. While many fungal pathogens appear to be notoriously non-immunogenic, spores of certain Mucorales species express surface structure such as the spore coat protein homologs (CotH) proteins that may be amenable targets for active immunization. Amongst others, CotH3 seems to be essential during infectious spore attachment, sporulation, and invasion. For proof-of-concept, we constructed an experimental vaccine candidate 17D-CotH3, that expresses multiple copies of a conserved 16-aa peptide derived from Rhizopus CotH3 on the surface of virus-encoded nanoparticles. Immunization of mice and hamsters with 17D-CotH3 induces spore-specific IgM and IgG antibodies that appear to interfere with the adhesion of spores to target cells, and possibly to enhance phagocytosis by macrophages. By this means 17D-CotH3 elicits humoral immune responses that mimic the activity of previously described therapeutic monoclonal antibodies shown to protect from lethal pulmonary mucormycosis in mice. Importantly, we could detect similar antibody responses to CotH3 in a select sample of hematologic patients recovering from mucormycosis. Vaccine efficacy will be evaluated against experimental exposure using Rhizopus sp. and related Mucorales in neutropenic and DKA small animal models that are prone to lethal IFD.

Session 11 - Epidemiology and resistance mechanisms

S11-01

Fungal Epidemiology and Resistance

A. Aldejohann [1], J. Zitzmann, M. Mushi, G. Walther, O. Kurzai
[1]*University Hospital Würzburg, Infection Control and Antimicrobial Stewardship Unit, Würzburg, Germany*

Background

Invasive fungal infections (IFIs) caused by Candida and Aspergillus species are a significant concern in critically ill patients. Analysis of pathogen distributions and resistance patterns help to improve patient outcomes. We provide insights of our epidemiological projects ranging from Covid associated invasive aspergillosis (CAPA) in Germany to a Candida point prevalence study in Mwanza, Tanzania.

Methods

We analysed incidence and resistance of 95 culture positive CAPA in three German tertiary care hospitals at COVID peak season. Inclusion criteria were SARS-CoV-2-positivity, Aspergillus culture-positivity of lower respiratory tract specimen, and ARDS. A point prevalence study at a tertiary care hospital in Tanzania was conducted assessing colonization predictors and evaluating the performance of selective-chromogenic media (CA+).

Results

Out analysis revealed differences in the incidence of culture-positive CAPA (0.6–19%). A. fumigatus was the most abundant species (93%). Most patients received steroids to treat COVID-19-ARDS and required respiratory support. We observed a significant association between galactomannan indices >3 in respiratory fluid and mortality (p=0.035 FE, OR=0.252, 95% CI=0.066-0.986). Therapy with convalescent plasma was associated with a reduction of mortality (p=0.024 FE; OR=0.208, 95% CI=0.051-0.845). No resistant phenotypes (73/95 tested isolates) were detected. In Tanzania, we processed 1082 samples from 448 eligible patients with a yield of 596 suspected Candida isolates classified by CA+. Of these, 541

were confirmed by MALDI-TOF showing good comparability for C. albicans and moderate for other species. Importantly, in 9 cases C. auris-like growth phenotypes on CA+ could not be confirmed by MALDI-TOF, indicating initial misclassification. In our setting, predictors of Candida colonization include prior hospital admission, prior antibiotic use, and low age.

Conclusion
We identified factors affecting survival and mortality of culture positive CAPA patients in Germany. A. fumigatus resistance seems to be low in the cohort. Our findings from Tanzania provide valuable insights into Candida epidemiology and the performance of selective-chromogenic media in East Africa.

S11-02

Dual use of antifungals as a hidden driver of global resistance

M. Lackner [1]
[1] *Institute for Hygiene and Medical Microbiology, Medical University of Innsbruck (MUI), Innsbruck, Austria*

Background

Mucormycosis is a life-threatening invasive fungal infection caused by fungi of the order Mucorales, primarily affecting immunocompromised individuals. Early and accurate diagnosis is critical for improving outcomes, as delayed treatment is associated with high mortality. Polymerase chain reaction (PCR) assays have emerged as a promising diagnostic tool, offering rapid and sensitive detection of fungal DNA. This systematic review and meta-analysis evaluated the diagnostic performance of PCR assays for mucormycosis across various specimen types.

Methods

A standardized search was conducted across PubMed, Embase, Global Health, and the Cochrane Library from inception to December 3, 2024. Original studies using PCR-based methods on human specimens were assessed for eligibility. Using a bivariate meta-analysis, PCR performance was analyzed against the modified European Organisation for Research and Treatment of Cancer–Mycoses Study Group Education and Research Consortium 2020 (EORTC-MSGERC) definitions. The study protocol was registered on PROSPERO (CRD42023478667).

Results

From 4,855 articles, 30 met inclusion criteria, covering 5,920 PCR reactions on 5,147 specimens from 819 proven/probable mucormycosis cases and 4,266 non-cases. Sensitivity varied significantly by specimen type ($p < 0.001$), while specificity remained consistent ($p = 0.662$). Bronchoalveolar lavage fluid (BALF) showed the highest sensitivity (97.5%) and specificity (95.8%), followed by tissue and blood. Formalin-fixed paraffin-embedded specimens had the lowest sensitivity (73.0%) but the highest specificity (96.4%).

Conclusion

This meta-analysis confirms PCR's high diagnostic accuracy for mucormycosis and supports its inclusion in future diagnostic guidelines, particularly for detecting free DNA in blood, BALF, and tissue, to facilitate early and accurate diagnosis.

S11-03

Outcome of invasive *Candida* infections in Europe and the US: results from an ongoing multinational study [2024-2026]

L. Rahimli[1,2], N. Azimli[1,2], N. Vasenda[1], J. Salmanton-García[1,2], R. Sprute[1], I. Falces-Romero[3], M. Valerio[4], A. Soriano[4], A. Gutierrez Villanueva[5], P. Monzo-Gallo[6], C. Garcia-Vidal[6], F. Hanses[7], J. Vazquez[8], P. Yu[8], U. Scharmann[9], O. A. Cornely[1,2,10,11], D. Seidel[1,2]
[1]*University Hospital Cologne, Köln, Germany*
[2]*University Hospital Cologne, Cologne Excellence Cluster On Cellular Stress Responses in Aging-Associated Diseases (CECAD), Köln, Germany*
[3]*Hospital Universitario La Paz, Microbiology and Parasitology, Madrid, Spain*
[4]*Hospital General Universitario Gregorio Marañón, Madrid, Spain*
[5]*Hospital Puerta de Hierro Majadahonda, Madrid, Spain*
[6]*Hospital Clinic of Barcelona, Barcelona, Spain*
[7]*Universitätsklnikum Regensburg, Abteilung für Krankenhaushygiene und Infektiologie, Regensburg, Germany*
[8]*Augusta University, Medical College of Georgia, Augusta, United States*
[9]*Universitätsklinikum Essen, Essen, Germany*
[10]*University Hospital Cologne, Zentrum für Klinische Studien zu Köln (ZKS Köln), Köln, Germany*
[11]*Deutsches Zentrum für Infektionsforschung (DZIF), Partnerstandort Bonn-Köln, Köln, Germany*

Objectives

Invasive *Candida* infection cause significant morbidity and mortality, especially in immunocompromised patients. The FungiScope Candida Campaign 2024–2026 aims to analyze clinical data to better understand risk factors, treatments, and outcomesacross different geographical regions.

Materials & Methods

Anonymized patient data were collected via an online questionnaire (www.clinicalsurveys.net for Europe, Carelane for the USA), capturing demographics, clinical history, diagnostic findings, antifungal treatment, source control and outcome.

Results

By April 2025, 463 patients with invasive *Candida* infection were included (median age 67 [18–102]; 62.2% male).Most cases were from Germany (213; 46.0%), followed by Spain (171; 36.9%) and Italy (39; 8.4%).

Frequent risk factors included CVC use (54.6%), ICU treatment (42.8%), chronic cardiovascular disease (40.6%), hematological/oncological conditions (38.7%), and major surgery (35.9%). Chronic kidney diseases/acute kidney injury and uncontrolled diabetes were present in 22.9% and 22.5% of cases, respectively.

Most patients received antifungal therapy (92%; median 14 days [1–306]. First-line agents included caspofungin (43.6%), anidulafungin (23.7%), and fluconazole (21.1%), while fluconazole (47.3%) and caspofungin (18.5%) predominated as second-line treatment.

Germany predominantly used caspofungin (75.1%), whereas Spain favored anidulafungin (51.2%) as the first-line agent. In Italy, fluconazole (35.9%) and caspofungin (33.3%) were the leading choices. Survival was not significantly influenced by either the initial antifungal

therapy (p = 0.131) or the *Candida* species (*albicans* vs. non-*albicans*; p = 0.462). Overall mortality was 39.4%.

Conclusion

In this cohort, echinocandins were predominantly used as first-line treatment and fluconazole for second-line. Neither initial antifungal choice nor *Candida* species significantly impacted survival.

S11-04

Epidemiology of human histoplasmosis cases in Germany in the years 2023 and 2024

S. Reusch[1], S. Ackermann[1], J. Gerkrath[1], T. Woelki[1], V. Rickerts[1]
[1]Robert Koch-Institut, Department of Infectious Diseases, Unit 16 Mycotic and Parasitic Agents and Mycobacteria, Berlin, Germany

Introduction

Histoplasmosis is a systemic fungal infection caused by the obligate pathogenic *Histoplasma* species complex. The infection can range from pneumonia, soft tissue infections to chronic pulmonary and disseminated forms. It can be fatal, particularly when diagnosis is delayed due to nonspecific symptoms and limitations in diagnostic tests. While the epidemiology of *Histoplasma* is best understood in North America, infections in Europe are typically linked to travel to highly endemic regions (Americas, Asia, Africa).

Methods

For diagnostic purposes, our reference laboratory for cryptococcosis and rare systemic mycoses has developed and implemented tests to detect histoplasma from infected tissues (e.g., BAL, biopsy, cerebrospinal fluid) through direct culture, microscopy and specific qPCR. Additionally, we use a commercial antigen detection test (IMMY Clarus) for urine samples and an antibody test (Immunodiffusion, IMMY). To be able to understand the emergence and distribution of different Histoplasma clades, we additionally perform multilocus sequence typing (MLST).

Results

In both years each, five proven human histoplasmosis cases (according to EORTC criteria) were diagnosed in Germany. One disseminated infection was diagnosed via culture of Histoplasma from a blood sample. The remaining patients had localized infections in the lung or in lymph nodes, with partial involvement of skin. All cases likely represent import infections after travel to highly endemic regions. The most sensitive diagnostic test was our in-house developed histoplasma qPCR, that was positive in 80% of the cases. MLST revealed infections predominantly with South American clades.

Discussion

Histoplasmosis is rarely diagnosed as an imported infection in Germany as suggested by travel history and molecular typing. A combination of laboratory tests applied to diverse clinical samples including infected tissue, urine and serum are necessary for diagnosis.

S11-05

Trends of azole-resistant *Aspergillus fumigatus* susceptibility over 12 years from a German ECMM Excellence center

H. L. Verhasselt[1], L. Thissen[1], U. Scharmann[1], S. Dittmer[1], P. M. Rath[1], J. Steinmann[2], L. Kirchhoff[1]
[1]*Universitätsklinikum Essen, Institute of Medical Microbiology, Essen, Germany*
[2]*Paracelsus Medical University, Klinikum Nürnberg, Institute of Clinical Microbiology, Infectious Diseases and Infection Control, Nürnberg, Germany*

Numbers of infections with azole-resistant *Aspergillus fumigatus* (ARAf) were rising in the last decades. We assessed ARAf susceptibility trends towards five antifungals amphotericin B (AMB), itraconazole (ITR), voriconazole (VCZ), olorofim (OLO) and manogepix (MGX)) over 12 years in a German ECMM Center. In addition, underlying mutations were studied and correlated with trends in minimum inhibitory concentration (MIC).

EUCAST broth microdilution (BMD) was performed for 143 clinical ARAf isolates collected between 2011 and 2022. Molecular assays on mutations associated with antifungal resistance were performed for all isolates (AsperGenius® 1.0) and for ten non TR34/L98H and TR46/Y121F/T289A mutated ARAf isolates *cyp51A* sequencing was carried out.

For all isolates, BMD revealed a MIC50 of > 8 mg/L for ITR, 4 mg/L for VCZ, 0.03 mg/L for OLO, 0.016 mg/L for MGX, and 0.5 mg/L for AMB. Considering EUCAST breakpoints, 97.9 % of the strains were resistant to VCZ, 1.4 % towards AMB and 92.3 % towards ITR. Molecular assays revealed 86 % isolates with the mutation TR34/L98H, 7 % with a TR46/Y121F/T289A mutation and 7 % with other *cyp51A* mutations. A comparison of triazole MICs of isolates collected from 2011 to 2019 with the MICs of isolates collected between 2020 and 2022 revealed no significant differences for itraconazole (p = 0.543) and for voriconazole (p = 0.148), with a trend of increased geometric mean for ITR and VCZ MICs over time. MICs for OLO and MGX did not significantly differ between isolates with the distinct mutations. Before 2016, the azole resistance underlying mutations were mainly TR34/L98H, but the portion of isolates with TR46/Y121F/T289A and other *Cyp51A* mutated isolates increased afterwards.

We showed almost stable MICs for ITR and VCZ over twelve years in ARAf isolates from West Germany while occurring azole resistance underlying mutations varied with an increase in the proportion of TR46/Y121F/T289A and other *Cyp51A* mutations after 2016.

S11-06

Human Coccidioidomycosis in Germany (2011 - 2023): Molecular epidemiology and *in vitro* resistance

M. Messal[1], T. Störiko[1,2], J. Michel[1], J. Gerkrath[1], S. Ackermann[1], S. H. Tausch[2], V. Rickerts[1]
[1]*Robert Koch-Institut, Department of Infectious Diseases, Unit 16 Mycotic and Parasitic Agents and Mycobacteria, Berlin, Germany*
[2]*Robert Koch-Institut, MF1 Bioinformatik-Support, Berlin, Germany*

Introduction

Coccidioidomycosis (cocci) is the second most prevalent travel associated systemic fungal infection, endemic to semi-arid regions in the Americas. However, epidemiology in Germany is poorly described.

Objective

Describe molecular epidemiology and *in vitro* resistance of cultivated *Coccidioides* isolates from Germany.

Methods

Culture-proven cocci cases at the German reference laboratory for rare systemic fungal infections were analysed. *In vitro* susceptibility testing was performed using Sensititre YeastOne YO10, covering licenced antifungals.

DNA from cultivated isolates was sequenced with Illumina technology. Whole-genome based maximum-likelihood phylogenies were constructed using the MycoSNP-nf pipeline (developed at CDC).

Results

Twelve cases were identified (female 25%, male 75%; aged 23-82). Patients originated from Germany (42%), US (25%) or other/unknown (33%). Underlying diseases were reported in two patients (rheumatoid arthritis, hepatitis C); six were healthy (50%), and data were missing for four (33%). Eight patients had pulmonary disease (67%), one an intracerebral abscess (8%). Three cases involved disseminated lung disease with mucocutaneous (n=2) or bone (n=1) involvement. Two relapses were noted.

Antifungal susceptibility testing showed good activity of amphotericin B (MIC50=minimum inhibitory concentration 50%, 0.5 µg/ml); fluconazole was the least active (8), while itraconazole (0.5), posaconazole (0.25) and voriconazole (0.06) were more active.

Phylogenetic reconstruction indicated endemic exposure largely consistent with reported travel history (Arizona:67%, Texas and Latin America:17%, California 17%).

Conclusion: Molecular epidemiology confirms Arizona as a typical origin of cocci imported to Germany. Amphotericin B, itraconazole and newer azoles demonstrate superior *in vitro* activity compared to fluconazole.

S11-07

Domestic bathrooms as reservoirs for eye-infecting *Fusarium* species

E. Garbe[1], A. Ullah[1], U. Farooq[1], A. Gille[1], S. Janevska[1], G. Walther[2]
[1]*Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), (Epi-)Genetische Regulation Pilzlicher Virulenz, Jena, Germany*
[2]*Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Nationales Referenzzentrum für Invasive Pilzinfektionen, Jena, Germany*

Fusarium is a diverse fungal genus comprising over 400 species, including major plant pathogens. Yet, several species are also opportunistic human pathogens, causing life-threatening invasive fusariosis in critically ill patients to superficial infections such as those of the cornea (keratitis) in usually immunocompetent patients. In Germany, the majority of these eye infections are caused by species of the *F. solani* (FSSC) and *F. oxysporum* (FOSC) species complexes. While certain risk factors are known, like the use of contact lenses, several questions about these infections remain unanswered, such as the actual reservoirs of the infecting species, which appear to be common in indoor environments. Thus, we collected *Fusarium* isolates from indoor environments in cooperation with building biologists, identified them to species level and compared their diversity with a set of clinical *Fusarium*

isolates received by the NRZMyk. In addition, we performed a systemic screening for *Fusarium* presence in domestic bathrooms of healthy volunteers and keratitis patients to identify potential reservoirs for eye-infecting species. The *Fusarium* diversity of indoor and clinical samples showed notable similarities and confirmed the indoor presence of most clinically relevant species. Opportunistic species were also frequently isolated in bathrooms, especially from drains, overflows, silicone joints and water samples, with a dominance of certain species, such as *F. veterinarium* (FOSC) and *F. keratoplasticum* (FSSC). Interestingly, other species from both complexes were also frequently isolated from bathrooms, but were nearly absent in the clinical set. Finally, *Fusarium* isolates of the same species and sequence type as those obtained from the eyes of keratitis patients were recovered from the patients' bathrooms. In sum, this study details the ecology of clinically relevant *Fusarium* species, their abundance in domestic bathrooms and confirms them as reservoirs for fungal eye infections.

Poster

Poster session I

LTP-01 | LT-01

Comparison of two Commercial Realtime PCR Assays for the Detection of Aspergillus-DNA

D. Schmidt[1], H. L. Verhasselt[1], L. I. Korth[1], A. Hain[1], J. Buer[1], P. M. Rath[1]
[1]*Universitätsklinikum Essen, Institute of Medical Microbiology, Essen, Germany*

Introduction

Invasive aspergillosis is a severe infection, associated with a high mortality and morbidity. Early and accurate diagnosis is paramount to improve patient outcome.

Objectives

Brochoalveolary lavage fluids from critically ill patients were analyzed with the AsperGenius2.0 assay (AG2.0) by PathoNostics (The Netherlands) and the VIASURE Aspergillus differentiation assay (VIASURE) by Certest Biotec (Spain) in comparison with culture and the PLATELIA ASPERGILLUS Ag assay (PLATELIA) by Bio-Rad (Germany), respectively.

Materials & Methods

DNA of 136 samples from 131 patients (mean age 60,5 years; 73% male) was analyzed using a RotorGeneQ instrument (Qiagen). For AG2.0 positivity was defined by a ct value below 39 (Outlier 10%), for VIASURE by a ct value below 40 (Outlier 30%), respectively. Results in the *Aspergillus spp.* channel of the AG2.0 assay were disregarded. For the galactomannan assay positivity was defined as an optical density index equal or higher than 1.0.

Results

Detection rate of the AG2.0 assay was 11.8% (n=16) versus 22.8% (n=31) of the VIASURE assay. Ct values were between 28.35 and 36.85 (mean=32.03) for the AG2.0 assay and between 23.6 and 35.46 (mean=28.35) for the VIASURE assay, respectively. The agreement between both assays was 80.9%. Despite the higher detection rate of the VIASURE assay agreements with PLATELIA and culture, respectively, was lower when compared with the

agreements between AG2.0, PLATELIA and culture (67.4%, 82.4% vs 88.2%, 89.7%). This was due to the fact that the VIASURE assay gave positive results in 14 samples (ct values 29.03-35.43) that could not be verified.

Conclusion

The VIASURE assay showed a higher sensitivity in comparison with the AG2.0 assay. Although this did not result in a higher specificity when compared with culture and with the PLATELIA assay, respectively, the assay can still be a useful molecular confirmation tool when other assays give indecisive results.

LTP-02 | LT-01

A PCR-based approach for the detection of dermatophytes: Insights from real-life clinical data

S. Steixner[1], S. Fuchs[1], R. Vahedi-Shahandashti[1], C. Lass-Flörl[1]
[1]Medizinische Universität Innsbruck, Institute of Hygiene and Microbiology, Innsbruck, Austria

Background

Dermatomycosis is among the most prevalent superficial fungal infections, and the emergence of antifungal resistance is contributing to a significant global disease burden. Accurate and timely diagnosis is essential for appropriate treatment and effective transmission control. This study highlights the performance of a PCR-based diagnostic workflow and provides epidemiological insights into real-life clinical data in Tyrol, Austria.

Methods

In this retrospective study, a total of 4483 specimens, collected in a 6-year period (2018-2024), were analyzed using a stepwise approach: pan-dermatophyte real-time PCR, followed by fluorescence microscopy and fungal culture as needed.

Results

PCR detected dermatophyte DNA in 1170 samples (26.1%), predominantly *Trichophyton rubrum* (76.4%). Among 3313 PCR-negative cases, 308 showed fungal elements microscopically, resulting in 402 cultured isolates – including dermatophytes, *Candida* spp., and non-dermatophyte molds like *Aspergillus* spp. and *Fusarium* spp. The PCR workflow had a low false-negative rate (1.49%) and significantly reduced diagnostic turnaround from 31 to 6 days.

Conclusion

Integrating PCR with conventional diagnostics enhanced sensitivity, speed, and accuracy of dermatomycosis detection. Our findings highlight *T. rubrum* as the dominant pathogen and support the combined use of molecular and conventional diagnostics in routine clinical practice.

LTP-03 | LT-03

NFDI4Microbiota supporting microbiology research providing data access, services, training and workflows

L. Junctorius[1], K. U. Förstner[1], A. C. McHardy[2]
[1]*ZB MED - Information Centre for Life Sciences, Köln, Germany*
[2]*Helmholtz Centre for Infection Research, Braunschweig, Germany*

Introduction

NFDI4Microbiota aims to support the microbiology research community by providing access to data, analysis services, data/metadata standards, and training. It belongs to the National Research data Infrastructure (NFDI), which aims to develop a comprehensive research data management. NFDI4Microbiota intends to facilitate the digital transformation in the microbiological community (bacteriology, virology, mycology, and parasitology).

Goals

NFDI4Microbiota aims to support the German microbiology research network through training and community building activities, and by creating a cloud-based system that will make the storage, integration, and analysis of microbial data and (microbial) omics data, consistent, reproducible, and accessible. Thereby, NFDI4Microbiota will promote the FAIR (Findable, Accessible, Interoperable and Re-usable) principles and Open Science.

Results

To enable FAIR data management, the NFDI4Microbiota consortium develops and provides computational infrastructure and analytical workflows to store, access, process, and interpret various microbiology-related data types. NFDI4Microbiota works on developing and implementing software and standardized workflows for users to analyze their own data. Further, NFDI4Microbiota offers trainings, spanning from metagenomics, over courses about programming, to research data management and ELN (electronic lab notebooks). To interact with young scientists, the consortium launched an ambassador program, thereby helping to identify the needs of their local community. All relevant information and specific services are available via the web portal.

Summary

NFDI4Microbiota has established community services providing access to data, analysis services, data/metadata standards, and training thereby promoting FAIR principles and Open Science in the microbiology community.

LTP-04 | LT-04

Elucidating the contribution of Ugp1 in *Aspergillus fumigatus* 5-fluorocytosine activity

L. Birštonas[1], F. Gsaller[1], A. Kühbacher[1]
[1]*Medizinische Universität Innsbruck, Institute of Molecular Biology, Innsbruck, Austria*

Introduction

Compared to the other antifungal agents used in the clinical setting, the antifungal 5-fluorocytosine (5-FC) is not toxic per sé. To unfold its toxicity, it has to be metabolized within the cell into 5-fluorinated nucleotides such as 5-fluorouridine triphosphate (5-FUTP), an analog of the RNA building block uridine triphosphate (UTP). 5-FUTP can be incorporated into RNA instead of UTP, leading to adverse effects in RNA and protein metabolism. In addition to its role in RNA metabolism, UTP is a crucial precursor for nucleotide sugars which provide essential components for cell wall polymers like glucans.

Objectives

In the first step of nucleotide sugar synthesis, the enzyme UDP-glucose pyrophosphorylase (Ugp1) catalyzes the formation of UDP-glucose from UTP and glucose-1-phosphate. Based on the hypothesis that 5-FUTP affects nucleotide sugar metabolism, for instance by directly acting on Ugp1 enzyme activity, in this work we aimed to elucidate a potential novel mode-of-action related to 5-FC.

Materials and methods

A. fumigatus conditional expression mutants of *ugp1* were generated to monitor 5-FC activity during its downregulation and overexpression. In addition to phenotypical assays, minimum inhibitory concentrations (MICs) were analyzed using a broth microdilution assay coupled with high-throughput microscopy. An assay is being developed to determine whether Ugp1 activity is altered in response to 5-FC treatment.

Results

Downregulation of *ugp1* led to severe defects in hyphal morphology and rendered *A. fumigatus* more susceptible to 5-FC. In line, its overexpression increased 5-FC resistance.

Conclusion

Taken together, our initial data suggests a new mode-of-action for 5-FC related to nucleotide sugar biosynthesis.

LTP-05 | LT-05

Antifungal tolerance – the ability of fungi to make therapy difficult

K. Góralska[1], M. Szybka[2], F. Karuga[3], D. Pastuszak-Lewandoska[2], E. Brzeziańska-Lasota[4]
[1]Medical University of Lodz, Department of Biology, Parasitology and Medical Mycology., Lodz, Poland
[2]Medical University of Lodz, Department of Microbiology and Medical Laboratory Immunology, Lodz, Poland
[3]Medical University of Lodz, Department of Biology and Parasitology, Lodz, Poland
[4]Medical University of Lodz, Department of Biomedicine and Genetics, Lodz, Poland

The increasing level of resistance among fungi poses a huge challenge to the effectiveness of therapy. The mechanisms of acquiring resistance by fungi, especially *Candida*, are currently being widely analyzed. Studies of this type have allowed us to establish the similarity of the resistance mechanisms of fungal cells and other eukaryotic cells, including human cells, which may favor the emergence of cross-resistance in fungi in response to other types of drugs. At the same time, it was found that exposure of fungi to drugs may result in cell adaptation manifested as antifungal terolance.

The aim of the study was to search for mechanisms of acquiring antifungal tolerance in *Candida albicans* and *Candida parapsilosis* as a result of fungal exposure to methotrexate (MTX).

The minimum inhibitory concentration level of selected azoles was determined for 16 isolates of *C. albicans* and *C. parapsilosis*, which were exposed to different concentrations of MTX. Then, the expression levels of genes: *ERG11*, *MDR1* and *CDR1*, potentially responsible for the occurrence of cross-resistance, were assessed before and after exposure to MTX.

We found that as a result of exposure to MTX, *C. albicans* and *C. parapsilosis* strains to MTX showed a high increase in resistance to fluconazole and a partial increase in resistance to voriconazole. For *C. albicans* strains, we found an increase in the expression of the *MDR1* gene, and a decrease in *ERG11* and *CDR1* after exposure. For *C. parapsilosis* after exposure, an increase in the expression of the *CDR1* gene and a decrease in *ERG11* and *MDR1* were recorded.

Our results suggest, there is a risk of resistance or tolerance to antifungal drugs in patients treated with MTX. Whereas the mechanisms by which fungi acquire tolerance and develop cross-resistance are highly complex and most likely involve several pathways simultaneously, including epigenetic mechanisms.

LTP-06 | LT-06

Detecting tolerance in non-*albicans Candida* species from blood culture – a pilot for the ECMM-Candida IV study

K. Rosam[1], R. Vahedi-Shahandashti[1], S. Wolfgruber[2], O. A. Cornely[3], M. Hönigl[2], C. Lass-Flörl[1]
[1]Medizinische Universität Innsbruck, Institut für Virologie und Klinische Mikrobiologie, Innsbruck, Austria
[2]Medical University Graz, Department of Internal Medicine, Department of Infectious Diseases, Graz, Austria
[3]University of Cologne, Department I of Internal Medicine, Köln, Germany

Introduction

Non-*albicans Candida* (NAC) species are increasingly common in candidemia cases and may exhibit elevated antifungal resistance. In addition, antifungal tolerance, defined by the persistent survival above the minimal inhibitory concentration (MIC) after prolonged incubation without a change in MIC, has emerged as contributing factor to treatment failure and resistance development.

Aim

To investigate NAC bloodstream isolates for heterogeneity in resistance and tolerance to fluconazole (FLC) and anidulafungin (ANI).

Methods

Within the ECMM *Candida* IV study, 45 NAC strains from 21 patients were retrospectively tested with Etest® for FLC and ANI. Readings were taken at 24h, 48h, and 72h. Microcolonies (MCs) within the inhibition zone at 72 hours were isolated and, alongside with their corresponding original isolates, retested using the EUCAST method to evaluate MICs and supra-MIC growth (SMG).

Results

After 72h, 15 isolates produced a total of 60 MCs in the E-test, comprising of *C. glabrata* (n=7), *C. parapsilosis* (n=6), and *C. orthopsilosis* (n=2). In *C. glabrata*, all MCs from five isolates exhibited a FLC-sensitive phenotype by EUCAST after 48h. Two isolates displayed phenotypic heterogeneity, each producing resistant (n=5) and sensitive (n=3) MCs, with all resistant MCs demonstrating elevated SMG values ranging from 0.18 to 0.27. In *C. parapsilosis*, all MCs were FLC-sensitive. Among *C. orthopsilosis* isolates, one isolate yielded only FLC-sensitive MCs, while the other produced two susceptible and four FLC-resistant MCs which displayed SMG values of 0.15–0.29. In the case of ANI, all MCs were sensitive, except for one *C. glabrata* strain that formed two resistant MCs with SMG values of 0.32–0.35.

Conclusion

Our data show that NAC isolates, especially *C. glabrata*, can form MCs with various tolerance levels indicated by elevated SMG. Undetectable by standard testing, this highlights the importance of identifying these variants to prevent treatment failure.

LTP-07 | LT-07

Employing human *in vitro* macrophage models to identify early immune response mediators against *Aspergillus fumigatus*

J. Söhnlein[1], S. Schäuble[2], Z. Abboud[1], K. Hünniger-Ast[3], M. Seif[1], H. Einsele[1], A. Beilhack[1], J. Löffler[1]
[1]*Universitätsklinikum Würzburg, Würzburg, Germany*
[2]*Hans-Knöll-Institut, Microbiome Dynamics, Jena, Germany*
[3]*Hans-Knöll-Institut, Fungal Septomics, Jena, Germany*

The saprophytic mold *Aspergillus fumigatus* (AF) forms 2 – 3 µm small conidia, which pose a potential threat to immunocompromised individuals after inhalation. In healthy individuals, alveolar macrophages (AMs) are the first line of defense, effectively eliminating inhaled conidia and maintaining lung homeostasis. However, the early immunological processes that determine whether the pathogen can be cleared or invades the epithelium to cause infection remain elusive. We aim to investigate early decision points in AMs upon initial encounter with AF by employing various human macrophage (MΦ) populations. Human CD14+ monocytes were differentiated into AM-L [1] cells and GM-CSF MΦs. Phenotypic characterization was performed using microscopy and flow cytometry. Both cell types were co-cultured with resting AF conidia for 6 and 9 hours. Transcriptional differences were analyzed using dual RNA sequencing and validated by ELISA and qPCR. Functional assessment of phagocytic and killing capacities was conducted using the FLARE [2] model. Furthermore, the AM-L model was compared to primary human AMs to assess similarity, and the impact of TNF signaling inhibition by etanercept on CXCL10 production will be evaluated. AM-L cells exhibited higher expression of AM markers, including MHC II and CD68. Genotypic comparison between AM-L and GM-CSF MΦs further proved the antigen-presenting phenotype of AM-L cells and visualized stronger cytokine expression already after 6h of AF encounter. Especially, CXCL10 secretion was increased in AF infected AM-L cells. FLARE infection demonstrated higher phagocytic capacity of AM-L cells after 2h post-infection. We established the AM-L cells as a robust human *in vitro* model for studying early AF infection and to model alveolar immune responses. Additionally, TNFa-mediated CXCL10 expression emerges as a possible early key factor in host defense against AF.

References

1. Pahari et al. mBio (2023)
2. Jhingran et al. Cell Reports (2012)

LTP-08 | LT-08

Responses of human monocytes to co-infection with *Candida albicans* and *Staphylococcus aureus*

G. Braune[1], N. Nieuwenhuizen[1], K. Hünniger-Ast[2], K. Ohlsen[3], O. Kurzai[1,2]
[1]Universitätsklinikum Würzburg, Institut für Hygiene und medizinische Mikrobiologie, Würzburg, Germany
[2]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Jena, Germany
[3]Universitätsklinikum Würzburg, Institut für Molekulare Infektionsbiologie, Würzburg, Germany

Introduction

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 the immune system.

Objective

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

Materials & Methods

Pan-monocytes were isolated by magnetic-activated cell sorting from human peripheral blood mononuclear cells. Monocytes were exposed *in vitro* to *C. albicans* and/or *S. aureus*, with and without opsonisation, and analyzed by flow cytometry to assess uptake kinetics across classical ($CD14^+CD16^-$), intermediate ($CD14^+CD16^+$), and non-classical ($CD14^-CD16^+$) subsets. To assess pathogen killing, colony forming units were analysed by plating assays.

Results

Pathogens were taken up mainly by inflammatory and intermediate monocyte subsets. Without opsonisation, the percentage of co-infected cells was very low. Opsonising pathogens with normal human serum significantly increased the uptake of both *C. albicans* and *S. aureus*, and in particular increased the percentage of co-infected cells. In cells exposed to both pathogens, approximately 50% of classical monocytes were co-infected by 60 min, with an additional 10% infected only with *C. albicans* and 20% only with *S. aureus*. Our preliminary data suggests simultaneous infection with *S. aureus* may impede the clearance of *C. albicans*.

Conclusion

Polymicrobial infection may affect the uptake and killing of individual pathogens by monocytes, influencing the outcome of infection. Future plans include transcriptomic analysis of single and dual-infected monocytes. Understanding these competitive phagocytic dynamics at the cellular level may inform the development of therapies against fungal-bacterial co-infections.

LTP-09 | LT-09

Intracellular survival of *Lichtheimia corymbifera* in macrophages

R. Zaher[1], F. Schmidt[1], T. Heinekamp[1], A. A. Brakhage[1]
[1]*Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Molekulare und Angewandte Mikrobiologie, Jena, Germany*

Introduction

Several pathogens have developed a wide range of strategies to survive within their hosts, including mechanisms that enable persistence within phagosomes. This also applies to clinically relevant human pathogenic fungi. Our research focuses on two human-pathogenic fungi that are both widespread in the environment and exhibit a saprophytic lifestyle: *Lichtheimia corymbifera*, a member of the Mucorales order, and the airborne ascomycete *Aspergillus fumigatus*, one of the most relevant fungal pathogens in humans. In immunocompromised patients, various Mucorales species -including *L. corymbifera*- can cause severe and often fatal infections known as mucormycosis. Moreover, *L. corymbifera* is increasingly recognized as a frequent cause of breakthrough infections, especially following illnesses such as invasive pulmonary aspergillosis. Despite its clinical relevance, the pathogenesis of mucormycosis remains poorly understood.

Aim

This project aims to elucidate the interactions between *L. corymbifera* spores and the host's innate immune system, with a comparative perspective on *A. fumigatus*.

Methods and results

To investigate this, we infected RAW 264.7 macrophages as well as primary immune cells with conidia from both fungal pathogens and monitored their interactions. We specifically focused on *L. corymbifera* and its interaction with macrophages, examining its capacity to survive and germinate intracellularly. In parallel, we analyzed the ability of macrophages to process fungal spores from both species, with particular attention to how they influence phagosome maturation.

Conclusion

Gaining insight into the molecular and cellular interactions between fungal spores and immune cells is essential for understanding *L. corymbifera* pathogenesis and could contribute to the development of novel therapeutic approaches for these life-threatening infections.

LTP-11 | LT-11

Establishment of a molecular system to assess RNA-DNA triple helix formation in *Aspergillus fumigatus*

V. Lazarova[1], L. Fabre[2], A. Mourya[1], A. E. Barber[2], H. Bierhoff[2], M. Blango[1]
[1]*Hans-Knöll-Institut, RNA Biology of Fungal Infections, Jena, Germany*
[2]*Friedrich-Schiller-Universität, Jena, Germany*

Aspergillus fumigatus, a WHO critical-priority human fungal pathogen, is responsible for millions of infections annually. In the Fungal RNA Transmission Impacting Human Epigenome Regulation (FuRTHER) Project funded by the Leibniz Association, we aim to understand the contribution of RNA-DNA triple helices (triplexes) to regulation of gene expression during fungal infections. Triplex structures typically form when a long non-coding RNA (lncRNA) binds to the major groove of a DNA helix. Mostly studied in humans, triplexes regulate gene expression through chromatin modulation, a mechanism that has not yet been assessed in pathogenic fungi. Here, we hypothesize that triplexes form both in fungal pathogens and between fungi and hosts as important regulators of gene expression during infection. Therefore, our main objective is first to confirm triplex formation in the fungus by discovering lncRNA candidates that form triplexes with dsDNA of fungal gene promoters. For this purpose, we have utilized *in silico* triplex prediction programs, DNA pulldowns, molecular tools development, and RNA/DNA sequencing. Triplex prediction using public datasets identified candidate fungal lncRNAs with high triplex forming potential. In parallel, we cloned a triplex-sensor protein into *A. fumigatus*. With this sensor, we are currently improving immunoprecipitation experiments for successful capture and sequencing of triplex structures. Finally, a major goal of the project is to test the potential for triplexes to form between kingdoms. For this purpose, extracellular RNA extracted from the fungus is being prepared for sequencing to predict triplex-forming lncRNAs, which could serve as cross-kingdom regulators during infection. Our study lays the groundwork to investigate fungal lncRNA-mediated triple helices involved in fungal infection, offering insights into gene modulation mechanisms and host-pathogen interactions.

LTP-12 | LT-12

Cytostatic drugs against Pancreatic Ductal Adenocarcinoma (PDAC) can cross-affect the viability of the pro-carcinogenic yeast *Malassezia globosa*

S. Mühlmann[1], F. Nocera[2], A. Amann[2], M. Maglione[3], N. Parth[2], C. Speth[1], G. Rambach[1]
[1]*Medizinische Universität Innsbruck, Institute of Hygiene and Microbiology, Innsbruck, Austria*
[2]*Medizinische Universität Innsbruck, University Hospital for Internal Medicine V, Innsbruck, Austria*
[3]*Medizinische Universität Innsbruck, Department of Visceral, Transplant, and Thoracic Surgery, Innsbruck, Austria*

Introduction

To improve the prognosis of PDAC, optimized therapies are needed. Since *Malassezia* is hypothesized to essentially contribute to tumor progression, a reduction of fungal viability represents a new promising strategy.

Aim

(i) to evaluate whether cytostatics commonly given to PDAC patients also affect the fungal viability; (ii) to study the influence of pancreatic environment on the antifungal effect of cytostatics.

Materials/Methods

Malassezia was incubated with the cytostatics 5-fluorouracil (5-FU), cisplatin or oxaliplatin; fungal proliferation was quantified by plating. Tumor microenvironment was simulated by homogenized murine pancreatic tissue (PH) and reduced oxygen content.

Results

5-FU, a commonly given anticancer drug for PDAC, significantly interferes with *Malassezia* proliferation. This inhibitory effect was strongly pronounced in MDA culture medium, but also in murine PH that was used to simulate the pancreatic environment. Even low 5-FU concentrations were effective against *Malassezia*. The long-term effect of 5-FU was also evaluated since cytostatic therapy lasts at least 3 weeks. No adaptation of the fungus was observed; the inhibitory effect of 5-FU was even more pronounced after 2 weeks. In contrast, cisplatin and its derivative oxaliplatin did not exert any effect on fungal proliferation in MDA or PH cultures.

The inhibitory effect of 5-FU is dependent on oxygen concentration. Whereas normoxic (21%) and hypoxic (1%) conditions did not differ in 5-FU effectiveness, an anaerobic environment, which is described for PDAC tissue, critically affected the 5-FU effect on the fungus.

Conclusions

The proliferation of *Malassezia* as a putative tumor-promoting factor can be reduced by an optimized choice of the cytostatic drugs used in chemotherapy. 5-FU not only affects proliferation of tumor cells, but also limits fungal proliferation, even in nutrient and oxygen conditions that are present in PDAC.

LTP-13 | LT-13

Diversity of pathogenic *Fusarium* species in outdoor environment

L. Lammers[1], G. Walther[1], E. Garbe[2], S. Janevska[2]
[1]*Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), National Reference Center for Invasive Fungal Infections, Jena, Germany*
[2]*Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), (Epi-)Genetic Regulation of Fungal Virulence, Jena, Germany*

Fusarium is a diverse fungal genus primarily infecting plants but also animals and humans. As an opportunistic pathogen it can lead to systemic infections in immunosuppressed patients but also to superficial infections like keratitis in otherwise healthy individuals. In Germany, *Fusarium* infections are mainly caused by species of the *F. solani* (FSSC), *F. oxysporum* (FOSC) and *F. fujikuroi* (FFSC) species complexes (SCs). The taxonomic revision of *Fusarium* started in 2013 and is still ongoing. Therefore, little is known about the ecology and geographic distribution of the newly recognized species. For example, the pathogenic FSSC species *F. keratoplasticum* and *F. petroliphilum* are mainly isolated from humans and indoor sources. While *F. keratoplasticum* has never been detected on a plant,

F. petroliphilum is described as a pumpkin pathogen from several countries including Spain. To investigate if pathogenic *Fusarium* species are occurring outdoors in Germany, we isolated *Fusarium* from pumpkins and soil samples across Germany and identified them by sequencing established marker regions TEF1 and RPB2. Overall, different SCs were obtained from pumpkins, with *F. tricinctum*, *F. incarnatum-equiseti* (FIESC) and *F. sambucinum* species complexes being most abundant. Out of 206 isolates, only 17 belonged to either FSSC, FOSC or FFSC, with *F. petroliphilum* being absent, but with the clinically relevant species *F. annulatum* detected 9 times. Preliminary results from soil samples show a different profile with the majority of isolates belonging to either FIESC or FOSC, including the clinically relevant species *F. nirenbergiae* (FOSC) and *F. solani* (FSSC). Important pathogenic species such as *F. veterinarium* (FOSC), *F. petroliphilum* or *F. keratoplasticum* (FSSC) have not been detected in Germany so far. Taken together, these results contribute to the understanding of the ecology of pathogenic *Fusarium* species, their reservoirs and their routes of infection.

PI-01

qPCR-based molecular detection of *Trichophyton indotineae* by targeting divergent sequences

E. Kaplan[1], O. Bingöl[2], H. Kandemir[3], A. S. Karakoyun[2], M. Durdu[4], M. Ilkit[2]
[1]*Istanbul University-Cerrahpaşa, Department of Pharmaceutical Microbiology, Istanbul, Turkey*
[2]*Çukurova University, Faculty of Medicine, Department of Microbiology, Sarıçam, Adana, Turkey*
[3]*Westerdijk Fungal Biodiversity Institute, Utrecht, Netherlands*
[4]*Başkent University Faculty of Medicine, Adana Dr. Turgut Noyan Application and Research Center, Department of Dermatology, Adana, Turkey*

Introduction

Trichophyton indotineae, formerly known as *T. mentagrophytes* internal transcribed spacer (ITS) genotype VIII, has been recognized over the last decade due to its high virulence and resistance to treatment. Its accurate identification in routine mycology laboratories remains challenging, as it shares phenotypic traits and substantial rDNA ITS similarity with *T. mentagrophytes* and *T. interdigitale*.

Objectives

This study aimed to identify more divergent and stable sequences via whole-genome comparisons between *T. indotineae* and *T. interdigitale* to facilitate highly specific targeting of *T. indotineae* using a validated quantitative polymerase chain reaction (qPCR)-based method.

Materials and Methods

Our whole-genome comparison revealed at least 22 unique sequences of *T. indotineae* compared to *T. interdigitale* and revealed the divergence of the former from the reference genomes of other *Trichophyton* species. Among these, a 499 bp segment was identified as the most genetically distinct sequence within the *T. indotineae* genome. Seventy-three dermatophyte strains [*T. indotineae* (*n*=66), non-*T. indotineae* (*n*=7)], were tested using our qPCR assay targeting the above-mentioned stable 499-bp region.

Results

Regarding analytical performance, our *T. indotineae*-specific qPCR assay exhibited high sensitivity (93.3%) and specificity (100%), with a detection limit of ~15 genomic copies. Our approach has the potential to establish highly sensitive and specific qPCR assays without relying on specialized assay designs for single nucleotide polymorphisms in the ITS or other loci.

Conclusion

This approach offers a practical solution for updating molecular diagnostics, particularly for novel taxa such as *T. indotineae*, for which limited gene data are available in public databases.

PI-02

Acute invasive fungal Rhinosinusitis in immunocompromised patients: How seminested PCR helps bridge the gap between clinical suspicion and fungal identification

N. Ahmed[1]
[1]*Alexandria University, Medical Research Institute (MRI), Molecular and Diagnostic Microbiology, Alexandria, Egypt*

Objectives

The main goal of the present study is to investigate the diagnostic value of molecular methods for the detection of *Aspergillus* and *Mucorales* in fresh tissue samples from AIFRS patients and compare it with conventional techniques.

Methods

This cross-sectional study was carried out on 50 clinically, endoscopically, and radiologically diagnosed AIFRS patients who were managed in a tertiary referral hospital from October 2021 to January 2023. Fresh tissue samples were collected during surgical debridement and subjected to histopathological, culture, and seminested PCR with specific primers for *Mucorales* and *Aspergillus*.

Results

Histopathology confirmed AIFRS diagnosis in 47 cases. Culture was positive in 39 samples. Seminested PCR was able to identify the causative fungi in all samples. *Mucorales* PCR was positive in 11 culture-negative samples. Also, the 19 samples, that histopathology diagnosed as positive but failed to specify the fungi type were diagnosed by PCR as *Mucorales* in 15, *Aspergillus* in 3, and mixed infection in 1 sample. Moreover, PCR detects *Mucorales* in all 3 histopathology-negative samples. Also, the 3 mixed infections detected by both culture and PCR were wrongly diagnosed by histopathology as *Mucorales* only in one sample, *Aspergillus* only in another one, and histopathology couldn't identify the hyphae type in the third.

Conclusions

Histopathology is the cornerstone of confirming the invasive nature of fungal infection; however, it couldn't distinguish between aspergillosis and mucormycosis in many cases. Also, culture and microscopy techniques yield a high percentage of false negative results even with avoiding tissue homogenization. Seminested PCR with species-specific primers is reliable in identifying the fungi in fresh tissue, and it is recommended to confirm the negative histopathology and culture results. Still, extreme caution must be taken to avoid false positive results by environmental contamination during the molecular detection.

Figure 1

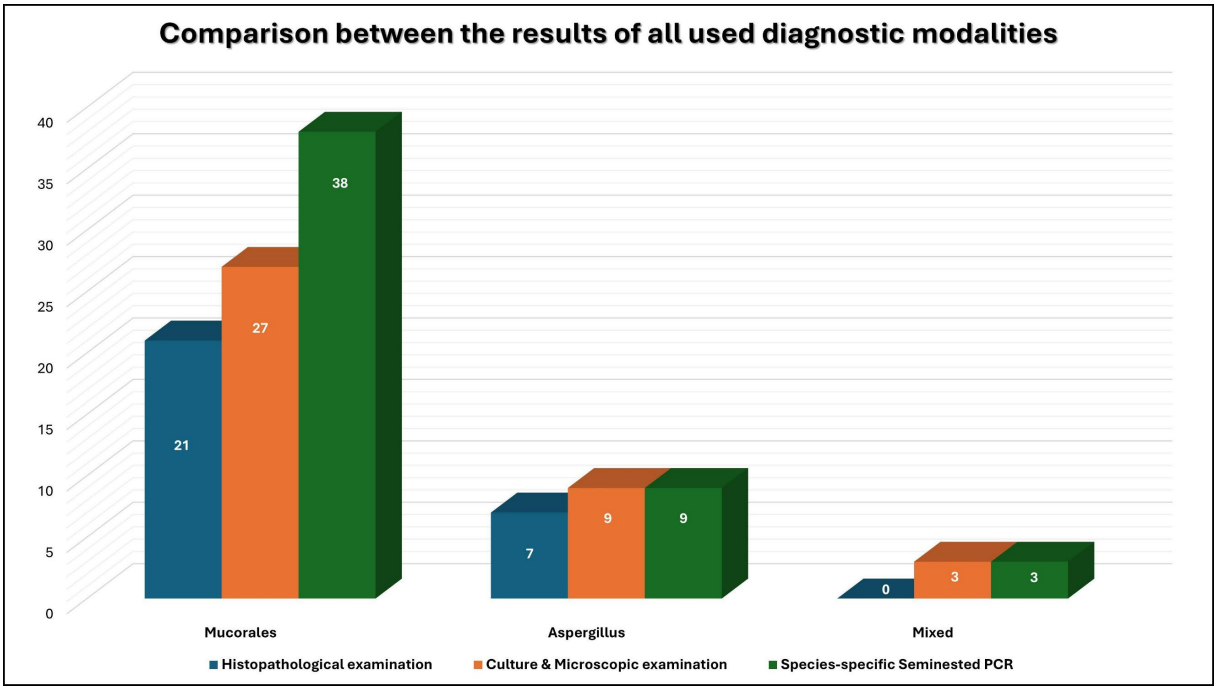
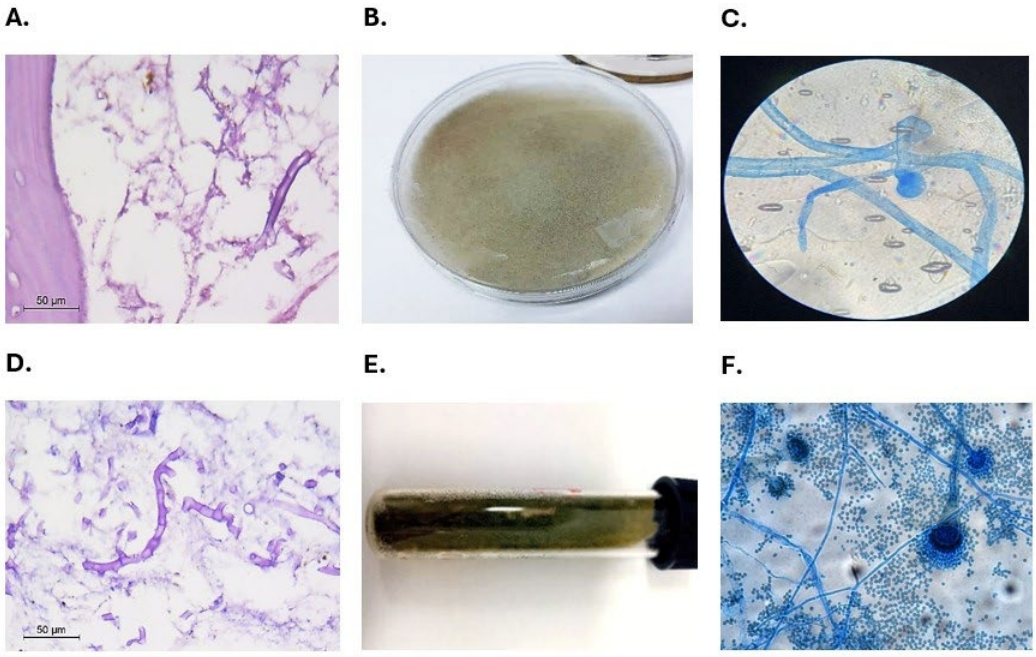


Figure 2



(A) Histopathological morphology of *Mucorales* aseptate hyphae *invading the bone* (PAS stain, x400),
(B) *Mucorales* colonies cover the entire PDA plate with distinctive areal hyphae of cottony-like appearance and grey spores,
(C) *Mucorales* microscopic morphology with broad ribbon-like and pauciseptate hyphae,
(D) Histopathological morphology of septate hyphae of *Aspergillus* spp. (PAS stain, x400),
(E) *Aspergillus Fumigatus* blue-green colonies growth on PDA slant,
(F) *Aspergillus Fumigatus* thin septate hyphae holding the vesicle with uniseriate phillade radiate from the upper two-third of it.

PI-03

Candida species culture positivity in patients with indwelling urinary catheters: the potpourri of white aggregates and inconsistent CFU counting

S. Steixner[1], A. Bauer[1], R. Bellmann-Weiler[2], C. Lass-Flörl[1]
[1]Medizinische Universität Innsbruck, Institute of Hygiene and Microbiology, Innsbruck, Austria
[2]Medizinische Universität Innsbruck, Department of Internal Medicine II, Innsbruck, Austria

Introduction

Urinary tract infection (UTI) is a common diagnosis in hospital and community settings. The presence of *Candida* spp. in urine can represent contamination, colonization, or UTI, and requires careful clinical interpretation. Diagnosis typically involves urine culture, but the use of colony forming unit (CFU) counting remains controversial. Additionally, white aggregates in urine are hypothesized to correlate with *Candida* cells. In this ongoing study, we investigate the phenomenon of white aggregates in patients with urinary catheters (UTC) and analyze the consistency of CFU counting in UTIs.

Material and Methods

UTC specimens with aggregates were analyzed by microscopy - gram and calcofluor white staining – CFU counting. In addition, we collected three consecutive UTC samples over the course of three days in *Candida* culture positive urine specimens to assess CFU

reproducibility. Species identification was performed by matrix-associated laser desorption/ionization – time of flight.

Results

A total of 28 UTC samples with aggregates were analyzed. Of these, 43% (12/28) contained human cells, leukocytes, cell debris, and *Candida* species, with *C. albicans* in 28% of specimens. For CFU reproducibility, 73 patients (219 specimens) were included. A statistical analysis revealed no significant differences in CFU counts across the three samples ($p=0.1499$). However, 31% of patients showed a variability of 10^1 CFU/mL, 15% of 10^2 CFU/mL, and 8% of 10^3 CFU/mL between samples. The most frequently identified species was *C. albicans* (53%).

Conclusions

The presence of white aggregates in UTC samples may include *Candida* species, but they are no reliable diagnostic marker for *Candida* UTIs. Additionally, CFU counting is an unreliable diagnostic tool due to considerable variability for different patients. These findings highlight the need for more accurate methods to diagnose *Candida* UTIs effectively, avoiding potential misdiagnosis and inappropriate antifungal treatment.

PI-04

Terbinafine-resistant *Trichophyton indotineae* infection: A case report

V. L. Müller[1], M. Vidakovic[1], S. Uhrlaß[2], P. Nenoff[2], A. Kreuter[1]
[1]Helios St. Johannes Klinikum Duisburg, Dermatologie, Duisburg, Germany
[2]labopart - Medizinische Laboratorien, Labor Leipzig-Mölbis, Partnerschaft Dr. Michael Gerber, Prof. Frank Bühling, Prof. Pietro Nenoff, Tobias Löwe, Erik von Rein, Rötha OT Mölbis, Germany

Introduction

Trichophyton indotineae has recently emerged as a global cause of treatment-resistant dermatophytoses. Terbinafine resistance, often due to squalene epoxidase (SQLE) gene mutations, presents major clinical challenges.

Objective

To report a case of terbinafine-resistant *T. indotineae* and discuss diagnostic and therapeutic strategies.

Patient & Methods

A 40-year-old Syrian woman presented with a 3-month history of annular, pruritic skin lesions. Her husband had similar symptoms. Despite oral terbinafine (250 mg/day for 3 weeks), no improvement was observed. Microscopy and culture identified *T. mentagrophytes*. Due to treatment failure, ITS rDNA sequencing was performed.

Results

Molecular analysis confirmed *T. indotineae* (100% identity). Resistance testing revealed an SQLE F397L mutation, indicating terbinafine resistance. Oral itraconazole (200 mg/day) led

to significant improvement within 2 weeks and near-complete remission after 8 weeks. Hygiene measures were implemented to prevent reinfection and transmission.

Conclusion

This case underliness the importance of molecular diagnostics in chronic dermatophytoses. In areas with rising terbinafine resistance, *T. indotineae* should be considered. Itraconazole is an effective alternative. Hygiene education is essential for control and prevention.

References

1. Uhrlaß S, Verma SB, Gräser Y, et al. Trichophyton indotineae—An Emerging Pathogen Causing Recalcitrant Dermatophytoses in India and Worldwide—A Multidimensional Perspective. *J Fungi (Basel)*. 2022;8(7):757.
2. Nenoff P, Verma SB, Ebert A, et al. Spread of Terbinafine-Resistant Trichophyton mentagrophytes Type VIII (India) in Germany—"The Tip of the Iceberg?" *J Fungi (Basel)*. 2020;6(4):207.
3. Khurana A, Masih A, Chowdhary A, et al. Correlation of In Vitro Susceptibility Based on MICs and Squalene Epoxidase Mutations with Clinical Response to Terbinafine in Patients with Tinea Corporis/Cruris. *Antimicrob Agents Chemother*. 2018;62(12):e01038-18.

Figure 1

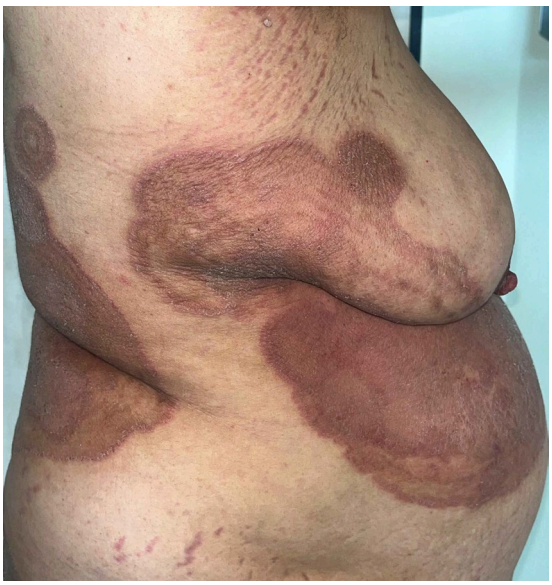
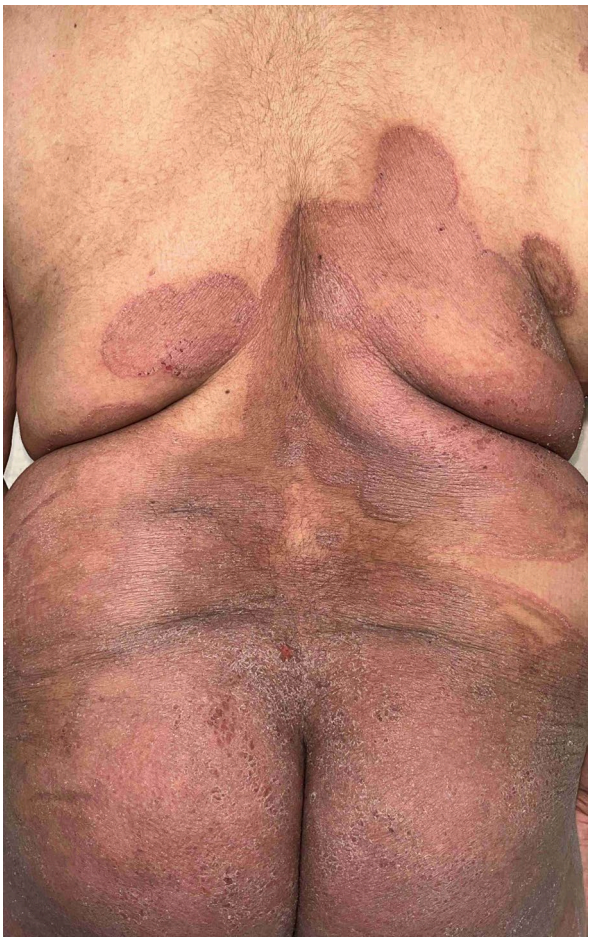


Figure 2



PI-05

Neurotropic fungal infection caused by *Cladophialophora bantiana*: Novel insights into antifungal susceptibility and genomic characterization

K. Spettel[1,2], F. Lötsch[1], R. Kriz[2], F. Thalhammer[3], S. Frank[1], M. Thurnher[4], B. Willinger[1]
[1]Medizinische Universität Wien, Klinisches Institut für Labormedizin, Abteilung für klinische Mikrobiologie, Wien, Austria
[2]FH Campus Wien, Biomedizinische Analytik, Wien, Austria
[3]Medizinische Universität Wien, Universitätsklinik für Urologie, Wien, Austria
[4]Medizinische Universität Wien, Universitätsklinik für Radiologie und Nuklearmedizin, Wien, Austria

Introduction

Cladophialophora bantiana is a neurotropic fungal organism capable of causing rare but life-threatening infections of the central nervous system and represents a significant clinical challenge. Due to its classification as a biosafety level 3 pathogen, handling *C. bantiana* requires stringent laboratory safety protocols, which often hinder broader research efforts. As a result, available data on antifungal susceptibility remain scarce, making treatment decisions particularly difficult.

Methods

We describe a case of a chronic cerebral infection caused by *C. bantiana* in a male patient from Austria, with neurological symptoms persisting over several years. Antifungal susceptibility testing was conducted following the EUCAST microdilution methodology including new antifungals such as olorofim and manogepix. Whole genome sequencing (WGS) was also used to provide comprehensive genetic characterization of the fungal strain.

Results

The susceptibility testing revealed variable MIC results. Fluconazole (64–128 mg/L) and olorofim (>8 mg/L) showed high MIC values, indicating limited activity. Amphotericin B demonstrated intermediate efficacy with an MIC of 2 mg/L. In contrast, lower MIC values were noted for manogepix (0.032–0.064 mg/L), posaconazole (0.032 mg/L), voriconazole (0.5 mg/L), and 5-flucytosine (0.125–0.25 mg/L), suggesting that these agents may be considered as potential treatment options, contingent on further clinical considerations.

Discussion

This study presents the first detailed MIC profile for *C. bantiana*, offering new insights into the pathogen's antifungal susceptibility. The genomic sequencing offered a more detailed understanding of antifungal targets, resistance mechanisms, and phylogenetic relationships, thereby strengthening the basis for optimized therapeutic strategies against this rare neurotropic pathogen.

PI-06

Trichophyton quinckeanum: Renaissance of a dermatophyte in Germany

C. Pelzer[1], P. Nenoff[2], D. Koch[2], H. Muetze[2], C. Krueger[2], A. Cozzio[1], S. Uhrlaß[2]
[1]Kantonsspital St. Gallen, Department of Dermatology, Venereology and Allergology, St. Gallen, Switzerland
[2]labopart - Medizinische Laboratorien, Rötha OT Mölbis, Germany

Introduction

Trichophyton (T.) quinckeanum is a zoophilic dermatophyte historically causing mouse favus (a special type of tinea capitis with bowl-shed scaly crusts), transmitted by mice, that was only sporadically detected in Germany for decades. Since 2014 an increasing number of isolates have been found in central Germany, giving rise to dermatophyte skin infections and skin appendix infections like tinea capitis or even kerion Celsi.

Objectives

The goal of this study was to characterize the specific features of dermatophyte infections due to *T. quinckeanum* according to its epidemiology, seasonality, clinical picture, growth properties and mode of transmission.

Methods

We collected the data of 550 isolates of *T. quinckeanum* from Germany between March 2014 and December 2024 in our laboratory in Mölbis, Germany, in order to identify specific

features of the dermatophyte infection. To our knowledge, this is the highest number of cases ever published.

Results

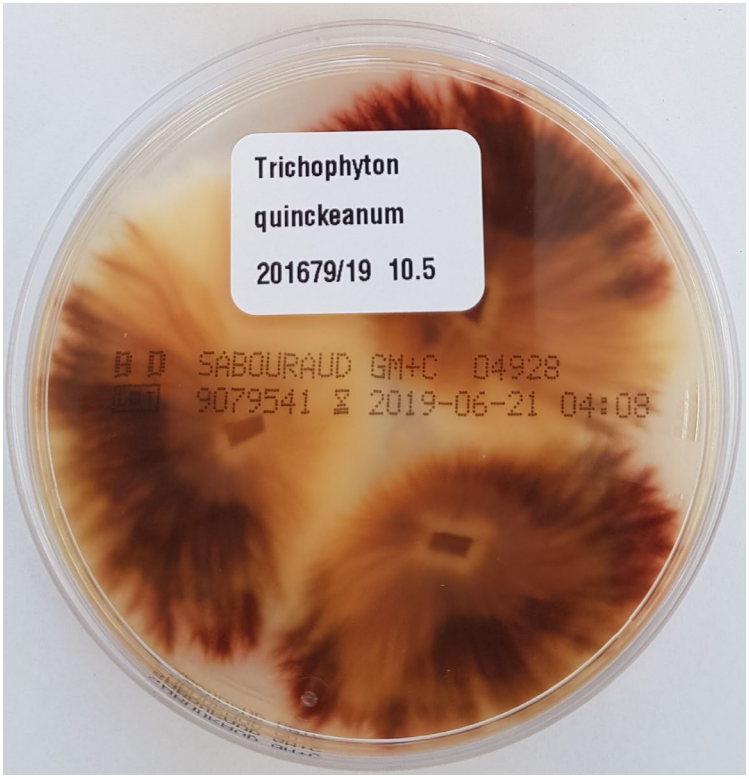
Infection rates show a yearly recurring increase in the second half of the year, whereas infection rates in the first half of the year are typically low. The peak of infections in the current epidemic in central Germany was seen in 2021. However, recent data from 2024 points to another increase. Mainly children, teenagers and young adults are affected. Clinically tinea corporis, faciei/capitis and manuum are predominant, while infections of the feet, nails and groin appear to be low.

Conclusions

T. quinckeanum has now become a relevant pathogen in Germany and surrounding countries. As 2024 data shows, it is to be expected that in the future infection rates will undulate again, possibly correlating with the cyclic mouse population numbers, as they are the main source of infection. Climate change may also play an important role for mouse populations. Transmission to humans typically occurs via an intermediate host like cats (and less likely dogs), which is why pet owners are most at risk.

Figure 1

Figure 2



PI-07

Current practices and challenges in antifungal stewardship for hematological malignancy patients

J. Salmanton-García[1,2,3,4,5,6], E. Gavriilaki[7], P. Evangelidis[7], N. Kotsiou[7], I. Sakellari[7], L. Pagano[8], O. A. Cornely[1,2,3,4,5,6,9]
[1]University of Cologne, Faculty of Medicine and University Hospital Cologne, Köln, Germany
[2]University of Cologne, Institute of Translational Research, Köln, Germany
[3]University of Cologne, Cologne Excellence Cluster On Cellular Stress Responses in Aging-Associated Diseases (CECAD), Köln, Germany
[4]University of Cologne, Department I of Internal Medicine, Köln, Germany
[5]University of Cologne, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD) and Excellence Center for Medical Mycology (ECMM), University of Cologne, Köln, Germany
[6]German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Köln, Germany
[7]Hematology Department - BMT Unit, G. Papanicolaou Hospital, Thessaloniki, Greece
[8]Universita Cattolica del Sacro Cuore, Department of Hematology, Fondazione Policlinico Universitario A. Gemelli -IRCCS-, Rom, Italy
[9]University of Cologne, Clinical Trials Centre Cologne (ZKS Köln), Köln, Germany

Background

Invasive fungal infections (IFIs) are a major cause of morbidity and mortality in patients with hematological malignancies (HM), particularly those undergoing hematopoietic cell transplantation (HCT). Immunosuppressive treatments and HCT increase the risk. While antifungal (AF) prophylaxis is standard, concerns about costs and resistance highlight the need for effective AF stewardship.

Methods

A web-based survey, conducted by the European Hematology Association"s Specialized Working Group on Infections in Hematology, assessed AF stewardship and prescription practices in HM and HCT centers. It included questions on expertise, AF practices, and IFI management, with data collected from July 8 to August 8, 2024.

Results

A total of 258 responses were received, representing departments with a median of 30 beds. The majority of respondents (85.5%) reported that IFIs were managed in consultation with infectious diseases (ID) specialists. However, adherence to ID guidelines was lower in departments with fewer than 30 beds and among professionals with over 15 years of experience. Additionally, inappropriate use of AF agents was more commonly reported by laboratory professionals and those with less than 15 years of experience. AF sensitivity testing was conducted by 78.5% of departments, with a greater frequency in smaller units. Despite this, 39.8% of respondents reported that routine therapeutic drug monitoring (TDM) of AF agents was not performed. Larger departments had a higher prevalence of Aspergillus spp. as the cause of mold infections, compared to smaller ones.

Conclusion

The survey reveals significant variability in AF stewardship across HM centers, particularly in adherence to ID consultancy, AF sensitivity testing, and TDM. Enhancing AF stewardship through tailored clinical guidelines, rapid diagnostics, and routine TDM could improve IFI management and clinical outcomes.

PI-08

Co-treatment with transporter inhibitors distinctly reduces inhibitory concentration levels of itraconazole in azole resistant *Trichophyton indotineae* isolates

A. Günther[1], A. Burmester[1], J. Tittelbach[1], M. Fabri[1], C. Wiegand[1]
[1]*Universitätsklinikum Jena, Klinik für Hautkrankheiten, Jena, Germany*

Many isolates of *Trichophyton indotineae*, a member of the *T. mentagrophytes/ interdigitale* complex exhibit resistance against itraconazole and voriconazole[1]. Resistance mechanisms include amino acid exchanges in the sterol 14-α demethylase gene *Erg11B*[2], as well as two types of *Erg11B* gene amplification[3], which are associated with overexpression of *Erg11B*[3, 4]. Additionally, efflux mechanisms mediated by transporters belonging to subfamilies of multiple drug resistance (MDR) or major facilitator (MFS) contribute to antifungal resistance[4-6]. Therefore, inhibition of fungal efflux transporters using known inhibitors could be a promising strategy to prevent treatment failure.

MLN methods were adapted based on the CLSI protocol with Sabouraud-glucose broth as growth medium. The inhibitory properties of itraconazole in combination with Inhibitors were analyzed in detail. Several *T. indotineae* isolates, previously characterized in a genomic study[3], were tested for known resistance mechanisms and azole resistance type[3].

Co-treatment with chinine hydrochloride and itraconazole did not result in a significant reduction of inhibitory concentration (IC) values in *T. indotineae* isolates. In contrast, ritonavir reduced IC values by 10-20%. The most pronounced effect was observed with sertraline, which, in higher concentrations, inhibited fungal growth independently. When combined with itraconazole, IC values were reduced to below 10% in both sensitive and resistant strains.

Increased resistance of fungi is a growing global health concern. Sertraline shows considerable potential as an adjunct therapy for dermatomycoses.

References

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. Yamada et al. Antimicrob Ag Chemother (2022) 66, e0005922

Poster session II

PII-01

Presence of *Trichophyton tonsurans* between 2008 and 2024 in Germany

G. Devdera[1], S. Uhrlaß[2], Z. Herrmann[2], D. Koch[2], H. Muetze[2], C. Krueger[2], P. Nenoff[2]
[1]*Dermatology practice, Ganna Devdera, Siegen, Germany*
[2]*labopart - Medizinische Laboratorien, Rötha OT Mölbis, Germany*

Introduction

Trichophyton (T.) tonsurans is an anthropophilic dermatophyte known among wrestlers as "mat fungus".

Objective

Dermatomycoses caused by this pathogen have recently been diagnosed more frequently in Germany. A new route of infection is the transmission of *T. tonsurans* in barbershops. Here, the laboratory detection of *T. tonsurans* is evaluated.

Methods

Skin and hair samples from routine examinations were evaluated in the laboratory. Mycological detection of *T. tonsurans* was performed using culture methods. From 2011 onwards, the diagnosis was supplemented by a PCR-ELISA (polymerase chain reaction enzyme immunoassay). To distinguish between morphologically similar dermatophytes, selected dermatophyte strains were identified by sequencing the ITS region of the rDNA. From 2022, RT-PCR with melting curve analysis was also used. Multiple isolates from one patient were counted only once for statistical purposes. If more than three months elapsed between two fungal detections, this was considered a new infection.

Results

T. tonsurans was a rarely diagnosed dermatophyte for many years. Until 2014, a maximum of 10 isolates were found per year. In 2015, the detection rate rose to 20 per year for the first time. From 2017 to 2019, there was a significant increase to 38 to 71 *T. tonsurans* per year due to an outbreak at the wrestling club Leipzig. From 2020 onwards, there was an even greater increase in *T. tonsurans*. Detection rates rose from 101 per year to 347 (2023) and 538 (2024). The average age of patients is between 15 and 20 years.

Conclusions

Dermatophytoses caused by *T. tonsurans* have been rare to date. However, since 2015, an initially slow increase in the prevalence of this highly contagious dermatophyte has been observed. This was accompanied by infections in the field of martial arts. Since the end of 2019 and the beginning of 2020, there has been an increase in tinea capitis, tinea barbae and tinea faciei following visits to barbershops.

Figure 1

PII-02

Clinical insights into invasive Aspergillosis among immunosuppressed patients: a single-centre experience from Argentina

J. Salmanton-García[1,2,3,4,5,6], J. Carballo[7], C. Bergallo[7], F. Romero[7], B. Palacio[7], L. Luque-Aguada[7], M. Marino[7], F. Riera[7,8,9,10]
[1]University of Cologne, Faculty of Medicine and University Hospital Cologne, Köln, Germany
[2]University of Cologne, Institute of Translational Research, Köln, Germany
[3]University of Cologne, Cologne Excellence Cluster On Cellular Stress Responses in Aging-Associated Diseases (CECAD), Köln, Germany
[4]University of Cologne, Department I of Internal Medicine, Köln, Germany
[5]University of Cologne, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD) and Excellence Center for Medical Mycology (ECMM), University of Cologne, Köln, Germany
[6]German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Köln, Germany
[7]Sanatorio Allende, Division of Infectious Diseases, Córdoba, Argentina
[8]Research Group of Immunology and Mycology, Córdoba, Argentina
[9]Universidad Nacional de Córdoba, Facultad de Medicina, Córdoba, Argentina
[10]Universidad Nacional de Córdoba, Primera Cátedra de Infectología, Córdoba, Argentina

Introduction

Invasive aspergillosis poses a significant threat to immunocompromised individuals. Diagnostic criteria incorporating biomarkers and imaging have improved identification and treatment options have expanded. However, in Argentina, diverse patient demographics and environmental factors add complexity to managing this infection. This study aims to explore

the epidemiology, diagnostic methods, and treatment of invasive aspergillosis in an Argentine hospital setting.

Methods

We collected data from patients suspected of invasive aspergillosis at our hospital in Central-Northern Argentina. Variables included demographics, underlying conditions, diagnostic criteria, treatment, and outcomes.

Results

With a median age of 44.5 years and a 51% of male patients, our institution conducted invasive aspergillosis screenings on 192 patients, many of whom were battling malignancies (90%). One third of them had the infection set as probable or possible. Imaging (31%) and positive microbiological results (16%) were examples of diagnostic evidence. With an overall mortality rate of 15%, half of the patients got antifungal treatment for a median of seven days. Mortality among the diagnosed patients was 22%; no specific treatments or cavitations were correlated with pulmonary nodules. Patients without HSCT had a high death rate (31%), however this difference was not statistically significant, as were patients with pulmonary nodules (15%). There were no discernible variations in mortality according to the type of treatment received.

Conclusion

This study provides insights into the epidemiology, diagnosis, and treatment of invasive aspergillosis in an Argentine hospital setting. Our study reveals that invasive aspergillosis remains a significant issue in high-risk patients despite prophylaxis, with a high diagnostic yield from CT scans and a notable mortality rate, particularly among those with pulmonary nodules.

PII-03

DBRMC – A novel database for resistance mutations in *Candida*

R. Kriz[1], K. Spettel[2,1], S. Galazka[3], N. Schweitzer[2], A. Graf[4], B. Willinger[2]
[1]FH Campus Wien, Biomedizinische Analytik, Wien, Austria
[2]Medizinische Universität Wien, Klinisches Institut für Labormedizin, Abteilung für klinische Mikrobiologie, Wien, Austria
[3]Agentur für Gesundheit und Ernährungssicherheit, Abteilung für integrative Risikobewertung, Daten und Statistik, Wien, Austria
[4]FH Campus Wien, Department für Applied Life Sciences, Bioengineering und Bioinformatik, Wien, Austria

Introduction

A major challenge in antifungal resistance research is distinguishing resistance mutations from natural genetic variations. Data on such mutations are scarce, fragmented, and inconsistently reported. To address this, we developed the Database for Resistance Mutations in *Candida* (DBRMC), a curated and structured resource that compiles genetic variants linked to antifungal resistance and enables their systematic evaluation in both research and diagnostic settings.

Methods

Resistance data were generated from 266 clinical isolates of *Candida albicans* and *Nakaseomyces glabratus*, focusing on eight key resistance genes. We designed a multiplex long-range PCR protocol enabling simultaneous amplification of all targets in a single reaction, providing a cost-effective alternative to whole-genome sequencing. Amplicons were sequenced on the Illumina MiSeq platform. Antifungal susceptibility was assessed for up to 12 agents and correlated with genetic findings. Variants were identified using a custom Python-based pipeline and integrated into an SQLite-backed relational database with a web interface.

Results

More than 3,500 mutations, representing 290 distinct types, were identified and systematically linked to antifungal susceptibility profiles. The database allows filtering by gene, mutation type, antifungal agent, and isolate metadata. Functional predictions and mutation frequency were used to highlight variants potentially involved in resistance.

Discussion

DBRMC provides a comprehensive collection of resistance-associated mutations linked to phenotypic data. By integrating genomic and susceptibility profiles, it enables the identification and prioritization of clinically relevant variants. The resource is designed to support research, surveillance, and the development of molecular diagnostics for antifungal resistance.

PII-04

Invasive fungal infections in B-cell lymphoma

S. Krishnan[1], N. Inadze[2], K. A. Merga[1], S. Vielreicher[1], S. M. Peter[1], C. Kosan[2], I. D. Jacobsen[1]
[1]Leibniz Institute on Natural Product Research and Infection Biology – Hans Knöll Institute (HKI), Jena, Germany
[2]Friedrich Schiller university, Center for molecular Biomedicine, Jena, Germany

Invasive fungal infections, including aspergillosis and disseminated candidiasis, are life-threatening conditions with a mortality rate exceeding 30% despite treatment. One significant factor contributing to this high mortality is the host's inadequate immune response, which can result from an underlying disease or the treatment of that disease. We aimed to investigate whether B-cell lymphoma influences susceptibility to fungal infections. To this end, C57BL/6 wildtype mice and Eμ-Myc transgenic mice, a model of B-lymphoma with varying stages of the disease, were challenged intranasally with *A. fumigatus*.

Bone marrow analysis revealed increased Lin− cells, while LSK and LK populations were reduced. Alternatively, a decreasing trend was observed in the CLP population. This indicates potential stem cell exhaustion and possible lymphoid suppression. In contrast, the CMP, GMP, and MEP numbers remained unchanged, suggesting that myeloid progenitor maintenance is preserved. Blood analysis showed normal mature myeloid and lymphoid cell counts; however, platelet counts were reduced. This reduction may be attributed to infection-induced suppression of thrombopoiesis or platelet consumption. These findings suggest a complex interaction between lymphoma and fungal infection, leading to selective hematopoietic remodelling that favours the maintenance of the myeloid lineage while impairing platelet production.

This preliminary study shows that lymphoma negatively affects antifungal immunity. Further investigations are underway to determine if tumour-associated changes are pathogen-specific and cytokine-influenced. In the future, these mouse models combining infection with an underlying disease can also be used to determine if the type of underlying disease affects the efficacy of antifungal therapies.

Keywords: *A. fumigatus*; B-Lymphoma; Bone marrow; Immunophenotyping; Transgenic mice

PII-05

The effect of lung colonisation with *Candida albicans* on *Staphylococcus aureus* infection

T. Köhler[1], N. Nieuwenhuizen[1], E. Ibrahim[2], I. D. Jacobsen[3], T. Hertlein[2], M. Batliner[1], W. Böhnke[3], A. Schöninger[1], K. Ohlsen[2], O. Kurzai[1,3]
[1]Universitätsklinikum Würzburg, Institut für Hygiene und medizinische Mikrobiologie, Würzburg, Germany
[2]Universitätsklinikum Würzburg, Institut für Molekulare Infektionsbiologie, Würzburg, Germany
[3]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Microbial Immunology, Jena, Germany

Background

The fungus *C. albicans* and the bacterium *S. aureus* are both commensal organisms that can cause severe systemic infections in immunocompromised patients and are often co-isolated. However, whereas *S. aureus* can cause pneumonia in mechanically ventilated patients and disseminate from the lung, *C. albicans* almost never causes invasive lung infections. We aim to investigate the different behaviour of *C. albicans* and *S. aureus* in the lung, and the effect of *C. albicans* on *S. aureus* infection.

Methods

We established a novel lung colonisation/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 day 2, lung, liver and kidney bacterial/fungal burdens as well as lung immune responses were analysed.

Results

Following intranasal administration, colony numbers of both *C. albicans* and *S. aureus* declined over time, however, the *C. albicans* Δ*ece1* mutant persisted until day 5. Only *S. aureus* disseminated to the liver and kidney, reflecting the clinical pattern where *C. albicans* does not cause invasive pulmonary infections, whereas *S. aureus* does. Colonisation with *C. albicans* and *S. aureus* increased the recruitment of neutrophils and $CD11b^+$ dendritic cells to the lungs. Cytokine analysis demonstrated a significant upregulation of IL-1β, IL-17, and IL-22 during *C. albicans* colonisation followed by *S. aureus* infection. Pre-colonisation with *C. albicans* conferred protection against lethal *S. aureus* lung infection. Blocking IL-22 abrogated this protective effect, suggesting a key role for IL-22 in mediating resistance to *S. aureus* infection.

Conclusion

We established a murine model that recapitulates *C. albicans* and *S. aureus* colonisation and infection dynamics in the lung. IL-22 appears to be a critical immunological mediator influencing the outcome of *S. aureus* infections.

PII-06

Victory in battle, defeat in war: Navigating isavuconazole implementation at an Argentinian tertiary centre

J. Salmanton-García[1,2,3,4,5,6], C. Niveyro[7], P. A. Villalba-Apestegui[7], V. I. Martín[7], . Compañy-Kec[7], V. E. Sosa[7], G. A. Méndez[7]
[1]University of Cologne, Faculty of Medicine and University Hospital Cologne, Köln, Germany
[2]University of Cologne, Institute of Translational Research, Köln, Germany
[3]University of Cologne, Cologne Excellence Cluster On Cellular Stress Responses in Aging-Associated Diseases (CECAD), Köln, Germany
[4]University of Cologne, Department I of Internal Medicine, Köln, Germany
[5]University of Cologne, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD) and Excellence Center for Medical Mycology (ECMM), University of Cologne, Köln, Germany
[6]German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Köln, Germany
[7]Hospital Escuela de Agudos Dr. Ramón Madariaga, Posadas, Argentina

Introduction

Isavuconazole, a second-generation triazole, is a broad-spectrum antifungal with activity against aspergillosis and mucormycosis. Its favorable safety profile enhances compliance and treatment outcomes.

Methods

We collected data on patients receiving isavuconazole from June 2019 to December 2023 at an Argentinian tertiary care center. Variables included demographics, underlying conditions, imaging, treatment details, and outcomes. Patients were classified using EORTC/MSG criteria for invasive fungal infections (IFI).

Results

Among 45 cases, malignancies were common (60.0%), with 27 cases showing active disease. Imaging findings included pulmonary nodules (66.7%) and ground-glass opacity (62.2%). Breakthrough IFI occurred in 12 cases (26.7%). Isavuconazole was primarily used as first-line therapy (68.9%), with a median duration of 59 days. Patients receiving first-line treatment were significantly older (51 vs. 32 years, p=0.001). At 30 days, 20.0% showed treatment response, while mortality was 15.6%. Pulmonary nodules were significantly more frequent in first-line cases (77.4% vs. 42.9%, p=0.039) and in patients with active IFI at day 30 compared to responders (84.0% vs. 44.4%, p=0.034).

Conclusion

Our findings highlight the complexities of isavuconazole use in clinical practice and the need for further research to optimize its role in IFI management. Mortality was primarily due to underlying disease progression rather than fungal infection, reinforcing the importance of broad-spectrum antifungals with fewer contraindications.

PII-07

Green synthesis, characterization and antimicrobial potential of silver nanoparticles from the mushroom *Ganoderma oregonense*

L. Ofodile[1], O. Victor[1], O. Asulewon[1,2]
[1]*Yaba College of Technology, Biological Science, Lagos, Nigeria*
[2]*Yaba College of Technology, Lagos, Nigeria*

Introduction

The rise of antibiotic-resistance has created an urgent need for alternative antimicrobial agents. Conventional nanoparticle synthesis methods often involve toxic chemicals, making eco-friendly approaches crucial. Mushrooms, rich in bioactive compounds, offer a sustainable source for green nanoparticle synthesis.

Objectives

Silver nanoparticle (AgNPs) was synthesized with the extract of *Ganoderma oregonense*, characterized chemically and morphologically to determine its properties and potential application. Its ability to inhibit some bacteria and fungi compared to conventional antibiotics was tested.

Materials & Methods

Methanol extraction of *Ganoderma oregonese* and the biosynthesis of AgNPs at 80°C were done. X-ray diffraction (XRD), Fourier-transform infrared spectroscopy (FTIR), UV-vis spectroscopy, and scanning electron microscopy (SEM), were also carried out. After which it was screened for antimicrobial activity using *Candida tropicalis, Klebsiella pneumonia, Staphylococcus aureus, Eschericia coli* by paper disc assay. The cultures were prepared using a novel growth media; whole powdered durum wheat waste glucose agar (WPDWWGA) medium, patent number NG/P/2024/91.

Results

XRD analysis confirmed the presence of crystalline structures, diffraction peaks aligning with AgNP formation. FTIR spectra revealed functional groups such as hydroxyl (-OH), carbonyl (C=O), and C–O–C stretching vibrations, suggesting the involvement of bioactive molecules. UV-vis spectroscopy showed a strong absorption peak around 300 nm, characteristic of AgNP surface plasmon resonance. SEM-EDS analysis revealed silver as the dominant element (61.67%), confirming nanoparticle composition. AgNP (1mg/ml) inhibited *Candida tropicalis* (13.8mm), *Klebsiella pneumonia* (13.8 mm) most and least inhibited *Staphylococcus aureus* (10 mm), but better than the streptomycin.

Conclusion

Ganoderma oregonense is a sustainable biogenic source for AgNP synthesis, with antibiotics application.

Figure 1

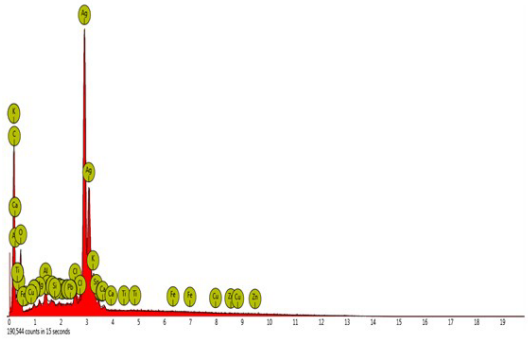


Figure 1: Composition of the Nanoparticle based on Scanning Electron Microscopy analysis (SEM)

Figure 2

Table 1: Antimicrobial activity of the silver nanoparticles from *G. oregonense*

Concentration	*Candida tropicalis*		*Klebsiella pneumoniae*		*Staphylococcus aureus*		*Escherichia coli*	
Nanoparticles	*D1*	*D2*	*D1*	*D2*	*D1*	*D2*	*D1*	*D2*
1mg	$2.25^{A}\pm3.18$	$2.25^{C}\pm3.18$	-	$3.00^{C}\pm0.00$	-	-	-	-
3mg	$4.95^{A}\pm0.07$	$5.05^{D}\pm0.07$	$4.50^{A}\pm0.71$	$5.00^{D}\pm0.00$	$4.00^{A}\pm0.71$	$4.75^{D}\pm0.35$	$5.40^{A}\pm0.14$	$6.45^{C}\pm0.07$
4mg	$10.83^{B}\pm0.76$	$11.33^{E}\pm0.58$	$6.25^{A}\pm1.77$	$6.75^{D}\pm1.06$	$4.17^{A}\pm3.82$	$5.00^{D}\pm4.36$	$9.83^{B}\pm1.26$	$10.00^{E}\pm1.50$
6mg	$12.67^{B}\pm0.76$	$13.17^{E}\pm0.76$	$13.25^{B}\pm1.77$	$13.75^{E}\pm1.77$	$9.50^{B}\pm8.41$	$10.00^{E}\pm9.01$	$11.17^{B}\pm1.61$	$12.00^{E}\pm1.32$
Streptomycin	*D1*	*D2*	*D1*	*D2*	*D1*	*D2*	*D1*	*D2*
6mg	ni	ni	ni	5.00±0.00	ni	ni	ni	ni

Key: ni = no inhibition, D1 = Day 1, D2 = Day 2.

PII-08

Correlation of bifonazole uptake in Bovine Hoof Sheet with *in vitro* antifungal efficacy for improved onychomycosis treatment formulations

U. Bock[1], A. L. Nellessen[2], S. Kappes[2], C. Kolb[3], S. Uhrlaß[4], P. Nenoff[4], A. Lamprecht[2]
[1]*Bock Project Management, Tawern, Germany*
[2]*University of Bonn, Department of Pharmaceutics, Institute of Pharmacy, Bonn, Germany*

[3]*Bayer Vital GmbH, Leverkusen, Germany*
[4]*labopart Medizinische Laboratorien, Rötha, Germany*

Introduction

In topical treatment of onychomycoses, the nail plate poses a significant barrier to the penetration of active pharmaceutical ingredients (APIs), which complicates the development of clinically effective formulations [1]. Predictive screenings to ensure penetration of antimycotic formulations are therefore essential. Bovine hoof sheet (BHS) is often used as a surrogate for human nail in *in vitro* permeation studies, however, data on API penetration into nail plate and its correlation with *in vitro* efficacy against pathogens is limited.

Objectives

This study investigates the correlation between bifonazole (BFZ) uptake in BHS from commercial formulations and BFZ in dimethyl sulfoxide (DMSO) reference solutions to the *in vitro* efficacy against *T. rubrum*.

Materials & Methods

Formulations included 1% (w/w) BFZ from Canesten® Extra Salbe (SAL) and Canesten® Extra Creme (CRE), along with BFZ solutions in DMSO at 10, 100, and 1000 µg/mL. BFZ uptake was analyzed by HPLC-UV after 1 day of incubation with DMSO and after 1 and 7 days with SAL and CRE. Following BFZ exposure in DMSO, BHS were incubated with *T. rubrum* for seven days, and the zones of inhibition were measured.

Results

After 1 day, BFZ mean uptake from SAL (44.2 µg BFZ per mL BHS) and CRE (26.4 µg/mL) was similar to that from 100 µg/mL DMSO (11.8 µg/mL) which demonstrate early inhibition on *T. rubrum*. Uptake of SAL was greater CRE likely due to the permeation enhancer urea [2]. After 7 days, uptake from SAL (159.5 µg/mL) approached that of 1000 µg/mL BFZ in DMSO (209.4 µg/mL), resulting in a significant zone of inhibition against *T. rubrum*.

Conclusion

This *in vitro* study demonstrates that correlating API uptake by BHS with inhibition zones against relevant pathogen *T. rubrum*, compared to reference solutions, offers a rapid and effective screening method for formulating topical antimycotics prior to *in vivo* testing.

References

1. Kobayashi *et al.,* J. Pharm. Pharmacol., 1999; 2. Kappes *et al.,* Pharmaceutics,2021

PII-09

***Spread of Trichophyton indotineae* (*Trichophyton mentagrophytes* ITS genotype VIII) after 6 years of data analysis in Germany**

S. Uhrlaß[1], D. Koch[1], H. Muetze[1], C. Krueger[1], P. Nenoff[1]
[1]*labopart - Medizinische Laboratorien, Rötha OT Mölbis, Germany*

Introduction

Trichophyton (*T.*) *indotineae* is the pathogen responsible for severe dermatophytosis in Asia.

Objective

Since 2018, isolates from patients in Germany with tinea caused by *T. indotineae* have been analysed.

Methods

The dermatophytes were detected by culture and RT-PCR. For confirmation, sequencing of the ITS region of the rDNA was performed on all isolates. Sensitivity tests to terbinafine and itraconazole were performed using the breakpoint method and additional sequencing of the squalene epoxidase gene (SQLE).

Results

T. indotineae was detected in 196 patients from Germany between 2018 and the end of 2024. One strain each from 2016 and 2017 was only identified as *T. indotineae* after the fact. In 2018, individual *T. indotineae* strains were found. From 2019 to 2022, an increase was observed, with between 16 and 23 *T. indotineae* strains found per year. There was a significant increase in patients with dermatophytosis caused by *T. indotineae* in 2023 (47 patients), followed by 2024 (73 patients). Of the 196 patients with dermatophytosis caused by *T. indotineae*, almost two-thirds (64%) were men. Looking at the age distribution, the 21–30 age group dominated with 89 patients (45.4%). *T. indotineae* most commonly caused tinea corporis in patients in Germany (148 out of 193 patients, 77%). In some patients, the disease manifested itself multilocularly. The point mutations associated with terbinafine resistance and the associated amino acid substitutions affected positions 397 (102 strains) and 393 (13 strains) of the SQLE gene. Further amino acid substitutions were found at positions 448, 415, 440 and 443. In 186 strains, 115 (61.8%) were resistant to terbinafine in vitro using the breakpoint test and 11 strains (5.9%) were resistant to itraconazole.

Conclusion

Reliable data on the occurrence of *T. indotineae* in Germany are available. Patients with *T. indotineae* are characterised by the clinical picture of extensive dermatophytosis with severe itching.

Figure 1

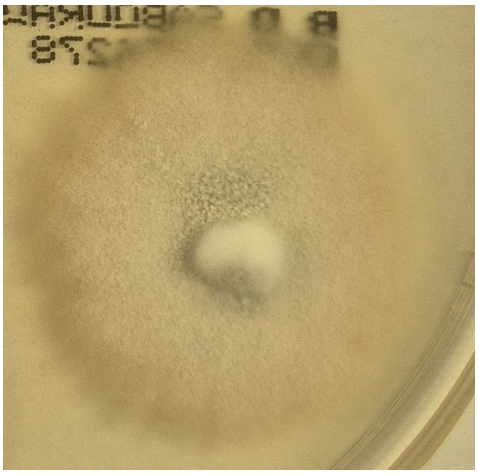
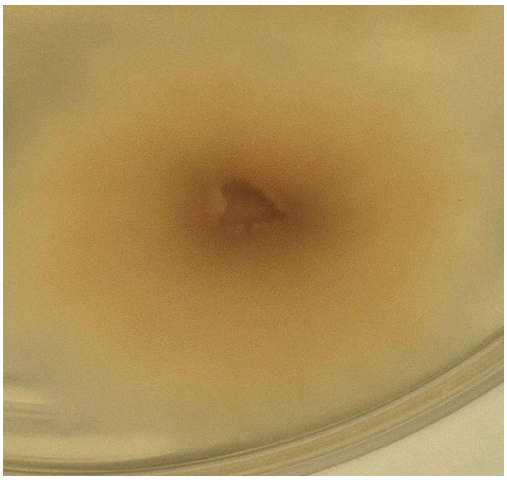


Figure 2



PII-10

The nutritional environment during sporulation alters fitness of *Aspergillus fumigatus* conidia

D. Soltan Esmaeili[1], J. Berges[2], S. Krappmann[1], H. Bruns[2]
[1]Uniklinik Erlangen, Mikrobiologisches Institut– Clinical Microbiology, Immunology and Hygiene, Erlangen, Germany
[2]Universitätsklinikum Erlangen, Medical Clinic 5 – Haematology and Internal Oncology, Erlangen, Germany

Aspergillus fumigatus is a saprophytic filamentous fungus that causes the majority of invasive aspergillosis cases in immunocompromised patients. Its omnipresent, small, and hydrophobic conidia serve as infectious agents. These dormant spores reflect the nutritional conditions supplied by the environment in which they were produced. Multiple factors determine the virulence of *A. fumigatus* in the host, among them its metabolic versatility, but how the nutritional status of this fungal pathogen impacts its interaction with cells of host immunity is rather unexplored. To elucidate the effect of varying sources of carbon and nitrogen on fitness of conidia and their interaction with immune cells, we nutritionally programmed the spores by growing an *A. fumigatus* wild-type isolate on culture media with defined combinations of C- and N-sources and harvesting the resulting asexual spores. Such adapted conidia were tested for fitness under stressful and clinically relevant conditions such as iron limitation, elevated temperature, presence of reactive oxygen species or agents interrupting cell wall integrity, and antifungals. Variation in C- and N- sources resulted in distinct transcriptional responses of genes involved in oxidative stress regulation, indicating that metabolic input strongly influences the activation of antioxidant defense pathways in *A. fumigatus*. Our experimental efforts offer the perspective to gain insights about the influence of metabolic pathways affecting conidial fitness and the cell wall, which serves as a dominant PAMP in fungal pathogen/host interactions.

PII-12

Clinical insights into Mucormycosis among immunosuppressed patients: a multicentre experience from Argentina

J. Salmanton-García[1,2,3,4,5,6], C. Niveyro[7,8], V. E. Sosa[8,9], V. Arce[10], M. A. Aguirre[11], P. A. Villalba-Apestegui[7], V. I. Martín[7,8], . Compañy-Kec[7,8], M. C. Tomasino[7], R. Solari[7], F. R. Achinelli[12], K. Nguyen[1,2,3,4], O. A. Cornely[1,2,3,4,5,6,13], G. A. Méndez[7,8]

[1]*University of Cologne, Faculty of Medicine and University Hospital Cologne, Köln, Germany*
[2]*University of Cologne, Institute of Translational Research, Köln, Germany*
[3]*University of Cologne, Cologne Excellence Cluster On Cellular Stress Responses in Aging-Associated Diseases (CECAD), Köln, Germany*
[4]*University of Cologne, Department I of Internal Medicine, Köln, Germany*
[5]*University of Cologne, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD) and Excellence Center for Medical Mycology (ECMM), University of Cologne, Köln, Germany*
[6]*German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Köln, Germany*
[7]*Hospital Escuela de Agudos Dr. Ramón Madariaga, Posadas, Argentina*
[8]*Universidad Católica de las Misiones, Facultad de Medicina, Misiones, Argentina*
[9]*Laboratorio de Alta Complejidad de Misiones (LACMI), Misiones, Argentina*
[10]*Hospital Julio C. Perrando, Chaco, Argentina*
[11]*Hospital de Alta Complejidad, Pte. Juan Domingo Perón, Formosa, Argentina*
[12]*Hospital Angela I. de Llano, Corrientes, Argentina*
[13]*University of Cologne, Clinical Trials Centre Cologne (ZKS Köln), Köln, Germany*

Introduction

Mucormycosis is a severe fungal infection with high mortality, primarily affecting immunocompromised patients. In Argentina, where healthcare resources are limited, outcomes remain poorly documented. This study evaluates clinical features, risk factors, treatment, and outcomes of mucormycosis patients at tertiary hospitals in Northern Argentina.

Methods

We collected data from mucormycosis patients at four tertiary hospitals between 2010 and 2024. Variables included demographics, underlying conditions, diagnostic criteria, treatment, and outcomes.

Results

Among 31 patients (median age 50 years, 58% male), diabetes mellitus (51%) and immunosuppression (35%) were common risk factors. Infections involved the paranasal sinuses (39%) or extended to the brain (29%). Rhizopus spp. was the predominant pathogen (74%). Imaging was consistent with mucormycosis in 77% of cases.

Liposomal amphotericin B was the most common initial treatment, used alone in 48% and in combination in 10%. Amphotericin B deoxycholate was used in 39%, while posaconazole was the primary salvage therapy (39%). Surgical debridement was performed in 94% of cases.

The overall mortality rate was 45%. Survivors were more likely to be female (64% vs. 35%, $p=0.032$) and had longer treatment durations (61 vs. 14 days, $p<0.001$). Mortality was not significantly associated with underlying conditions, pathogens, or antifungal choice.

Conclusion

Survival was linked to effective clinical management, with liposomal amphotericin B as first-line therapy and posaconazole as salvage treatment. Timely, guideline-driven interventions are crucial for improving outcomes in mucormycosis patients.

PII-13

Fusarium keratoplasticum displays a high virulence potential in a 3D cornea infection model

A. Schöninger[1], A. Zimmermann[2], G. Walther[3], O. Kurzai[1,4,5], R. Martin[1]
[1]*Julius-Maximilians-Universität Würzburg, Institute of Hygiene and Microbiology, Würzburg, Germany*
[2]*Julius-Maximilians-Universität Würzburg, Institute of Hygiene and Microbiology, Würzburg, Germany*
[3]*Hans-Knöll-Institut, Nationales Referenzzentrum für Invasive Pilzinfektionen, Jena, Germany*
[4]*Hans-Knöll-Institut, Research Group Fungal Septomics, Jena, Germany*
[5]*Hans-Knöll-Institut, Nationales Referenzzentrum für Invasive Pilzinfektionen, Jena, Germany*

Introduction

Fungal keratitis is an infection of the human eye which frequently leads to a loss of eyesight or even the whole eye. Members of the *Fusarium solani* species complex (FSSC) are major causes of this disease. However, the underlying fungal pathogenicity mechanisms are not well understood, partially caused by the lack of suitable complex in vitro infection models.

Aims

To address the question of how FSSC species invade human cornea cells, we examined keratitis isolates of the FSSC species *F. falciforme*, *F. keratoplasticum* and *F. petroliphilum* in different *in-vitro* infection models.

Material and Methods

FSSC strains were obtained by the German National Reference Center for Invasive Fungal Infections (NRZMyk) and were originally isolated from patients with diagnosed fungal keratitis. We infected either monolayers of the hTCEpi cornea cell line or a hemi-cornea 3 model which consisted of a multilayer eptithelium of hTCEpi cells, and a stromal layer made of collagen and primary human fibroblasts. Fluorescence and electron microscopy were used to study the invasion of fungal cells. Host cell damage was measured by the release of lactate dehydrogenase (LDH).

Results

In both used in-vitro infection models, *F. keratoplasticum* emerged as the most virulent species, showing extensive invasion and causing massive host cell damage. As shown by electron microscopy, filaments of this species were able to induce the formation of trans cellular tunnels between infected host cells. In contrast to *F. keratoplasticum*, the capacities for invasion and damage were limited in the other two tested FSSC species.

Conclusion

Our results indicate a good adaptation of *F. keratoplasticum* to the ecological niche of the human eye and to further invade and destroy human cornea cells. The formation of trans cellular tunnels might be beneficial for immune evasion and nutrient acquisition.

PII-15

Activin A in the response to *Candida albicans* infection

N. Nieuwenhuizen[1], R. Sprute[2,3], G. Braune[1], J. Patitz[1], A. Shehata[1,4], K. Hünniger-Ast[1,4], O. A. Cornely[2,3]
[1]Julius-Maximilians-Universität Würzburg, Institute of Hygiene and Microbiology, Würzburg, Germany
[2]University of Cologne, Faculty of Medicine and University Hospital Cologne, Köln, Germany
[3]German Centre for Infection Research (DZIF), Köln, Germany
[4]Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie e. V. – Hans-Knöll-Institut (HKI), Fungal Septomics, Jena, Germany

Introduction

The cytokine activin A is a member of the TGF-beta superfamily. Activin A exhibits a wide range of effects on both innate and adaptive immune cells, including the differentiation of Th17 cells, regulated in a context and spatiotemporal-dependent manner. To date, no studies have examined the presence or functions of activin A during fungal infection.

Objective

We aim to determine whether activin A is raised in response to infection with *Candida albicans* and whether it plays a role in the outcome of infection.

Patients & Methods

Peripheral blood was collected from healthy volunteers and neutrophils and monocytes were isolated by magnetic bead sorting. Cells were infected with *Candida albicans* and cell supernatants were collected for measurement of activin A by ELISA. In addition, activin A was measured in the serum of patients with diagnosed candidiasis and in healthy donors.

Results

Activin A was significantly raised after infection of both monocytes and neutrophils with *C. albicans* compared to mock-infected controls. Pre-opsonization of *C. albicans* before neutrophil infection did not alter activin A levels compared to non-opsonized *C. albicans*, suggesting that the activin A may be induced by a pathogen component. In candidiasis patients, serum activin A levels were significantly increased and tended to be higher in patients with polymicrobial infections.

Conclusion

C. albicans infection triggers the release of activin A by human monocytes and neutrophils. In future studies, we will neutralize activin A signalling in whole blood assays and in mouse models of *C. albicans* infection to determine its role in the immune response to fungal infection.

Further Abstracts

OC-01

Dem Pionier der medizinischen Mykologie Friedrich Staib zum 100. Geburtstag

B. Buchberger[1,2], V. Rickerts[1]
[1]Robert Koch-Institut, Berlin, Germany
[2]Universität Essen-Duisburg, Institute for Health Care Management and Research, Essen, Germany

Zu Beginn des akademischen Werdegangs von Friedrich Staib in den 1950er Jahren war die medizinische Mykologie in Deutschland ein junges Fach, in dem überwiegend zu klinischen Fragen aus Dermatologie und Gynäkologie geforscht wurde. Systemische Mykosen galten als äußerst selten. Aufgrund besserer Behandlungsmöglichkeiten bakterieller Infektionen, der Einführung zytotoxischer Chemotherapeutika und Immunsuppressiva gewannen Systemmykosen zunehmend an Bedeutung, insbesondere durch Ausbreitung des HI-Virus ab 1980.

Auf der Basis von Literatur und Interviews mit Wegbegleitern, Doktoranden und der Familie wird der Wissenschaftler Staib und seine international geschätzte Forschung vorgestellt.

Nach Einberufung zur Wehrmacht und Kriegsgefangenschaft studierte Staib Veterinär- und Humanmedizin in München und Würzburg und wurde doppelt promoviert. 1953 begann er mit dem Aufbau eines mykologischen Labors am Institut für Hygiene und Mikrobiologie der Universität Würzburg und habilitierte sich 1962 im Fach Mikrobiologie. Von 1968 bis 1990 wirkte er am Robert Koch-Institut in Berlin als Leiter des Fachgebiets Mykologie, zu dessen internationalem Ruf er wesentlich beitrug. Intensiv und mit großem Einfluss auf Forschungserfolge pflegte er die Zusammenarbeit mit klinisch tätigen Ärzten.

Schwerpunkte seiner Arbeit waren die Verbesserung der Diagnostik von Mykosen und die Vertiefung des Verständnisses für Pathogenitätsmechanismen von Pilzen. Internationale Anerkennung fand Staibs Forschung zu *Cryptococcus neoformans* (Staib-Agar-Indikatormedium auf Basis des Virulenzfaktors Melanin zur Anzucht aus nicht sterilen klinischen und Umweltproben). Daneben beschrieb er sezernierte Proteasen von *Candida albicans* als Virulenzmechanismus.

Staibs breites Interesse von Pilzdiagnostik, fungalen Virulenzfaktoren bis hin zu Umweltnischen von Mykoseerregern war in einer Zeit zunehmender Bedeutung von Systemmykosen richtungsweisend für die medizinische Mykologie in Deutschland und weit darüber hinaus.

No abstract available / Talks cancelled:

S2-01; S2-06; 3-03; S7-02; S7-03; S10-04

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