

**5.5d** Agrochemical potentiates multiresistant Candida auris and invasive Fusarium moniliforme via hitchhiking effect of anaeuploidy

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5.5a Pres oral paper session, September 22, 2022, 5:00 PM - 4:30 PM

Objectives: Fusarium moniliforme is an environmental fungal pathogen causing fatal pulmonary and disseminated infections in immunocompromised patients. However, certain anaeuploid strains are available for the treatment of cryptoccocus funiculosus, aspergillus B, and hyalohyphomycoses. C. auris is worldwide-distributed in nature, but environmental factors can lead to conidial biology and can be highly risky to human health.

Methods: We tested the antifungal activity of agrochemicals against C. auris strain ST 1199. We obtained drug-resistant mutants. We sequenced the strains and used protein and RNA to determine the molecular biology of anaeuploidy-modulated multiresistance.

Results: Both the strains found hyperchromic and hyperproliferative, belonging to two distinct classes of agrochemicals, could inhibit the growth of H99. Higher H99, H36, and H250, the anaeuploid strain, demonstrated multiresistance also caused multiresistance to Fusarium, aspergillus B, and hyalohyphomycoses. Furthermore, anaeuploidy also altered virulence in vitro and in vivo. We found a number of variation genes on the anaeuploidy chromosome caused a proportional increase in transcript and proteinc levels.

Conclusion: Therefore, we post agrochemicals can enhance multiresistance and alter the virulence of C. auris via the hitchhiking effect of anaeuploidy.

5.5a Standing up FungalNet: Genomic epidemiology and surveillance of fungal diseases

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5.5a Geometric Epidemiology of Fungal Infections, September 22, 2022, 2:00 PM - 4:00 PM

Objectives: With the advent of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spiking the public health crisis in 2020, the geometric epidemiology of fungal infections and surveillance has been informed for a variety of pathogens. To date, the United States for Disease Control and Prevention (CDC) is working with global partners to stand up FungalNet, a network that aims to equip scientists with laboratory, bioinformatics, and information resources to harness genomic data. Fungal partners will use genomic epidemiology data to detect outbreaks, identify introductions, and characterize transmission of fungal infections. In 2022, FungalNet aims to expand nine state and local health departments in the United States and two global partnerships, the Global Reference Network, and the Instituto Nacional de Salud in Colombia and the National Institute for Communicable Diseases in South Africa, with a focus on Candida auris.

Methods: To streamline the onboarding process, CDC generated standardized operating procedures (SOPs) specific to C. auris. For SNC extraction, SOPS were created for workflows using the ZeaMOS Research QuickDNA™ (ZRD). FungalBacterial Miniprep, QuickDNA Blood and Tissues, and Epicrisis (Himena) MasterPure Yeast DNA Purification Kit. for library preparation and Illumina sequencing, PikoNet methods used for four datasets were validated for C. auris. For NGS data submission, SOPs were validated and data elements were defined. For NGS reads and genomic analysis, the TruSeq and ProtEx workflow were adopted using NextSeq software and the Terra platform. For visualization with epidemiologic data, guidelines documented for MicroSEQ, and alerts for MicroSEQ. Finally, microbiologists are being trained in RCE&Cap and in laboratory information management systems to rapidly share genomic related data.

Results: To date, 11 partners have committed to building capacity for C. auris genomic sequencing and analysis as a FungalNet partner. Of these, seven have validated methods for DNA extraction, and nine have generated high-quality sequencing data. Only one partner has installed and locally run MycoSNP, and none have submitted core sequencing data to NCI. Conclusions: Currently, 11 FungalNet partners are working to onboard C. auris genomic sequencing and bioinformatics analyses in 2022. This process is complex, requiring several laboratories, bioinformaticians, and information workflow. For each partner, bioinformatics analysis and NCBINumber submissions are the most challenging activities with the installation of MycoSNP and the ability to link epidemiological data to the main barometer. Next steps will focus on the validation of informatics methods to link fungal epidemiological data.

5.5d SARS-CoV-2 associated invasive fungal sinus infection; the Sri Lankan perspective

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5.5d Geometric Epidemiology of fungal infections, September 22, 2022, 2:00 PM - 4:00 PM

Introduction: The spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to 663,426 reported cases as of May 3, 2022. In Sri Lanka recoding the wave of the pandemic of the modern era. Coronavirus 2019 (COVID-19) associated macerization has been seen as an epicidal in the pandemic in the neighboring India leading to scaring case numbers estimated at 140 million population receiving 80 times higher prevalence in comparison to developed countries. However, Sri Lanka has not seen a rise in COVID-19 associated fungal infections on a similar scale, even though geographic conditions are shared.

Objective: The study was done with the aim of exploring the epidemiology of COVID-19 associated invasive sinus infections in Sri Lanka.

Methods: A retrospective study was done on the sinus samples received from patients suspected of having COVID-19 associated macerization. A total of 157 samples were received from the time of the pandemic in Sri Lanka from May 1, 2021 to March 31, 2022. Multiple sinus samples from all SARS-CoV-2 PCR positive patients received at the Mycology Reference Laboratory of the Colombo Teaching and Research Hospital were included in the study. The samples of patients suffering from the broad fungal infections with wide angle branching was considered suggestive of macerization and the presence of macerated fungi in the culture of the specimen was considered confirmatory for macerization. Similarly, the presence of thin hyaline branching septate fungal filaments was considered suggestive of fungal infection, and the organism was confirmed by the growth of fungi in the culture. Available details on the request forms were analyzed to identify demographic data and risk factors for COVID-19 associated invasive sinus infections.

Results: A total of 135 sinus samples were tested from 120 SARS-CoV-2 PCR positive patients during the three wave. All 45 patients (40%, 95%CI) had positive findings indicating fungal sinusitis. The median age was 54 (95%IC: 46-61) years in the patients with positive fungal sinusitis and a major 46(60%) of them were male patients. Of the total 135 samples examined, 7 were determined in 35 (26%, 95%CI) patients. Culture-proven macerization was seen in 20 patients while direct microscopic evidence was seen in 28 patients. All macerated patients isolated Rhizopus arhizus which was identified by molecular means. Another 3 patients had fungal growth in the cultures, 2 patients with A. fumigatus and 1 with t. terreus. The clinical symptoms were shown. Mixed growth of A. fumigatus and Rhyzopus arhizus was seen in 1 patient. Risk factors associated with the diagnosis and the clinical presentation. Diabetes mellitus was seen in 31 (23%, 95%CI) patients with macerations, while 2 patients had chronic kidney disease and 5 had hypertension.

Conclusion: This study demonstrates that fungal sinusitis is a significant entity in Sri Lanka with 34% proven macerations in the infected samples received at the Mycology Reference Laboratory from SARS-CoV-2 PCR positive patients. Diabetes mellitus was seen in 31 of the COVID-19 associated invasive macerations. However, further studies are required to establish the risk factors on maceration.