Medical Mycology, 2022, **60**, myac072
https://doi.org/10.1093/mmy/myac072

Oral Presentations

S1.1d
Risk factors a ssociated with oropharyngeal candidiasis in COVID-19 patients: a casecontrol study

Mohammadreza Salehi[1], Reyhaneh Sadat Kiyaei[2], Sadegh Khodavaisy[3], Nasim Khajavirad[4], Seyed Ali Dehghan Manshadi[5], Ilad Alavi Darazam[6], Arash Seifi[7]
[1]Tehran University of Medical Sciences, Tehran, Iran
[2]Tehran Universityof Medical Sciences, Tehran, Iran
[3]Tehran University of Medical Sciences, Tehran, Iran
[4]Tehran University of Medical Sciences, Tehran, Iran
[5]Tehran University of Medical Sciences, Tehran, Iran
[6]Shahid Beheshti University of Medical Sciences, Tehran, Iran
[7]Tehran University of Medical Sciences, Tehran, Iran

S1.1 Controversies in the clinical management of invasive candidiasis in critically ill patients, September 21, 2022, 11:00 AM - 12:30 PM

Objectives: With the emergence and spread of the coronavirus disease-19 (COVID-19) in the world, humans have been faced with the biggest challenge in health care systems in recent decades. The aim of the present study is to identify risk factors associated with oropharyngeal candidiasis (OPC) in COVID-19 patients.

Methods: The total number of confirmed COVID-19 patients was 218 (105 participants as cases who experienced OPC and 113 participants as controls without any evidence of OPC). The questionnaire used in this study consists of demography data, treatment strategy, clinical and laboratory data, and underlying diseases to collect information at the time of clinical OPC and follow them until the end of hospitalization.

Results: Pseudomembranous candidiasis (77/105, 73.3%) was the most prevalent form of OPC in case patients. The majority of cases (58.1%) and control (58.4%) groups were male. Increasing age of COVID-19 patients ($P = .03$) and length of hospitalization ($P = .016$) were significantly associated with OPC. Diabetes ($P = .003$), solid tumor ($P = .019$), and hypertension ($P = .000$) were the most common underlying conditions. Use of dentures ($P = .003$) and poor oral hygiene ($P = .000$) were related to OPC in case groups. Therapy with chloroquine ($P = .012$), IVIG ($P = .001$), diuretics ($P = .000$), and corticosteroid pulse therapy ($P = .000$) were significantly associated with the development of OPC in case patients.

Conclusion: It is reasonable to consider that old age, length of hospitalization, poor oral hygiene, corticosteroid usage, diabetes, solid tumor, and hypertension may predispose to the development of OPC in COVID-19 patients.

S1.2c
Diagnosis of fungal infections in animals: Combining the old and the new to maximize results

Andrea Peano

University of Turin, Grugliasco, Italy

S1.2 Emerging and Expanding Endemic Mycoses, September 21, 2022, 11:00 AM - 12:30 PM

There is a broad spectrum of fungal infections involving companion, zootechnical and wild animals. Some fungi are distributed worldwide and act as opportunistic pathogens. Others, such as the dimorphic fungi *Blastomyces dermatitidis* and *Sporothrix brasiliensis*, are primary pathogens with a more defined geographical distribution. Dermatophytes cause less severe diseases limited to the skin. However, they are relevant since they are widely diffused. Moreover, some dermatophytes are transmitted from animals to humans; therefore, these infections represent a public health problem.

In recent years, opportunistic fungal infections (e.g., Aspergillosis, Candidiosis, Cryptococcosis) in human medicine have increased. The main reason is the rise of people with immunosuppression of various origins (AIDS, chemotherapy, immunosuppressive therapies in organ transplant) (Kozel and Wickes, 2014. Cold Spring Harb Perspect Med, 4: a019299). Moreover, the spectrum of fungi causing infections is expanding, which constitutes an identification challenge for even the most experienced mycologists. To achieve an even earlier and more precise diagnosis, new methods for the detection of fungal elements in tissue samples (e.g., PCR based techniques, serological tests) and fungal identification (e.g., matrix assisted laser desorption/ionisation time-of-flight analyzer technology) are now available in adjunction to traditional methods (microscopic examination of clinical samples, histopathology, and culture). Cases of opportunistic deep mycosis are more rarely reported in animals because the situations leading to immunosuppression in human patients are not mirrored in veterinary medicine. However, there is an increasing interest in these cases involving animals. Thus, new diagnostic procedures are being applied more and more to animal infections (Elad and Segal, 2018. Front Microbiol, 9:1303).

Direct microscopy retains its importance as a quick and inexpensive tool to 'intercept' a fungal infection. It also allows observing the cellular population involved in the immune response and finding other pathogens. It is helpful to interpret the results of more advanced tests (culture, PCR). The sensitivity of microscopic exams varies with the individual agent, source and quality of the specimen, and the skills and experience of the laboratorian. Diagnosis of invasive fungal infection by direct microscopy and histopathology may require the use of biopsies of deep tissues, which may pose a risk for the patient. Often it does not allow fungal identification.

Fungal culture can yield the specific etiological agent if positive, which allows antifungal susceptibility testing (AST). It may take many days to achieve a result. Identification of less common fungi requires a high level of expertise and equipment.

A widely employed identification method is PCR + sequencing of the ITS region (other DNA regions used are: LSU, SSU, β-Tubulin, and Calmodulin). Data generated from an unknown fungus can be used to search public databases, such as GenBank, using the web-based BLASTn algorithm. Database searches must be performed with caution owing to the public nature of the database and the high frequency of erroneous deposits. The suggestion is to employ verified, published, recent sequences.

The most popular non-nucleic acid sequence-based molecular diagnostic assay for fungi is Matrix Assisted Laser Desorption Ionization Time of Flight (MALDI-TOF). The technique generates spectra that are screened against a library of reference spectra, which correspond to individual species. The strength of MALDI-TOF technology lies in the rapid sample analysis (minutes) and the absence of any downstream data manipulation. Weaknesses of this system include the need for an existing library to compare generated spectra to and potential variability in results of unknown fungi if they are not grown under conditions similar to reference spectra.

Thanks to the improvement of the identification methods in veterinary medicine, it has been possible to describe new cryptic species responsible for specific diseases, e.g., the species included in the *Aspergillus viridinutans* complex, agents of the sino-orbital Aspergillosis in cats) (Talbot and Barrs, 2017. Med Mycol, 56 [1]: 1:12). Another example is represented by the recently described dermatophyte species within the *T. benhamiae*-complex (Čmoková et al. 2020, Fungal Diver, 104 [1]: 333-387; Peano et al. 2022, Vet Dermatol, Online ahead of print).

PCR-based methods targeting specific fungi are now used to detect several fungal pathogens directly from clinical samples. Real-time PCR uses fluorescent dyes to enhance specificity through either a nonspecific DNA binding dye, SYBR green, or a specific fluorescently labeled probe directed to a target sequence. Since one (or more, in the case of multiplex PCR) specific pathogen is targeted, it is possible to work on 'contaminated' samples. These techniques are very 'clinical-friendly' since they are presented as 'panels' (e.g., PCR panel for 'seizure episodes in cats' to detect the main agents responsible for neurologic infections, Cryptococcus, Toxoplasma, Neospora).

The use of serological tests (e.g., the search for wall fungal components, such Beta-Glucan) may be a precious tool to diagnose and monitor the therapy response in a variety of diseases (e.g., disseminated Aspergillosis in dogs; avian Aspergillosis) (Burco et al., 2012. Avian Dis, 56 [1]: 183-191). New diagnostic tools likely will reveal animal infection cases that the traditional methods would have missed.

S1.3a
Genetics andgenomics of *Malassezia* species

Giuseppe Laniri
University of Molise, Campobasso, Italy

S1.3 *Malassezia*: genetics, genomics, and biology, September 21, 2022, 11:00 AM - 12:30 PM

Malassezia includes yeasts belonging to the subphylum *Ustilaginomycotina* within the *Basidiomycota*. *Malassezia* yeasts are attracting the interest of both basic and applied scientists for their unique biological features, and for their importance in clinical and cosmetic settings. Although *Malassezia* yeasts are commonly found as commensal on human and animal skin, they are also associated with several skin disorders, such as dandruff/seborrheic dermatitis, atopic eczema, pityriasis versicolor, and folliculitis. More recently, an association of *Malassezia* with Crohn's disease, pancreatic ductal adenocarcinoma, and psoriasis exacerbation has been reported. To understand the genetic basis of *Malassezia* commensalism and pathogenicity, the availability of genomic and molecular tools plays a crucial role. Genomics advances in *Malassezia* reveal karyotype variations and gene turnover events, including genes horizontally transferred from bacteria. Moreover, the increasing availability of transcriptomic data allows us to prioritize studies on novel key genes that potentially characterize the pathophysiology of *Malassezia* fungi. For gene function studies, protocols for *Agrobacterium tumefaciens*-mediated transformation were developed and utilized in strategies of random insertional mutagenesis or targeted gene replacement through CRISPR/Cas9. Developed tools can be combined with the use of host-pathogen interaction models, such as the easy-to-use wax moth larvae of *Galleria mellonella* or the more complex murine skin model, enabling the characterization of both the fungal components that trigger skin damage and inflammation, and the inflammatory and antifungal response of the host to prevent fungal infection through immunological and molecular analyses of experimentally infected tissue.

S1.3c
Diversity and hybridization in *Malassezia* furfur

Bart Theelen
Westerdijk Fungal Biodiversity Institute, Utrecht, Netherlands

S1.3 *Malassezia*: genetics, genomics, and biology, September 21, 2022, 11:00 AM - 12:30 PM

The Basidiomycetous yeast *Malassezia* is the most abundant fungal genus on healthy human skin but may also cause various skin disorders such as seborrheic dermatitis, dandruff, and pityriasis versicolor. In recent years, *Malassezia* has increasingly been implicated in health and disease beyond the skin: as an underestimated cause of *Malassezia* bloodstream infections (BSIs) in immunocompromised patients and neonates, associated with Crohn's disease, promoting pancreatic oncogenesis, and exacerbating cystic fibrosis. *Malassezia furfur* is the number one *Malassezia* BSI cause and is also implicated in many skin disorders. With these new discoveries of *Malassezia*'s impact on human health, the need for a better understanding of its evolution and pathobiology also became more pressing. Hybridization has been suggested as a biological mechanism of adaptation to new hosts, and may lead to increased pathogenicity. Many examples of major hybrid yeast pathogens exist, such as *Candida albicans*, *C. orthopsilosis*, *C. metapsilosis*, and multiple examples in the *Cryptococcus gattii/Cryptococcus neoformans* species complex. Here the multiple hybridization events of the *Malassezia furfur* species complex will be discussed. Two distinct hybridization events occurred between the same parental lineages, and these parental strains were originally also hybrids. The identification of a pseudobipolar mating system and the analysis of the mating-type loci provide evidence that sexual liaisons of mating compatible cells from these parental lineages led to a diploid/aneuploid state in the hybrid lineages. Sequence similarity percentages suggest that both parental lineages in fact are two different species. The genetic diversity of ca 300 strains belonging to this species complex is evaluated in relationship to host background and phenotype.

S1.3d
The human pathobiont *Malassezia furfur* secreted protease MfSAP1 regulates cell dispersal and exacerbates skin inflammation

Joleen Goh[1], Fiorella Ruchti[2], Si En Poh[3], Winston L.C. Koh[3], Kiat Yi Tan[4], Yan Ting Lim[4], Steven T.G. Thng[5], Radoslaw M. Sobota[4], Shawn S. Hoon[3], Chenxi Liu[6], Anthony J. O'Donoghue[6], Salomé LeibundGut-Landmann[2], Hazel H. Oon[5], Hao Li[3,7], Thomas L. Dawson[1,8]

[1]A*STAR Skin Research Labs, Agency for Science, Technology and Research, Singapore, Singapore
[2]Section of Immunology, Vetsuisse Faculty, University of Zürich, , Switzerland
[3]Molecular Engineering Lab, Institute of Molecular and Cell Biology, Agency for Science, Technology and Research, Singapore, Singapore
[4]Functional Proteomics Laboratory, Institute of Molecular and Cell Biology, Agency for Science, Technology and Research, Singapore, Singapore
[5]National Skin Centre, National Health Group, Singapore, Singapore
[6]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California-San Diego, La Jolla, USA
[7]Department of Chemistry, National University of Singapore, Singapore, Singapore
[8]Department of Drug Discovery, School of Pharmacy, Medical University of South Carolina, Charleston, USA

S1.3 Malassezia: genetics, genomics, and biology, September 21, 2022, 11:00 AM - 12:30 PM

Objectives: *Malassezia* forms the dominant eukaryotic microbial community on the human skin. The *Malassezia* genus possesses a repertoire of secretory hydrolytic enzymes involved in protein and lipid metabolism which alter the external cutaneous environment. The exact role of most *Malassezia* secreted enzymes, including those in interaction with the epithelial surface, is not well characterized.

Methods and Results: In this study, we compared the expression level of secreted proteases, lipases, phospholipases, and sphingomyelinases of *M. globosa* in healthy subjects and seborrheic dermatitis or atopic dermatitis patients. We observed upregulated gene expression of the previously characterized secretory aspartyl protease MgSAP1 in both the lesional and non-lesional skin sites of affected compared to healthy subjects. To explore the functional roles of MgSAP1 in skin disease, we generated a knockout mutant of the homologous protease MfSAP1 in the genetically tractable *M. furfur*. We observed the loss of MfSAP1 resulted in dramatic changes in the cell adhesion and dispersal in both culture and a human 3D reconstituted epidermis model. In a murine model of *Malassezia* colonization, we further demonstrated MfSAP1 contributes to inflammation as observed by reduced edema and myeloid pustule formation with the knockout mutant versus wildtype.

Conclusion: Taken together, we show that this dominant secretory *M. aspartyl* protease has an important role in enabling a planktonic cellular state that can potentially aid in colonization and additionally as a virulence factor in barrier-compromised