S8.3d Characterization of glycylcephalosporin/cephalosporin-resistant espyrto protein in Candida glabrata Role in pathogenicity
Reinder Kaur
Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad, India
S8.3 Hoon the Pungal Cat Wall Gican Can Modulate the Immune Response?, September 23, 2022, 3:00 PM - 4:10 PM
Candida glabrata is the second most frequent most pathogen found in Candida bloodstream infections, depending upon the geographical location. C. glabrata, which belongs to the Nakasonea clade, possesses a distinct set of virulence attributes which can be either acquired or pre-established in macrophages, adhere to host cells and bacterial surface and survive a wide range of stresses. Our research is focused on unraveling the strategies that C. glabrata employs to survive the nutrient-poor hostile environment and evade host immune responses. Toward this end, we are delineating the cellular processes, that are involved in these pathways. Furthermore, we are also exploring whether these pathways are specific to C. glabrata, or are shared by other members of the same clade. These findings underline the importance of multidrug resistance C. glabrata is a serious threat.

S8.4b Population biology of hedgehog fungus Tephrocytopus erinacei
Vit Hulka1
1Charles University, Faculty of Science, Prague, Czech Republic
S8.4b Cause of animal mycoses, September 23, 2022, 3:00 PM - 4:30 PM
Tephrocytopus erinacei is a main cause of dematiaceous fungi in hedgehogs and is currently reported from human infections worldwide. It is found in wild European hedgehogs (Erinaceus europaeus) but also in the African four-toed hedgehog (Atelerix albiventris), a popular pet animal worldwide. Little is known about the reservoir and population genetics of this pathogen despite its increasing importance in clinical practice. Notably, whether there are different populations or even species associated with different hosts or geographic regions is not known. To answer these questions, we collected 161 isolates, performed molecular analyses, determined genotypes and identified morphological and physiological differences. Multiple phylogenetic and morphology analysis supported T. erinacei as a morphological species, in contrast to highly incongruent results among different molecular markers in previous studies. Our multilocus analysis identified distinct genotypes, one mainly linked to hedgehogs and the second to Erinaceus. These results shed light on the validity of mycolopsis hybrid in combination with other clinical molecular markers to understand the species boundaries of dematiaceous fungi.

S8.5c MLST genotyping and phylogenetics of AD-hybrids
Massimo Cogliati,1 Min Chen1, Jinyu Xu1, Megan Hitchcock,1 Junse Xia1, Cong-Hong Yang1,2, Violker Robert1, mans Deen Oliveira1, Joan-Enric Silve1, Walter Meier1,2, Magdalena Florea1,3, Ursula Neumeier4,5, Patricia Escardón6, Andreas Puhl7, Frederik Rogler8,15, Sebastien Bertolino9
1Institut f. Medizin. Mikrobiologie, Universitaets-Klinik Heidelberg, Germany 2Zentrum f. Molekulare Medizin, Campus Benjamin Franklin, Berlin, Germany 3Istituto di Micologia, Universita’ di Firenze, Firenze, Italy 4Zhejiang Hospital, Shanghai, China 5McMaster University, Hamilton, Canada 6IPPC, Beijing, China 7Robert Koch Institute, Berlin, Germany 8Institut Pasteur, Paris, France 9University of Brighton, Brighton, UK 10Sydney University, Sydney, Australia 11Gurtin University, Perth, Australia 12University of Wroclaw, Wroclaw, Poland 13Institut Pasteur, Paris, France 14Ministerio de Salud Pública, Instituto de Higencia, Montevideo, Uruguay 15University of Montpellier, Montpellier, France
S8.5a Genotyping of Cryptococcus neoformans and C. gattii, September 23, 2022, 3:00 PM - 4:30 PM
Objectives: In a previous study a set of new molecular-type-specific primers were designed to apply the standard DHSAM consumes multi-locus sequence typing (MLST) scheme to Cryptococcus neoformans AD-hybrids. In the present study, we report the preliminary results of the investigations by MLST of a large number of AD hybrids with the aim to identify the circulating genotypes, their phylogenetic relationships.
Methods: A total of 50 AD hybrids isolates were analyzed by performing MLST analysis. The strategies and the results of the study will be reported at the conference.

Conclusions: These preliminary results suggest that the AD hybrids have evolved independently from the mating of a haploid very common in both clinical and environmental isolates and AD haploids that are not circulating at present or very rare. Therefore, it is likely that AD hybrids originated in the environment where VNN gattii/neoformans diversity is higher and suitable AD combinations can occur. Sequencing of further AD hybrids is in progress to confirm these results.

S8.5d Cryptococcus neoformans and Cryptococcus gattii clinical isolates from Colombia develop heteroresistance to fluconazole at high concentrations
Javier Meiller1, Silvia Carvalho-Valencia1, Patricia Escardón3, Camilla Farinacite1
1Studies in Translational Microbiology and Emerging Infectious Disease Research Group (MICROS), School of Medicine and Health Sciences, Universidad Del Rosario, Bogota, Colombia 2Group of Microbiology, National Institute of Health, Bogota, Colombia
S8.5a Genotyping of Cryptococcus neoformans and C. gattii, September 23, 2022, 3:00 PM - 4:30 PM
Introduction: Cryptococcus is a worldwide mycoses caused by Cryptococcus neoformans and Cryptococcus gattii. Although resistance to antifungals is inefrective, isolates with decreased susceptibility to fluconazole have been reported globally, including Colombia, which may be due to 1) heteroresistance, defined as the ability to adapt to increasing concentrations of this antifungal compound, and 2 point mutations in the ERG11 gene encoding the fluconazole target enzyme, lanosterol 14α-demethylase.
Objective: To determine the development of heteroresistance to fluconazole in C. neoformans and C. gattii clinical isolates from Colombia and to evaluate and sequent ERG11 gene of the isolates to study for mutations that might characterize resistant or heteroresistant phenotype.
Methods: The minimum inhibitory concentration (MIC) to fluconazole was determined in 38 and 24 isolates of C. neoformans and C. gattii, respectively, using broth microdilution. Heteroresistance was evaluated by placing each isolate on twoYPD agar that contained fluconazole at concentrations equal to the MIC of each isolate. Heteroresistant colonies were then replated in increasing concentrations of fluconazole. Results: All isolates were susceptible to fluconazole with MICs of 1 g/ml (n = 1), 2 g/ml (n = 4), 4 g/ml (n = 17), 8 g/ml (n = 23), 16 g/ml (n = 5), and 32 g/ml (n = 1). However, all isolates developed heteroresistance colonies, with increased MICs 4 g/ml (n = 2) and 8 g/ml (n = 1). To elucidate this process, genotypes and function of C. neoformans in pate joke, were performed. These findings underline the importance of multidrug resistance C. neoformans and pathogenic C. gattii will be presented.
discovery (Yi et al., 2021). We herein screened ~2000 crude extracts from mycobiota in an in situ C. albicans-mammalian epithelial cell infection model. Typically, when oral epithelial cells (TR146) are infected by C. albicans, the fungus proliferates, forms hyphae, and invades and damages the monolayer. In our assay, we estimate the damage to epithelial cells by released lactate dehydrogenase. We also note changes to the growth and morphology of the fungus. Based on these readouts we assign antivirulence and antifungal ranks to each extract, and confirm top-ranked hits with an independent prophylactic stable-based assay for host cell damage, and a colorimetric assay of fungal metabolic activity. We found that several of the top-ranked antifungal extracts also showed effects on a multi-drug resistant strain of C. albicans.

Using an established pipeline, we identified several of the antifungal and antivirulent bioactive components in these extracts. After scaling the production of promising lead compounds, we will test their druggability on clinical Candida spp. strains, and identify their mode of action using large-scale Candida spp. knock-out libraries and multi-omics approaches.

Our novel extracts are likely to contain new classes of non-toxic antifungals that can potentially treat infections by multi-drug resistant fungi. We identified and confirmed several mycobiota extracts that protected mammalian epithelial cells without severely affecting the fungus’ growth, which are, therefore, considered antivirulent.

5. Kumanan, C.A., Groszny, M.S., Holb, B., 2020. The gut, the bad and the harmless. Candida albicans as a commensal and opportunistic pathogen in the intestine. Curr. Opin. Microbiol. 54, 7–13. https://doi.org/10.1016/j.mib.2020.09.006
6. Vui, B., Holb, B., Brink, K., 2021. Uncharted territories in the discovery of antifungal and antivirulence natural products from bacteria. Comput. Struct. Biotechnol. J. 19, 1244–1252. https://doi.org/10.1016/j.csbj.2021.02.013

52.4a
Oral infections by melanized fungi Curvularia lunata and Lasiodiplodia theobromae: Antifungal susceptibility and clinical outcome
Sanhitra Mitra, Prashant Garg, Somaiahala Murthy, Vivek Pravin Dave
LV Prasad Eye Institute, Hyderabad, Hyderabad, India

55.4 Free oral presentations (late breaking), September 23, 2022, 4:45 PM - 6:15 PM

Purpose: To report antifungal susceptibility and clinical correlations in melanized fungal isolates of Curvularia lunata and Lasiodiplodia theobromae from ocular infections.

Methods: Antifungal susceptibility testing was performed by broth microdilution testing, following Clinical and Laboratory Standard Institute guidelines, of 17 C. lunata and 11 L. theobromae isolates from monomicrobial infections of microbial keratitis or fungal endophthalmitis patients. Isolates resistant to ≥2 classes of antifungals were considered as multidrug-resistant (MDR). The panel of antifungals tested were amphotericin B, natamycin, voriconazole, fluconazole, itraconazole, posaconazole, and caspofungin.

Results: Voriconazole showed the highest susceptibility (83.3% isolates) followed by natamycin (80%), fluconazole (80%), itraconazole (74.7%), ketoconazole (70%), posaconazole, and caspofungin (66.7%-70%) and least amphotericin B (63.5%).

For treatment, all patients received topical natamycin, and few received additional oral ketoconazole or intravenous voriconazole. MDR isolates led to the poorer clinical outcomes (P<0.05) in patients. But natamycin resistance alone did not show unfavorable outcomes (P>0.25), though this was the most frequent drug used topically in fungal ocular infections.

Conclusions: Melanized fungi causing ocular infections have varying susceptibility to different antifungal agents. Most effective drug as seen in vitro in our study was voriconazole. Significant resistance to amphotericin B, which is the most common antifungal used in intravitreal injections, was noted. MDR isolates overall had poorer clinical outcomes.

MDR isolates overall had poorer clinical outcomes.