Issue 27-June 2024

ISMM MYCOSES Newsletter

Message of the President

It is indeed wonderful to be writing to you all once again.

To begin with, the primary objective of this council was to strengthen the fungal diagnostic capabilities across the institutions. Realising this is possible only by increasing the number of young faculty and students in the ISMM body our membership drive helped us to grow in strength in the past one year. This is very encouraging for the future of medical mycology.

The members of the council especially the young brigade have been hosting and participating in many academic programs both national and international taking mycoses management to better levels. Happy to share that their exciting plans to deliver interactive programs online will begin in the next couple of months.

The council has extended all support to Dr. Anupma to host our biennial conference at Chennai. Knowing Anupma and her team, it will be a great academic feast. Requesting the students and young faculty to participate in large numbers and make the oral and poster presentations highly competitive as there are many prestigious awards to be won. Chennai is also a travellers' treasure trove with many sites to visit. This outing is worth both for academics and entertainment. Looking forward to great participation.

We as a team are happy working and strengthening Medical Mycology in our country. The collective effort by the council thus far has been commendable. Let us ensure we spread the message across.

I sincerely urge and request the microbiology fraternity (working, interested, non-interested in medical mycology) to send in your valuable feedback to the team.

Thank you and God bless.

Dr. Jayanthi Savio

President, Indian Society of Medical Mycologists

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President, Indian Society of Medical Mycologists

Report of General Secretary

Greetings ISMM members,

I hope everyone is safe and doing good after the scorching heat wave that just passed through the country. Being the General Secretary of the Indian Society of Medical Mycologists (ISMM), my duty is to provide information regarding the recent activities to our members. I am glad to report some positive updates.

We have conducted two Executive Council (EC) Meetings (5th & 6th) since the last Newsletter of December 2023.

The 5th EC meeting was held on 9th March 2024 and the following topics were discussed:

- Dr. Anupama Jyoti Kindo informed the EC members that the official website for the 2025 ISMM conference has been launched and will be fully functional.
- Dr. Shukla Das discussed about the WHO sponsored CME, to be organized under the aegis of ISMM in either October or November. The exact date is yet to be decided.
- Dr. Vinay, Dr. Harsimran, Dr. Arghadeep and Dr. Pratibha discussed about the panel discussion for students. It was decided to invite Google Forms to populate about various topics.
- Dr. Savitri Sharma discussed her Newsletter and possible date of publication to be in either June or July.

The 6th EC meeting was held on 7th June 2024. The following agenda was discussed:

- Dr. Anupama, the organizing secretary of the ISMM conference 2025, informed that she received financial help from ISHAM and ECMM for the upcoming ISMM conference. She also informed the EC members that an amount of Rs. 1.5 lakh seed money was received from ISMM. She confirmed that the groundwork is going on as per plans and they are going to open the conference website on 15 June, 2024. She requested Dr. Pratibha to put the conference link on the ISMM website. She also informed us that 5 international faculty members have confirmed their participation in this conference, and they are exploring about the number of travel grants they can provide to encourage students. EC members are happy with the progress and assured her of additional assistance if needed. Dr. Harsimran apprised the last newsletter quiz winner, who will be awarded in the conference so that it can be coordinated directly by the organizers.
- Dr. Ranjana, who held the last ISMM conference at Manipur in 2023, informed that there is approximately a Rs. 4 Lakhs surplus in their budget. They have decided to transfer Rs. 3.5 lakhs to ISMM account and requested to make a fixed deposit in the bank. She suggested that the interest amount generated could be used as travel grant awards to students in future conferences. She also informed Dr. Anupama that Rs. 50,000 will be contributed towards the ISMM 2025 conference travel grants. All the EC members applauded Dr. Ranjana for her generous contribution to ISMM.
- Dr. Savitri Sharma informed us that the next issue of ISMM newsletter is due in June 2024, and requested everyone to send their materials to her at the earliest. She also requested the President and General Secretary to give their reports for the upcoming issue of the newsletter.
- Dr. Vinay and his team explained that for the initiation of online master classes or "Meet the Expert" online sessions they are going to generate some questions through a Google Form. They will communicate with some eminent personalities to conduct the ISMM proposed online session within the next month. They are thinking of starting this online program by the end of August.

The next ISMM conference will be held in February 2025 at the Sri Ramchandra Medical College, Chennai. Dr. Anupama has already published the brochure and launched the website. We, the council members, are requesting all ISMM members to try and participate actively to make the conference a success. We assured all the help from our society for the successful execution of this important event. I am signing off with best wishes for the rest of the year!

Dr. Anup K Ghosh
General Secretary, Indian Society of Medical Mycologists

1. **Dr. M. J. Thirumalachar Life Time Achievement Award.**

   The Life Time Achievement award is established to honor members of the ISMM, who during the span of his/her lifetime have demonstrated a longstanding commitment to the cause of Medical Mycology in India. The award is made possible by a generous donation by one of the senior most and revered member of the Society, Dr. Arvind A. Padhye,

   The award would recognize the significant contribution to the understanding and application of the knowledge pertaining to the Medical Mycology in India, over the entire course of his /her life time, with a definable body of work through one or more of the following:-

   - Teaching /Training.
   - Research.
   - Publications/patents.
   - Patient care.

Who may receive the award?

The nominee should be a Life member of the ISMM in good standing,

He should be in the field for at least 25 years but not necessarily active professionally at the time of receiving the award.

He must be alive at the time the selection committee's choice is announced. In case of an unfortunate event of death of the awardee after selection, the award may be presented posthumously.

How will the recipients be chosen?

The president, with the approval of the executive committee, will appoint a Life Time Achievement Awards committee consisting of five active members of the Society. One committee member shall be a current member of the ISMM executive council, who would co-ordinate the committee meeting. The committee will invite nominations from the members for the award. The nomination is to be made by at least two life members of the society at least 6 months in advance to the next annual conference of the society. Self-Nomination will not be accepted.

The nominations will be scrutinized by the award committee and the best among the nominations will be selected for the award.

When will the award be presented?

The award may be presented to the deserving individual at the Annual Conference of the Society. The awardee will be introduced to the august gathering duly stating his/her achievements during the inaugural function of the conference.

The award will consist of a citation and a memento.

No travelling or daily allowance will be provided to the awardee to attend the function.

The decision of the award committee will be final.

2. **G. P. Agarwal young scientist Award**

   The best paper award will be given to a young scientist below the age of 35 years (proof of age to be submitted). Applicant must submit the full length original research paper on any area of the medical mycology. Oral presentation of the research should be done in the separate award session during the conference.

3. **Dr. Pankajalakshmi Venugopal Glaxo Meritorious Award**

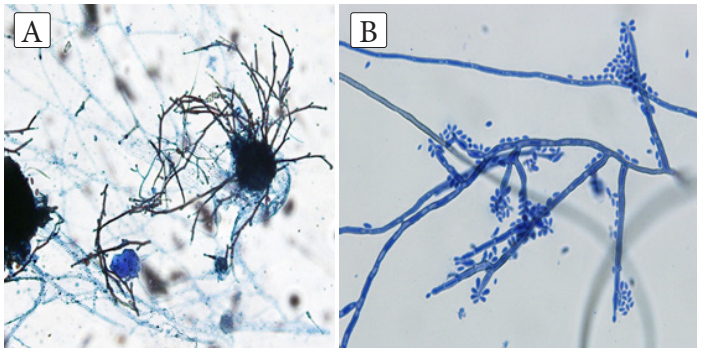
   Age limit -35 years (proof of age to be submitted). Must submit the curriculum vitae with list of publications and reprints of the papers in the field of medical mycology. Award will be given on the basis of the CV for the outstanding work in the field of medical mycology.

4. **Dr Kamalam Glaxo award in Dermatomycology**

   Applicant must submit full length research paper in duplicate in the field of dermatomycology. Award will be given based on oral presentation in the separate award session during the conference.

Answer for the last issue's identify the fungus (ISMM mycoses, Issue 26, Quiz December 2023)

A 40-year-old female presented with rhinorrhoea, and right nasal obstruction for past 2 weeks. She had no history of any comorbidity or illness. X-ray of maxillary region showed complete opacity of the right maxilla. The erosion of the antral bone was also appreciated. Computerized tomography (CT) scan of paranasal sinuses revealed opaque mass in the right maxillary sinus. The debris from the antrum was removed and subjected to potassium hydroxide (KOH) mount which showed branched septate hyphae and grew yellowish white colony on Sabouraud dextrose agar (SDA) after 4 days of incubation. The lactophenol cotton blue (LCB) mount from culture is shown in figures A & B.

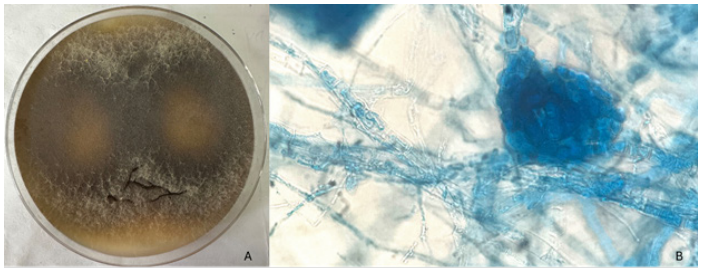


Correct identification: *Ascotricha chartarum*

(Correct answer was not received for this quiz)

Quiz: Can you identify the fungus?

A 59-year-old manual labourer presented with an injury to right eye while handling soil. He complained of pain, redness and decreased vision in the affected eye over the past 3 days. Slit lamp examination (SLE) showed a central corneal infiltrate affecting the inferior visual axis and hypopyon. Corneal scraping showed septate hyphae in potassium hydroxide (KOH) mount and grew white colonies on Sabouraud dextrose agar (SDA) within 48 hours of incubation, which later developed into a light brown colour. The culture on SDA and lactophenol cotton blue (LCB) mount are shown in figures A & B, respectively. Please identify the fungus to species level.



Send your answer to Dr. Harsimran Kaur at drharsimranpgi@gmail.com

Results of ISMM Mycology External Quality Assurance Program

Results of ISMM Mycology External Quality Assurance Program conducted at PGIMER, Chandigarh

Performance Report of the Participants (30th Batch, Jan 2024)

Total number of participating laboratories -178

S No.	Sample/ Code	Clinical details			Correct identification	Interpretation	Laboratory (%) given correct results
		Age/Sex	Clinical feature/ Diagnosis	Source of specimen			
1	EQMM-1	27/M	Itchy and scaly lesion on thigh	Skin scraping	*Trichophyton rubrum*	Dermatophytosis	93.3%
2	EQMM-2	61/F	Renal transplant, pneumonia	Bronchoalveolar lavage	*Aspergillus candidus*	Probable case of invasive aspergillosis	65.8%
3	EQMM-3	42/M	H/O Diabetes mellitus, orbital cellulitis	Orbital tissue biopsy	*Mucor racemosus*	Rhino-orbital mucormycosis	60.3%
4	EQMM-4	37/M	Yellowish brittle index fingernail	Nail clippings	*Scopulariopsis brevicaulis*	Onychomycosis due to non dermatophytic mold	93.9%
5	EQMM-5*	50/F	Sepsis	Blood culture	*Candida parapsilosis*	Candidemia	95.7%

Results of antifungal susceptibility testing performed for EQMM -5; Laboratories participating in AFST: 82.9 %

(EQMM-5) Minimum inhibitory concentration	**Amphotericin B 1mg/L**	**Fluconazole 2.0mg/L**	**Voriconazole 0.06mg/L**	**Itraconazole 0.25mg/L**	**Posaconazole 0.12mg/L**	**Anidulafungin 1mg/L**	**Micafungin 0.5mg/L**
Participant results %	81.7%	81.9%	79.2%	67.1%	63.4%	62.16%	71.9.%

Abstracts (January – June 2024)

Compiled by Dr. Joveeta Joseph

Microbiologist, Jhaveri Microbiology Centre, L V Prasad Eye Institute, Hyderabad

1. Naringenin-Zinc Oxide Nanocomposites Amalgamated Polymeric Gel Augmented Drug Delivery and Attenuated Experimental Cutaneous Candidiasis in Balb/c Mice: *In Vitro* and *In Vivo* Studies

Chanti Babu Katta[1], Deepankar Bahuguna[1], Harithasree Veerabomma[1], Spandana Gollapalli[1], Arbaz Sujat Shaikh[2], Nagesh A Bhale[3], Amol G Dikundwar[3], Venkat Rao Kaki[2], Pankaj Kumar Singh[1], Jitender Madan[4]

Affiliations

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AAPS PharmSciTech. 2024 Jun 6;25(5):130. doi: 10.1208/s12249-024-02841-7.

Abstract

Naringenin (NRG) inhibits the fungal 17β-hydroxysteroid dehydrogenase accountable for ergosterol synthesis in *Candida albicans* (*C. albicans*), a causative agent for cutaneous candidiasis. In present research, NRG was complexed with ZnO nanomaterial (NRG-Zn2+) to synthesize NRG-Zn2+ nanocomposites. The particle size and ζ-potential of NRG-Zn2+ nanocomposites were respectively estimated to be 180.33 ± 1.22-nm and - 3.92 ± 0.35-mV. In silico data predicted the greater affinity of NRG-Zn2+ nanocomposite for 14α-demethylase and ceramide in comparison to NRG alone. Later, NRG-Zn2+ nanocomposites solution was transformed in to naringenin-zinc oxide nanocomposites loaded chitosan gel (NRG-Zn-CS-Gel) with viscosity and firmness of 854806.7 ± 52386.43 cP and 698.27 ± 10.35 g, respectively. The ex-vivo skin permeation demonstrated 70.49 ± 5.22% skin retention, significantly greater ($P < 0.05$) than 44.48 ± 3.06% of naringenin loaded chitosan gel (NRG-CS-Gel) and 31.24 ± 3.28% of naringenin solution (NRG Solution). NRG-Zn-CS-Gel demonstrated 6.71 ± 0.84% permeation of NRG with a flux value of 0.046 ± 0.01-μg/cm2/h. The MIC50 of NRG-Zn-CS-Gel against *C. albicans* was estimated to be 0.156-μg/mL with FICI (fractional inhibitory concentration index) of 0.018 that consequently exhibited synergistic efficacy. Further, NRG-Zn-CS-Gel demonstrated superior antifungal efficacy in *C. albicans* induced cutaneous candidiasis infection in Balb/c mice. The fungal burden in NRG-Zn-CS-Gel treated group was 109 ± 25 CFU/mL, significantly lower ($P < 0.05$) than positive control (2260 ± 446 CFU/mL), naringenin loaded chitosan gel (NRG-CS-Gel; 928 ± 127 CFU/mL) and chitosan gel (CS-Gel; 2116 ± 186 CFU/mL) treated mice. Further, histopathology examination and cytokine profiling of TNF-α, IL-1β and IL-10 revealed the healing of skin and inflammation associated with cutaneous candidiasis infection. In conclusion, NRG-Zn-CS-Gel may be a potential candidate for translating in to a clinical viable topical nanotherapeutic.

PMID: 38844611

2. A chemically induced attenuated strain of *Candida albicans*

generates robust protective immune responses and prevents systemic candidiasis development

Swagata Bose[1], Satya Ranjan Sahu[1], Abinash Dutta[1], Narottam Acharya[1]

Affiliations

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Elife. 2024 May 24:13:RP93760. doi: 10.7554/eLife.93760.

Abstract

Despite current antifungal therapy, invasive candidiasis causes >40% mortality in immunocompromised individuals. Therefore, developing an antifungal vaccine is a priority. Here, we could for the first time successfully attenuate the virulence of *Candida albicans* by treating it with a fungistatic dosage of EDTA and demonstrate it to be a potential live whole cell vaccine by using murine models of systemic candidiasis. EDTA inhibited the growth and biofilm formation of C. albicans. RNA-seq analyses of EDTA-treated cells (CAET) revealed that genes mostly involved in metal homeostasis and ribosome biogenesis were up- and down-regulated, respectively. Consequently, a bulky cell wall with elevated levels of mannan and β-glucan, and reduced levels of total monosomes and polysomes were observed. CAET was eliminated faster than the untreated strain (Ca) as found by differential fungal burden in the vital organs of the mice. Higher monocytes, granulocytes, and platelet counts were detected in Ca- vs CAET-challenged mice. While hyper-inflammation and immunosuppression caused the killing of Ca-challenged mice, a critical balance of pro- and anti-inflammatory cytokines-mediated immune responses are the likely reasons for the protective immunity in CAET-infected mice.

PMID: 38787374

3. Carbon substrates promotes stress resistance and drug tolerance in clinical isolates of *Candida tropicalis*

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#Contributed equally.

Arch Microbiol. 2024 May 20;206(6):270. Doi: 10.1007/s00203-024-04000-9.

Abstract

Candida tropicalis is a human pathogen and one of the most prevalent non-*Candida albicans* Candida (NCAC) species causing invasive infections. Azole antifungal resistance in *C. tropicalis* is also gradually increasing with the increasing incidence of infections. The pathogenic success of *C. tropicalis* depends on its effective response in the host microenvironment. To become a successful pathogen, cellular metabolism, and physiological status determine the ability of the pathogen to counter diverse stresses inside the host. However, to date, limited knowledge is available on the impact of carbon substrate metabolism on stress adaptation and azole resistance in *C. tropicalis*. In this study, we determined the impact of glucose, fructose, and sucrose as the sole carbon source on the fluconazole resistance and osmotic (NaCl), oxidative (H2O2) stress adaptation in *C. tropicalis* clinical isolates. We confirmed that the abundance of carbon substrates influences or increases drug resistance and osmotic and oxidative stress tolerance in *C. tropicalis*. Additionally, both azole-resistant and susceptible isolates showed similar stress adaptation phenotypes, confirming the equal efficiency of becoming successful pathogens irrespective of drug susceptibility profile. To the best of our knowledge, our study is the first on *C. tropicalis* to demonstrate the direct relation between carbon substrate metabolism and stress tolerance or drug resistance.

PMID: 38767668

4. Innate and adaptive immune responses in subjects with CPA secondary to post-pulmonary tuberculosis lung abnormalities

Naresh Kumar Chirumamilla[1], Kanika Arora[2], Mandeep Kaur[3], Ritesh Agarwal[3], Valliappan Muthu[3], Amit Rawat[2], Sahajal Dhooria[3], Kuruswamy Thurai Prasad[3], Ashutosh Nath Aggarwal[3], Shivaprakash M Rudramurthy[4], Arunaloke Chakrabarti[5], Hansraj Choudhary[4], Arnab Pal[6], Inderpaul Singh Sehgal[3]

Affiliations

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[5]Doodhadhari Burfani Hospital, Haridwar, Uttarakhand, India.

Mycoses. 2024 May;67(5):e13746. Doi: 10.1111/myc.13746.

Abstract

Background: Post-tuberculosis lung abnormality (PTLA) is the most common risk factor for chronic pulmonary aspergillosis (CPA), and 14%-25% of the subjects with PTLA develop CPA. The pathogenesis and the host immune response in subjects with PTLA who develop CPA need to be better understood.

Methods: We prospectively compared the innate and adaptive immune responses mounted by patients of PTLA with or without CPA (controls). We studied the neutrophil oxidative burst (by dihydrorhodamine 123 test), classic (serum C3 and C4 levels) and alternative (mannose-binding lectin [MBL] protein levels) complement pathway, serum immunoglobulins (IgG, IgM and IgA), B and T lymphocytes and their subsets in subjects with PTLA with or without CPA.

Results: We included 111 subjects (58 CPA and 53 controls) in the current study. The mean ± SD age of the study population was 42.6 ± 15.7 years. The cases and controls were matched for age, gender distribution and body weight. Subjects with CPA had impaired neutrophil oxidative burst, lower memory T lymphocytes and impaired Th-1 immune response (lower Th-1 lymphocytes) than controls. We found no significant difference between the two groups in the serum complement levels, MBL levels, B-cell subsets and other T lymphocyte subsets.

Conclusion: Subjects with CPA secondary to PTLA have impaired neutrophil oxidative burst and a lower Th-1 response than controls.

PMID: 38767275

5. The Hog1 MAPK substrate governs *Candida glabrata*-epithelial cell adhesion via the histone H2A variant

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Affiliations

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PLoS Genet. 2024 May 14;20(5):e1011281. doi: 10.1371/journal.pgen.1011281. eCollection 2024 May.

Abstract

CgHog1, terminal kinase of the high-osmolarity glycerol signalling pathway, orchestrates cellular response to multiple external stimuli including surplus-environmental iron in the human fungal pathogen *Candida glabrata* (Cg). However, CgHog1 substrates remain unidentified. Here, we show that CgHog1 adversely affects Cg adherence to host stomach and kidney epithelial cells in vitro, but promotes Cg survival in the iron-rich gastrointestinal tract niche. Further, CgHog1 interactome and in vitro phosphorylation analysis revealed CgSub2 (putative RNA helicase) to be a CgHog1 substrate, with CgSub2 also governing iron homeostasis and host adhesion. CgSub2 positively regulated EPA1 (encodes a major adhesin) expression and host adherence via its interactor CgHtz1 (histone H2A variant). Notably, both CgHog1 and surplus environmental iron had a negative impact on CgSub2-CgHtz1 interaction, with CgHTZ1 or CgSUB2 deletion reversing the elevated adherence of Cghog1Δ to epithelial cells. Finally, the surplus-extracellular iron led to CgHog1 activation, increased CgSub2 phosphorylation, elevated CgSub2-CgHta (canonical histone H2A) interaction, and EPA1 transcriptional activation, thereby underscoring the iron-responsive, CgHog1-induced exchange of histone partners of CgSub2. Altogether, our work mechanistically defines how CgHog1 couples Epa1 adhesin expression with iron abundance, and point towards specific chromatin composition modification programs that probably aid fungal pathogens align their adherence to iron-rich (gut) and iron-poor (blood) host niches.

PMID: 38743788

6. *In silico* genome wide identification of long non-coding RNAs differentially expressed during *Candida auris* host pathogenesis

Kartavya Mathur, Bharti Singh, Rekha Puria, Vikrant Nain

Affiliation

School of Biotechnology, Gautam Buddha University, Greater Noida, India.

Arch Microbiol. 2024 May 10;206(6):253. doi: 10.1007/s00203-024-03969-7.

Abstract

Candida auris is an invasive fungal pathogen of high concern due to acquired drug tolerance against antifungals used in clinics. The prolonged persistence on biotic and abiotic surfaces can result in onset of hospital outbreaks causing serious health threat. An in depth understanding of pathology of *C. auris* is highly desirable for development of efficient therapeutics. Non-coding RNAs play crucial role in fungal pathology. However, the information about ncRNAs is scanty to be utilized. Herein our aim is to identify long noncoding RNAs with potent role in pathobiology of *C. auris*. Thereby, we analyzed the transcriptomics data of *C. auris* infection in blood for identification of potential lncRNAs with regulatory role in determining invasion, survival or drug tolerance under infection conditions. Interestingly, we found 275 lncRNAs, out of which 253 matched with lncRNAs reported in Candidamine, corroborating for our accurate data analysis pipeline. Nevertheless, we obtained 23 novel lncRNAs not reported earlier. Three lncRNAs were found to be under expressed throughout the course of infection, in the transcriptomics data. 16 of potent lncRNAs were found to be coexpressed with coding genes, emphasizing for their functional role. Noteworthy, these ncRNAs are expressed from intergenic regions of the genes associated with transporters, metabolism, cell wall biogenesis. This study recommends for possible association between lncRNA expression and *C. auris* pathogenesis.

PMID: 38727738

7. Dermatophytosis in domestic cats: Identification, and treatment in an Indian context

Mathew Salomi Sheetal[1], Archana Chandran[2], Abdulkhaderkunju Janus[1], Ollukkara Krishnan Sindhu[3], Deepa Padinjare Melepat[1], Vijayakumar Kaithathara[4], Ramachandran Latha Rathish[1]

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[4]College of Veterinary and Animal Sciences, Mannuthy, Kerala, India.

Acta Trop. 2024 Jul:255:107237. doi:10.1016/j.actatropica.2024.107237. Epub 2024 May 7.

Abstract

The surge in domestic cat adoption across India, particularly the rising preference for high-pedigree cats, coupled with environmental factors, has resulted in increased incidence of dermatophytosis among feline companions. Despite this growing concern, there is a noticeable scarcity of studies in India delving into the etiological factors contributing to dermatophytosis in cats. This disease is a threat to animal health and carries public health significance, given that cats are recognized reservoir hosts for *Microsporum canis*, a common dermatophyte affecting humans and animals. This study endeavours to identify the dermatophytes affecting cats and establish a standardized therapeutic regimen while accounting for the local stigma surrounding the regular bathing of cats. The study involved the examination of 82 cats presenting dermatological lesions, when subjected to cultural examination in dermatophyte test medium revealed 36 afflicted with dermatophytes. Isolates were presumptively identified by staining using lactophenol cotton blue, Chicago sky blue 6B, and Calcofluor white stains. Molecular-level identification of the isolates was confirmed through PCR-RFLP, amplifying the Internal Transcribed Spacer Sequence of 16 s rDNA, followed by restriction digestion using the Mva1 enzyme. Among the thirty-six isolates, 29 were identified as *M. canis*, while the remaining 7 were *M. gypseum*. The cases were categorized into five groups and treated with Lime Sulphur dip, 4 % chlorhexidine shampoo, a shampoo containing 2 % miconazole and 4 % chlorhexidine, oral itraconazole alone, and a combination of oral itraconazole with lime-Sulphur dip. Statistical analysis revealed that the response was notably swifter with lime Sulphur dip when considering only topical therapy. Moreover, the mycological cure was most expeditious when combining Lime Sulphur dip with oral itraconazole. These findings underscore the pivotal role of topical biocides in feline dermatophytosis treatment, potentially reducing the reliance on specific antifungals and thereby contributing to the mitigation of antimicrobial resistance emergence.

PMID: 38723739

8. A novel indirect ELISA for serodiagnosis of mucormycosis using antigens from *Rhizopus arrhizus*

Hansraj Choudhary[1], Harsimran Kaur[2], Shreya Singh[3], Rachna Singh[4], Valliappan Muthu[5], Roshan Verma[6], Shivaprakash M Rudramurthy[2], Ritesh Agarwal[5], Sanjay Jain[7], Amanjit Bal[8], Anup K Ghosh[2], Arunaloke Chakrabarti[9]

Affiliations

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[9]Doodhdhari Burfani Hospital, Bhupatwala, Haridwar, Uttarakhand, India.

Mycoses. 2024 May;67(5):e13730. doi: 10.1111/myc.13730.

Abstract

Background: Due to a delay in diagnosis by conventional techniques and high mortality, the development of a standardised and rapid non-culture-based technique is an unmet need in pulmonary, gastrointestinal, and disseminated forms of mucormycosis. Though limited studies have been conducted for molecular diagnosis, there are no established serologic tests for this highly fatal infection.

Objective: To develop and evaluate an indirect in-house enzyme-linked immunosorbent assay (ELISA) utilising antigens of *Rhizopus arrhizus* for detecting anti-Rhizopus antibodies (IgG and IgM) in sera of patients with mucormycosis.

Methods: We extracted both secretory and mycelial Rhizopus antigens using standardised protocols. Bradford assay was used for protein quantification. We then standardised an indirect ELISA using *R. arrhizus* mycelial and secretory antigens (10.0 µg/mL in bicarbonate buffer pH 9.2) for detecting anti-Rhizopus IgG and IgM antibodies in patient sera. We included patients with mucormycosis, other fungal infections, and healthy controls. Antibody index value (E-value) was calculated for each patient sample.

Results: Asparagine broth culture filtrate utilising 85% ammonium sulphate salt fractionation and mycelial homogenate grown in yeast extract peptone dextrose (YPD) broth precipitated with trichloroacetic acid (TCA) yielded a large amount of good-quality protein for the assay. We included 55 patients with mucormycosis (rhino-orbito-cerebral mucormycosis [ROCM, n = 39], pulmonary [n = 15], gastrointestinal [n = 1]), 24 with other fungal infections (probable aspergillosis [n = 14], candidiasis [n = 10]), and healthy controls (n = 16). The sensitivity of the antibody test for diagnosing mucormycosis ranged from 83.6-92.7% for IgG and 72.7-87.3% for IgM, with a specificity of 91.7-92.5% for IgG and 80-82.5% for IgM. The sera from patients with other fungal infections and healthy individuals did not show significant cross-reactivity.

Conclusion: The detection of anti-Rhizopus IgG antibody performed significantly better in comparison to IgM-based ELISA for diagnosing both ROCM (sensitivity of 84.6% vs. 69.2%) and pulmonary cases (86.6% vs. 80.0%). More extensive studies are required to confirm our findings.

PMID: 38712824

9. Microbiological Profile of Culture-Positive Fungal Keratitis

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Eye Contact Lens. 2024 Jun 1;50(6):265-269. doi: 10.1097/ICL.0000000000001089. Epub 2024 Apr 30.

Abstract

Purpose: To examine the microbiological profile of cases of culture-positive fungal keratitis presenting to a tertiary eye care center in eastern India.

Methods: Microbiology records of all culture-positive microbial keratitis patients presenting to L V Prasad Eye Institute, Bhubaneswar, between January 2020 and December 2021, were retrospectively reviewed. Collected data included smear results of culture-positive fungal or mixed infections, the species isolated, and the time taken for organisms to grow in each media.

Results: Fungal keratitis formed 36% of all culture-positive microbial keratitis, whereas mixed infections (fungi and other organisms) formed 8.5%. The most common fungal species isolated was *Fusarium spp.* (25.8%). The most common bacteria involved in mixed infection with fungi was *Staphylococcus spp.* (54.8%). The positivity of potassium hydroxide+calcofluor white stain in detecting fungal filaments was 89.0% and that of Gram stain was 76.1%. Culture-positive cases of fungal keratitis showed most frequent growth on potato-dextrose agar (77.6%). A similar pattern was observed in culture-positive mixed infections (Sabouraud dextrose agar [SDA]: 84%). Most frequent growth of bacteria in mixed infections was seen in thioglycolate broth (54.7%). The shortest time to achieve significant fungal growth was observed in blood agar (BA) and chocolate agar (CA) (2.2/2.3 days, and 1.8/2 days for fungal keratitis and mixed infections, respectively). Filamentous hyaline fungi took the shortest time to achieve significant growth (2.8 days), whereas yeast forms took the longest (5 days).

Conclusion: This study highlights the importance of combined use of both solid and liquid culture media, especially potato dextrose agar (PDA)/SDA and CA, to arrive at a definitive diagnosis of fungal keratitis and possible bacterial co-infection, which forms a significant proportion of cases with fungal keratitis. In resource-poor laboratories, two culture media, either SDA or PDA, along with BA, may be plated to detect mixed infections. Examination of stained smears of corneal samples provides an inexpensive method of rapid diagnosis of fungal keratitis when culture media is not available.

PMID: 38687618

10. Impact of sphingolipid synthesis inhibition on the drug susceptibility patterns of *Trichophyton* species

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Diagn Microbiol Infect Dis. 2024 Jun;109(2):116283. doi: 10.1016/j.diagmicrobio.2024.116283. Epub 2024 Mar 24.

Abstract

The well-known dermatophyte infections caused by *Trichophyton species* are an ambiguous problem to treat using the present arsenal of antifungals. This study expounds on the effect of inhibition of sphingolipid pathway on Trichophyton growth. Findings from the drug susceptibility assays suggest sphingolipid inhibition severely restricts the growth of *T. interdigitale* and *T. tonsurans*. The observed synergistic effects of combinations of sphingolipid inhibitor and conventional drugs provide a promising treatment strategy against Trichophyton infection.

PMID: 38574446

11. Dermatological disease prediction and diagnosis system using deep learning

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Ir J Med Sci. 2024 Jun;193(3):1295-1303. doi: 10.1007/s11845-023-03578-1. Epub 2023 Nov 30.

Abstract

The prevalence of skin illnesses is higher than that of other diseases. Fungal infection, bacteria, allergies, viruses, genetic factors, and environmental factors are among important causative factors that have continuously escalated the degree and incidence of skin diseases. Medical technology based on lasers and photonics has made it possible to identify skin illnesses considerably more rapidly and correctly. However, the cost of such a diagnosis is currently limited and prohibitively high and restricted to developed areas. The present paper develops a holistic, critical, and important skin disease prediction system that utilizes machine learning and deep learning algorithms to accurately identify up to 20 different skin diseases with a high F1 score and efficiency. Deep learning algorithms like Xception, Inception-v3, Resnet50, DenseNet121, and Inception-ResNet-v2 were employed to accurately classify diseases based on the images. The training and testing have been performed on an enlarged dataset, and classification was performed for 20 diseases. The algorithm developed was free from any inherent bias and treated all classes equally. The present model, which was trained using the Xception algorithm, is highly efficient and accurate for 20 different skin conditions, with a dataset of over 10,000 photos. The developed system was able to classify 20 different dermatological diseases with high accuracy and precision.

PMID: 38036757

12. Identification of potential anti-mucor agents by targeting endothelial cell receptor glucose-regulated protein-78 using in silico approach

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J Biomol Struct Dyn. 2024 May;42(8):4344-4355. doi: 10.1080/07391102.2023.2220809. Epub 2023 Jun 8.

Abstract

Mucormycosis is a fungal infection of the sinuses, brain and lungs that is the cause of approximately 50% mortality rate despite the available first-line therapy. Glucose-Regulated Protein 78 (GRP78) is already reported to be a novel host receptor that mediates invasion and damage of human endothelial cells by *Rhizopus oryzae* and *Rhizopus delemar*, the most common etiologic species of Mucorales. The expression of GRP78 is also regulated by the levels of iron and glucose in the blood. There are several antifungal drugs in the market but they pose a serious side effect to the vital organs of the body. Therefore, there is an immediate need to discover effective drug molecules having increased efficacy with no side effects. With the help of various computational tools, the current study was attempted to determine potential antimucor agents against GRP78. The receptor molecule GRP78 was screened against 8820 known drugs deposited in DrugBank library using high-throughput virtual screening method. Total top 10 compounds were selected based on the binding energies greater than the reference co-crystal molecule. Furthermore, molecular dynamic (MD) simulations using AMBER were performed to calculate the stability of the top-ranked compounds in the active site of GRP78. After extensive computational studies, we propose that two compounds (CID439153 and CID5289104) have inhibitory potency against mucormycosis and can serve as potential drugs that can form the basis of treating mucormycosis disease.Communicated by Ramaswamy H. Sarma.

PMID: 37288794

13. Covid-19-Associated Mucormycosis: Histopathology of the Deadly Fungal Infection

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Int Arch Otorhinolaryngol. 2024 Jan 24;28(2):e240-e246. doi: 10.1055/s-0043-1776729. eCollection 2024 Apr.

Abstract

Introduction: Many patients suffered from rhino-orbital-cerebral mucormycosis during the coronavirus disease 2019 (COVID-19) pandemic in India. Diabetes is a known risk factor of COVID-19 infection and mucormycosis. Objective The present study was done to describe the clinical spectrum and histopathological findings of mucormycosis in COVID-19 patients and their outcomes.

Methods: A cross-sectional study was done over a period of two and half months. The biopsy samples or scrapings from sinonasal or periorbital tissue of 38 patients were analyzed. Hematoxylin & Eosin (H&E stain) slides were evaluated along with Grocott-Gomori methenamine-silver and Periodic acid-Schiff stains to highlight the fungal elements.

Results: The male to female ratio was 2.5:1, and the mean age of the subjects was 53 years old. A total of 68.4% (n = 26/38) of the patients had diabetes as a comorbidity, 84.2% (n = 32/38) had a history of steroid intake, and 55.3% (n = 21/38) were given supplemental oxygen during their treatment. The common presentations were nasal blockage, discharge, eye pain, headache, and altered mentation. The sites of biopsy were: nasal cavity 76.3% (n = 29/38), periorbital fat/orbit 21.1% (n = 8/38), maxillary sinus 15.8% (n = 6/38) and ethmoid sinus 13.2% (n = 5/38). In 76.3% (n = 29/38) cases, broad, irregular, nonseptate, and right-angle branching hyphae were seen on H&E-stained tissue sections.

Conclusion: COVID-19 led to various complications in individuals affected by it. Mucormycosis was one such lethal complication. An early diagnosis and prompt treatment is crucial to control the progression of the disease and improve outcomes.

PMID: 38618587

14. Rapid detection of Mucorales in human blood and urine samples by functionalized Heusler magnetic nanoparticle assisted customized loop-mediated isothermal amplification

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Med Mycol. 2024 Jan 27;62(2):myae007. doi: 10.1093/mmy/myae007

Abstract

Mucormycosis is a rare disease with scarce diagnostic methods for early intervention. Available strategies employing direct microscopy using calcofluor white-KOH, culture, radiologic, and histopathologic testing often are time-intensive and demand intricate protocols. Nucleic Acid Amplification Test holds promise due to its high sensitivity combined with rapid detection. Loop-mediated isothermal amplification (LAMP) based detection offers an ultrasensitive technique that does not require complicated thermocyclers like in polymerase chain reaction, offering a straightforward means for improving diagnoses as a near-point-of-care test. The study introduces a novel magnetic nanoparticle-based LAMP assay for carryover contaminant capture to reduce false positives. Solving the main drawback of LAMP-based diagnosis techniques. The assay targets the cotH gene, which is invariably specific to Mucorales. The assay was tested with various species of Mucorales, and the limit of detections for *Rhizopus microsporus*, *Lichtheimia corymbifera*, *Rhizopus arrhizus*, *Rhizopus homothallicus*, and *Cunninghamella bertholletiae* were 1 fg, 1 fg, 0.1 pg, 0.1 pg, and 0.01 ng, respectively. This was followed by a clinical blindfolded study using whole blood and urine samples from 30 patients diagnosed with Mucormycosis. The assay has a high degree of repeatability and had an overall sensitivity of > 83%. Early Mucormycosis detection is crucial, as current lab tests from blood and urine lack sensitivity and take days for confirmation despite rapid progression and severe complications. Our developed technique enables the confirmation of Mucormycosis infection in < 45 min, focusing specifically on the RT-LAMP process. Consequently, this research offers a viable technique for quickly identifying Mucormycosis from isolated DNA of blood and urine samples instead of invasive tissue samples.

PMID: 38327232

15. Host antimicrobial peptide S100A12 disrupts the fungal membrane by direct binding and inhibits growth and biofilm formation of Fusarium species

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J Biol Chem. 2024 Mar;300(3):105701.doi: 10.1016/j.jbc.2024.105701. Epub 2024 Jan 30.

Abstract

Fungal keratitis is the foremost cause of corneal infections worldwide, of which *Fusarium spp*. is the common etiological agent that causes loss of vision and warrants surgical intervention. An increase in resistance to the available drugs along with severe side effects of the existing antifungals demands for new effective antimycotics. Here, we demonstrate that antimicrobial peptide S100A12 directly binds to the phospholipids of the fungal membrane, disrupts the structural integrity, and induces generation of reactive oxygen species in fungus. In addition, it inhibits biofilm formation by *Fusarium spp*. and exhibits antifungal property against *Fusarium spp*. both in vitro and in vivo. Taken together, our results delve into specific effect of S100A12 against *Fusarium spp*. with an aim to investigate new antifungal compounds to combat fungal keratitis.

PMID: 38301897

16. Development of a machine learning model to predict risk of development of COVID-19-associated mucormycosis

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Future Microbiol. 2024 Mar:19:297-305. doi: 10.2217/fmb-2023-0190. Epub 2024 Jan 31

Abstract

Aim: The study aimed to identify quantitative parameters that increase the risk of rhino-orbito-cerebral mucormycosis, and subsequently developed a machine learning model that can anticipate susceptibility to developing this condition.

Methods: Clinicopathological data from 124 patients were used to quantify their association with COVID-19-associated mucormycosis (CAM) and subsequently develop a machine learning model to predict its likelihood.

Results: Diabetes mellitus, noninvasive ventilation and hypertension were found to have statistically significant associations with radiologically confirmed CAM cases.

Conclusion: Machine learning models can be used to accurately predict the likelihood of development of CAM, and this methodology can be used in creating prediction algorithms of a wide variety of infections and complications.

PMID: 38294306

17. Effect of volume of instillate on the diagnostic utility of bronchoalveolar lavage galactomannan in patients with suspected chronic pulmonary aspergillosis-A pilot study

Anuj Ajayababu[1], Gagandeep Singh[2], Ved Prakash Meena[1], Ashish Datt Upadhyay[3], Bhaskar Rana[2], Prayas Sethi[1], Bindu Prakash[1], Amandeep Singh[1], Surabhi Vyas[4], Sanjeev Sinha[1], Immaculata Xess[2], Naveet Wig[1], Sushil Kumar Kabra[5], Animesh Ray[1]

Affiliation

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Mycoses. 2024 Jan;67(1):e13695. doi: 10.1111/myc.13695.

Abstract

Background: Bronchoalveolar lavage (BAL) galactomannan (GM) is commonly used to diagnose Aspergillus-related lung diseases. However, unlike serum GM, which is measured in undiluted blood, BAL-GM is estimated using variable aliquots and cumulative volume of instillates during bronchoscopy.

Objective: Since different studies have reported varying diagnostic accuracy and cut-offs for BAL-GM in CPA, we hypothesized that the total volume of instillate and 'order/label' of aliquots significantly affects the BAL-GM values, which was evaluated as part of this study.

Patients & methods: We obtained 250 BAL samples from 50 patients (five from each) with suspected chronic pulmonary aspergillosis. BAL fluid was collected after instilling sequential volumes of 40 mL

of normal saline each for the first four labels and a fifth label was prepared by mixing 1 mL from each of the previous labels. The GM level of each label was measured by PLATELIA™ ASPERGILLUS Ag enzyme immunoassay. This study measured the discordance, level of agreement, diagnostic characteristics (sensitivity, specificity and AUROC) and best cut-offs for BAL-GM in the different aliquots of lavage fluid.

Results: The study population, classified into CPA (28%) and non-CPA (72%) groups, based on ERS/ESCMID criteria (excluding BAL-GM) were not different with respect to clinico-radiological characteristics. The discordance of BAL-GM positivity (using a cut-off of >1) between the serial labels for the same patient ranged between 10% and 22%, while the discordance between classification using BAL-GM positivity (using a cut-off of ≥1) and clinic-radio-microbiological classification ranged between 18% and 30%. The level of agreement for serial labels was at best fair (<0.6 for all except one 'label'). The AUROC for the serial samples ranged between 0.595 and 0.702, with the '40 mL and the 'mix' samples performing the best. The best BAL-GM cut-off also showed significant variation between serial labels of varying dilutions (Range:1.01 - 4.26).

Interpretation: This study highlights the variation in BAL-GM measured and the 'positivity' between different 'labels' of aliquots of BAL, with the first aliquot and the mixed sample showing the best performances for diagnosis of CPA. Future studies should attempt to 'standardise' the instilled volume for BAL-GM estimation to standardise the diagnostic yield.

PMID: 38282361

18. Immune and metabolic perturbations in COVID-19-associated pulmonary mucormycosis: A transcriptome analysis of innate immune cells

Manpreet Dhaliwal[1], Valliappan Muthu[2], Arunima Sharma[3], Khem Raj[4], Shivaprakash M Rudramurthy[3], Ritesh Agarwal[2], Harsimran Kaur[3], Amit Rawat[1], Surjit Singh[1], Arunaloke Chakrabarti[3]

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Mycoses.2024 Jan;67(1):e13679.doi: 10.1111/myc.13679

Abstract

Background and objectives: The mechanisms underlying COVID-19-associated pulmonary mucormycosis (CAPM) remain unclear. We use a transcriptomic analysis of the innate immune cells to investigate the host immune and metabolic response pathways in patients with CAPM.

Patients and methods: We enrolled subjects with CAPM (n = 5), pulmonary mucormycosis (PM) without COVID-19 (n = 5), COVID-19 (without mucormycosis, n = 5), healthy controls (n = 5) without comorbid illness and negative for SARS-CoV-2. Peripheral blood samples from cases were collected before initiating antifungal therapy, and neutrophils and monocytes were isolated. RNA sequencing was performed using Illumina HiSeqX from monocytes and neutrophils. Raw reads were aligned with HISAT-2 pipeline and DESeq2 was used for differential gene expression. Gene ontology (GO) and metabolic pathway analysis were performed using Shiny GO application and R packages (ggplot2, Pathview).

Results: The derangement of core immune and metabolic responses in CAPM patients was noted. Pattern recognition receptors, dectin-2, MCL, FcRγ receptors and CLEC-2, were upregulated, but signalling pathways such as JAK-STAT, IL-17 and CARD-9 were downregulated; mTOR and MAP-kinase signalling were elevated in monocytes from CAPM patients. The complement receptors, NETosis, and pro-inflammatory responses, such as S100A8/A9, lipocalin and MMP9, were elevated. The major metabolic pathways of glucose metabolism-glycolysis/gluconeogenesis, pentose phosphate pathway, HIF signalling and iron metabolism-ferroptosis were also upregulated in CAPM.

Conclusions: We identified significant alterations in the metabolic pathways possibly leading to cellular iron overload and a hyperglycaemic state. Immune responses revealed altered recognition, signalling, effector functions and a pro-inflammatory state in monocytes and neutrophils from CAPM patients.

PMID: 38214399

19. Quality by Design Assisted Development of Luliconazole Transethosomes in Gel for the Management of *Candida albicans* Infection

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Assay Drug Dev Technol. 2024 Jan;22(1):1-17.doi: 10.1089/adt.2023.059. Epub 2023 Dec 29.

Abstract

The objective of this study was to develop and evaluate a novel vesicular formulation of luliconazole (LUL) for the management of *Candida albicans* infection through a topical route. LUL-loaded transethosomes (LUL-TE) were prepared by the film hydration method and various independent and dependent variables were optimized using the Box-Behnken design. Selected critical material attributes were the content of phospholipids (X1), concentration of ethanol (X2), and amount of sodium cholate (X3). Formulated LUL-TE were characterized for percent entrapment efficiency, percent drug loading, vesicle size, and polydispersity index (PDI) and were incorporated into the carbomer gel base and further evaluated for gel characterizations. The prepared transethosomal gel (LUL-TE-CHG) was evaluated for pH, spreadability, viscosity, antifungal activity, and in vitro study. From the observed results, it was evident that the prepared LUL-TE-CHG was in the desired pH (6.2 ± 0.45), spreadability [8.3 ± 0.42 g/(cm·s)], viscosity (236.1-19.2.26 mPa·s), nanovesicle size (252 ± 9.82), entrapment efficiency (85% ± 5.24%), zeta potential (-34.05 ± 3.52 mV), and PDI (0.233 ± 0.002). The zone of inhibition results suggested that the LUL-TE-CHG formulation has the highest antifungal activity, that is, 5.83 ± 0.15 mm3. The in vitro results showed that drug release within 2 h was 18.1% ± 2.0% and after that sustained release action, 83.2% ± 1.7% within 8 h. Finally, to confirm the therapeutic efficacy of the developed formulation, fungal infection was induced by using *C. albicans* in Wistar rats. In vivo, skin irritation study and histopathology studies were performed in the disease-induced model. Animal experiments revealed that LUL-TE-CHG has significantly improved the diseased condition in Wistar rats. The results observed from the skin permeation and skin deposition profile ensure that the prepared novel LUL-loaded TE system had a higher permeation rate and increased retention time compared with LUL-CHG. The hydrogel incorporated with LUL could be a novel approach with safe and effective fungal treatment.

PMID: 38156818

20. Polymorphisms in Innate and Adaptive Immune Genes in Subjects with Allergic Bronchopulmonary Aspergillosis Complicating Asthma

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Mycopathologia 2024 Feb 26;189(2):23. doi: 10.1007/s11046-024-00834-5.

Abstract

Innate and adaptive immunity play a crucial role in allergic bronchopulmonary aspergillosis (ABPA) pathogenesis. We performed next-generation sequencing using the Illumina TruSight One panel (4,811 human disease-associated genes, at least 20 × coverage) and selected 22 known immune genes (toll-like receptors (TLRs), C-type lectin, interleukin-4 receptor, and others). We included ABPA (n = 18), asthma without ABPA (n = 12), and healthy controls (n = 8). We analyzed 3011 SNPs from 22 genes and identified 145 SNPs (13 genes) that were present only in the disease groups and absent in controls. The SNP frequency overall was significantly higher in ABPA than in asthmatics (89/145 [61.4%] vs. 56/145 [38.6%], p = 0.0001). The SNP frequency in the TLR10 gene was also significantly higher in ABPA than in asthma (p = 0.017). Association analysis further revealed three genes having significant associations. Of these, NOS3 and HLA-DQB1 are associated with antimicrobial activity and adaptive immunity. More extensive studies are required to confirm our findings.

PMID: 38407762

21. Fungal coexistence in the skin mycobiome: a study involving *Malassezia*, *Candida*, and *Rhodotorula*

Bharati Naik[1], Jayaprakash Sasikumar[1], Vishal B[2], Shankar Prasad Das[3]

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AMB Express 2024 Feb 20;14(1):26. doi: 10.1186/s13568-024-01674-8.

Abstract

Evidence of fungal coexistence in humans points towards fungal adaptation to the host environment, like the skin. The human commensal Malassezia has evolved, especially residing in sebum-rich areas of the mammalian body where it can get the necessary nutrition for its survival. This fungus is primarily responsible for skin diseases like Pityriasis versicolor (PV), characterized by hypo or hyperpigmented skin discoloration and erythematous macules. In this manuscript, we report a 19-year-old healthy female who presented with a one-year history of reddish, hypopigmented, asymptomatic lesions over the chest and a raised erythematous lesion over the face. Upon clinical observation, the patient displayed multiple erythematous macules and erythematous papules over the bilateral malar area of the face, along with multiple hypopigmented scaly macules present on the chest and back. Based on the above clinical findings, a diagnosis of PV and Acne vulgaris (AV) was made. Interestingly, the patient was immunocompetent and didn't have any comorbidities. Upon isolation of skin scrapings and post-culturing, we found the existence of three fungal genera in the same region of the patient's body. We further went on to confirm the identity of the particular species and found it to represent Malassezia, Rhodotorula, and Candida. We report how Malassezia, the predominant microbial resident skin fungus, coexists with other fungal members of the skin mycobiome. This study on an applied aspect of microbiology also shows how important it is to identify the fungal organism associated with skin infections so that appropriate therapeutics can be advised to avoid cases of relapse.

PMID: 38376644

22. Sensitivity and specificity of LDBio *Aspergillus* ICT lateral flow assay for diagnosing allergic bronchopulmonary aspergillosis in adult asthmatics

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[6]Doodhadhari Burfani Hospital, Haridwar, Uttarakhand, India.

Mycoses 2024 Feb;67(2):e13700. doi: 10.1111/myc.13700.

Abstract

Background: *Aspergillus fumigatus*-specific IgG estimation is crucial for diagnosing allergic bronchopulmonary aspergillosis (ABPA). A point-of-care LDBio immunochromatographic lateral flow assay (LFA) had 0%-90% sensitivity to detect IgG/IgM antibodies against *A. fumigatus*.

Objective: To assess the accuracy of LDBio-LFA in diagnosing ABPA, using the modified ISHAM-ABPA working group criteria as the reference standard. The secondary objective was to compare the diagnostic performance between LDBio-LFA and *A. fumigatus*-specific IgG (cut-offs, 27 and 40 mgA/L), using a multidisciplinary team (blinded to *A. fumigatus*-IgG and LDBio-LFA results) diagnosis of ABPA as the reference standard.

Methods: We prospectively enrolled adult subjects with asthma and ABPA. We performed the LDBio-LFA per the manufacturer's recommendations. We used the commercially available automated fluorescent enzyme immunoassay for measuring serum *A. fumigatus*-specific IgG. We used the same serum sample to perform both index tests. The tests were performed by technicians blinded to the results of other tests and clinical diagnoses.

Results: We included 123 asthmatic and 166 ABPA subjects, with a mean ± SD age of 37.4 ± 14.4 years. Bronchiectasis and high-attenuation mucus were seen in 93.6% (146/156) and 24.3% (38/156) of the ABPA subjects. The sensitivity and specificity of LDBio-LFA in diagnosing ABPA were 84.9% and 82.9%, respectively. The sensitivity of serum *A. fumigatus*-specific IgG ≥27 mgA/L was 13% better than LDBio-LFA, with no difference in specificity. There was no significant difference in sensitivity and specificity between LDBio-LFA and serum *A. fumigatus*-IgG ≥40 mgA/L.

Conclusion: LDBio-LFA is a valuable test for diagnosing ABPA. However, a negative test should be confirmed using an enzyme immunoassay.

PMID: 38369615

23. An integrated method for targeted Oxford Nanopore sequencing and automated bioinformatics for the simultaneous detection of bacteria, fungi, and ARG

Sanjana Kuruwa[1], Amrutraj Zade[1], Sanchi Shah[1], Rameez Moidu[1], Shailesh Lad[1], Chhaya Chande[2], Ameeta Joshi[2], Nilma Hirani[2], Chaitali Nikam[1,3], Sanjay Bhattacharya[4], Aruna Poojary[5], Mahua Kapoor[1], Kiran Kondabagil[6], Anirvan Chatterjee[1]

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J Appl Microbiol 2024 Feb 1;135(2):lxae037. doi: 10.1093/jambio/lxae037.

Abstract

Aims: The use of metagenomics for pathogen identification in clinical practice has been limited. Here we describe a workflow to encourage the clinical utility and potential of NGS for the screening of bacteria, fungi, and antimicrobial resistance genes (ARGs).

Methods and results: The method includes target enrichment, long-read sequencing, and automated bioinformatics. Evaluation of several tools and databases was undertaken across standard organisms (n = 12), clinical isolates (n = 114), and blood samples from patients with suspected bloodstream infections (n = 33). The strategy used could offset the presence of host background DNA, error rates of long-read sequencing, and provide accurate and reproducible detection of pathogens. Eleven targets could be successfully tested in a single assay. Organisms could be confidently identified considering ≥60% of best hits of a BLAST-based threshold of e-value 0.001 and a percent identity of >80%. For ARGs, reads with percent identity of >90% and >60% overlap of the complete gene could be confidently annotated. A kappa of 0.83 was observed compared to standard diagnostic methods. Thus, a workflow for the direct-from-sample, on-site sequencing combined with automated genomics was demonstrated to be reproducible.

Conclusion: NGS-based technologies overcome several limitations of current day diagnostics. Highly sensitive and comprehensive methods of pathogen screening are the need of the hour. We developed a framework for reliable, on-site, screening of pathogens.

PMID: 38346849

24. Immunohistochemical analysis of chronic and recurrent dermatophytosis

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Mycoses. 2024 Mar;67(3):e13714. doi: 10.1111/myc.13714.

Abstract

Background: Dermatophytosis has assumed epidemic proportions with rising resistance, recalcitrance and recurrence, especially in tropical regions. While various factors contribute to high prevalence worldwide, yet little is known about the interactions between host defence mechanisms and dermatophytes, particularly in chronic and recalcitrant dermatophytosis.

Objectives: We aimed to compare the population of various immune cells in specimens of chronic recurrent dermatophytosis and those with acute superficial dermatophytosis.

Methods: We investigated the density of various immune cells-Langerhans cells (CD1a+), macrophages (CD68+), dermal dendrocytes (Factor XIIIa+) in the skin of chronic dermatophytosis patients and those with successfully resolved lesions (controls).

Results: Langerhans cells were significantly decreased in the epidermis of patients, both in affected and unaffected areas in comparison with controls. In the dermis, however, no differences in the density of immune cells (macrophages and fibroblasts) were observed.

Limitations: The limited sample size and immune cells evaluated could be expanded further in future research.

Conclusion: These results indicate that the decreased number of Langerhans cells could be a potential risk factor for the development of chronic and recurrent dermatophytosis.

PMID: 38488272

25. Metagenomic insights into fungal community composition of the nasopharyngeal region of COVID-19 associated mucormycosis patients from India

Bharathi Arunan[1], Daizee Talukdar[2], Satish Swain[1], Ashwin Varadarajan[1], Radhika Sarda[1], Gagandeep Singh[3], Neeraj Nischal[1], Manish Soneja[1], Susmita Bakshi[2], Pradipta Jana[2], Subhash Tanwar[2], Kapil Sikka[4], Hitesh Verma[4], Arulselvi Subramanian[5], Immaculata Xess[3], Naveet Wig[1], Bhabatosh Das[2], Animesh Ray[1]

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J Med Virol. 2024 Apr;96(4):e29601. doi: 10.1002/jmv.29601.

Abstract

Coronavirus disease 2019 (COVID-19) associated mucormycosis (CAM) was reported predominantly from India during the second wave of COVID-19 and has a high mortality rate. The present study aims to understand the fungal community composition of the nasopharyngeal region of CAM-infected individuals and compare it with severe COVID-19 patients and healthy controls. The fungal community composition was decoded by analyzing the sequence homology of the internal transcribed spacer-2-(ITS-2) region of metagenomic DNA extracted from the upper respiratory samples. The alpha-diversity indices were found to be significantly altered in CAM patients ($p < 0.05$). Interestingly, a higher abundance of *Candida africana*, *Candida haemuloni*, *Starmerella floris*, and *Starmerella lactiscondensi* was observed exclusively in CAM patients. The interindividual changes in mycobiome composition were well supported by beta-diversity analysis ($p < 0.05$). The current study provides insights into the dysbiosis of the nasal mycobiome during CAM infection. In conclusion, our study shows that severe COVID-19 and CAM are associated with alteration in mycobiome as compared to healthy controls. However, the sequential alteration in the fungal flora which ultimately leads to the development of CAM needs to be addressed by future studies.

PMID: 38597375

26. Formulation and evaluation of itraconazole-loaded nanoemulgel for efficient topical delivery to treat fungal infections

Archana S Patil[1], Samradni S Chougale[1], Umashri Kokatanr[1], Sujay Hulyalkar[1], Ravindra D Hiremath[2], Veerkumar Japti[3], Rajashree Masareddy[1]

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Ther Deliv. 2024 Mar;15(3):165-179. doi: 10.4155/tde-2023-0062.

Abstract

Aim: The clinical application of conventional oral dosage form of itraconazole is limited due to its poor bioavailability. The aim of the study was to develop nanoemulgel of Itraconazole for topical delivery.

Method: Nanoemulsions were prepared, optimized and further incorporated into a gel and evaluated for homogeneity, pH, viscosity, spreadability, in vitro drug release and skin irritation studies.

Results: Cumulative drug release from nanoemulsions was within the range of 37.24 to 47.63% at 10 h. Drug release % for all the nanoemulgel formulations at10 h was 32.39, 39.75 and 45.9% respectively. Nanoemulgel was non-irritant as demonstrated by skin irritation studies in animals.

Conclusion: Itraconazole nanoemulgels were proved to be potential for effective topical delivery of drug with enhanced bioavailability.

PMID: 38282577

27. Nanomicelles empower natamycin in treating fungal keratitis: An *in vitro*, *ex vivo* and *in vivo* study

Priyadarshini Sathe[1], Velmurugan Kailasam[1], Vasagiri Nagarjuna[2], Hanuman Sharma[3], Thirumurthy Velpandian[3], Prashant Garg[2], Jayabalan Nirmal[4]

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Int J Pharm. 2024 May 10:656:124118. doi: 10.1016/j.ijpharm.2024.124118.

Abstract

Fungal infections of cornea are important causes of blindness especially in developing nations with tropical climate. However, the challenges associated with current treatments are responsible for poor outcome. Natamycin is the only FDA-approved antifungal drug to treat fungal keratitis, but unfortunately due to its poor water solubility, it is available as suspension. The marketed suspension (5% Natamycin) has rapid precorneal clearance, poor corneal permeability, a higher frequency of administration, and corneal irritation due to undissolved suspended drug particles. In our study, we developed clear and stable natamycin-loaded nanomicelles (1% Natcel) to overcome the above challenges. We demonstrated that 1% Natcel could permeate the cornea better than 5% suspension. The developed 1% Natcel was able to provide sustained release for up to 24 h. Further, it was found to be biocompatible and also improved the mean residence time (MRT) than 5% suspension in tears. Therefore, the developed 1% Natcel could be a potential alternative treatment for fungal keratitis.

PMID: 38615806

28. Utility of an in-house real-time PCR in whole blood samples as a minimally invasive method for early and accurate diagnosis of invasive mould infections

Mragnayani Pandey[1], Immaculata Xess[2], Janya Sachdev[1], Neha Sharad[3], Sonakshi Gupta[1], Gagandeep Singh[1], Renu Kumari Yadav[1], Bhaskar Rana[1], Stephen Raj[1], M Nizam Ahmad[1], Neha Nityadarshini[1], Upendra Baitha[4], Manish Soneja[4], Shalimar[5], Bindu Prakash[4], Kapil Sikka[6], Purva Mathur[3], Viveka P Jyotsna[7], Rakesh Kumar [6], Naveet Wig[4], Sudesh Gourav[1], Ashutosh Biswas[4], Alok Thakar[6]

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J Infect. 2024 May;88(5):106147. doi: 10.1016/j.jinf.2024.106147.

Abstract

Introduction: Invasive mould infections (IMIs) are a leading cause of death in patients with compromised immune systems. Proven invasive mould infection requires detection of a fungus by histopathological analysis of a biopsied specimen, sterile culture, or fungal DNA amplification by PCR in tissue. However, the clinical performance of a PCR assay on blood samples taken from patients suspected of invasive mould disease has not been fully evaluated, particularly for the differential diagnosis of invasive aspergillosis (IA) and invasive Mucormycosis (IM).

Objectives: To assess the diagnostic utility of our previously validated in-house real-time PCR in blood samples for diagnosis of invasive aspergillosis and mucormycosis in patients with suspected invasive mould infection.

Methods: All patients with suspected invasive mould infection were prospectively enrolled from May 2021 to July 2021. Conventional fungal diagnosis was performed using tissue and respiratory samples. In-house PCR was performed on blood samples and its diagnostic performance evaluated.

Results: A total of 158 cases of suspected invasive mould infection were enrolled in the study. The sensitivity and specificity of in-house PCR performed on blood samples was found to be 92.5% and 81.4% respectively for diagnosis of probable IA, and 65% and 84.62% respectively for diagnosis of proven and probable IM. It was also able to detect 3 out of 5 cases of possible IM where no other microbiological evidence of IM was obtained.

Conclusions: This assay could be helpful in minimally invasive diagnosis of IMIs for patients in whom invasive sampling is not feasible, especially as a preliminary or screening test. It can help in early diagnosis, anticipating conventional laboratory confirmation by days or weeks. Possible correlation between fungal load and mortality can help in initiating aggressive treatment for patients with high initial fungal load.

PMID: 38555035

29. Global Transcriptomic Profiling of Innate and Adaptive Immunity During *Aspergillus flavus* Endophthalmitis in a Murine Model

Agimanailiu Khapuinamai[1,2], Dhanwini Rudraprasad[1,2], Suchita Pandey[1], Jaishree Gandhi[1], Dilip Kumar Mishra[3], Joveeta Joseph[1]

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Invest Ophthalmol Vis Sci. 2024 Apr 1;65(4):44. doi: 10.1167/iovs.65.4.44.

Abstract

Purpose: Fungal endophthalmitis is characterized by chronic inflammation leading to the partial or complete vision loss. Herein, we analyzed the transcriptomic landscape of *Aspergillus flavus* (*A. flavus*) endophthalmitis in C57BL/6 mice to understand the host-pathogen interactions.

Methods: Endophthalmitis was induced by intravitreal injection of *A. flavus* spores in C57BL/6 mice and monitored for disease progression up to 72 hours. The enucleated eyeballs were subjected to histopathological analysis and mRNA sequencing using the Illumina Nextseq 2000. Pathway enrichment analysis was performed to further annotate the functions of differentially expressed genes (DEGs) and validation of cytokines was performed in vitreous of patients with fungal endophthalmitis using multiplex ELISA.

Results: Transcriptomic landscape of *A. flavus* endophthalmitis revealed upregulated T-cell receptor signaling, PI3K-AKT, MAPK, NF-κB, JAK-STAT, and NOD like receptor signaling pathways. We observed significant increase in the T-cells during infection especially at 72 hours infection along with elevated expression levels of IL-6, IL-10, IL-12, IL-18, IL-19, IL-23, CCR3, and CCR7. Furthermore, host-immune response associated genes, such as T-cell interacting activating receptor, TNF receptor-associated factor 1, TLR1, TLR9, and bradykinin receptor beta 1, were enriched. Histopathological assessment validated the significant increase in inflammatory cells, especially T-cells at 72 hours post-infection along with increased disruption in the retinal architecture. Additionally, IL-6, IL-8, IL-17, TNF-α, and IL-1β were also significantly elevated, whereas IL-10 was downregulated in vitreous of patients with Aspergillus endophthalmitis.

Conclusions: Regulating T-cell influx could be a potential strategy to modulate the excessive inflammation in the retina and potentially aid in better vision recovery in fungal endophthalmitis.

PMID: 38687493

Glimpse of CME on Fungal Infections

Dr. Malini Kapoor conducted a preconference workshop under the aegis of UP-UK Microcon at GMC Agra on Clinical and Diagnostic Mycology on 9th and 10th February 2024. Thirty one participants from UP, UK, Delhi, Haryana , MP and Rajasthan attended the workshop.

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WHO SHOULD ATTEND?

ISMM 2025 is for all clinical and scientific professionals involved in the diagnosis and management of invasive fungal infection

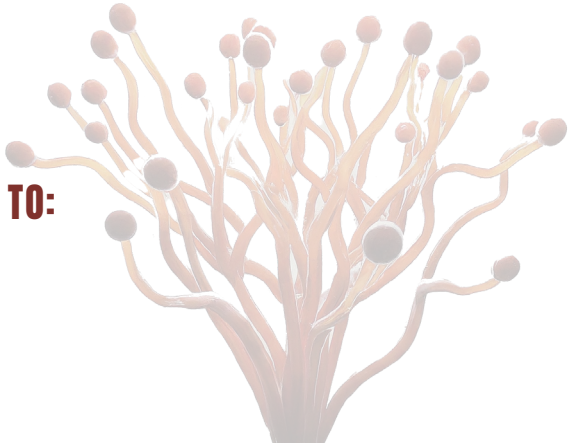
- Doctors, trainees and researchers in infectious disease, critical care, transplantation, hemato-oncology, dermatology and the spectrum of clinical specialties managing these infections
- Clinical and laboratory microbiologists
- Microbiology/ Mycology laboratory professionals
- PG students/ PhD scholars

REGISTRATION DETAILS

	ISMM Members	NON-ISMM Members	Young ISHAM* Members & PG/PhD Students	ISHAM Members
Early bird (1st July till Nov 30th 2024)	₹9500	₹11500	₹6000	₹8500
1st Dec 2024 to 16th Feb 2025	₹10500	₹12500	₹7000	₹8800
Spot registration	₹13000	₹15000	₹9000	₹11000
Accompanying person	₹5000	₹5000	₹5000	₹5000
One day/ Workshop	₹2000	₹2000	₹1500	₹2000

* Young ISHAM members (Below 40 years age) – Age proof to be uploaded

Few eligible participants will be given travel grant for presenting their poster/oral in ISMM 2025
Preference will be given to young ISHAM members for the travel grant.



REGISTRATION STARTS FROM 1ST JULY 2024

FOR REGISTRATION AND MORE DETAILS, PLEASE LOG ON TO:
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ABSTRACT SUBMISSION GUIDELINES

Last date for abstract submission: 30th December 2024

Word limit: Not more than 500 words

Oral presentation: 7 minutes and 3 minutes for discussion

Poster size: 24 inches by 36 inches in Portrait orientation

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AWARDS

AWARDS CATEGORY	REQUIREMENTS
1. Dr. MJ Thirumalachar Life-time achievement Award	Nominations must be sent in the prescribed Format.
2. G.P. Agarwal Young scientist award	Young scientist below the age of 35 yrs. (proof of age must be submitted). Applicants must submit the full length original research paper in duplicate on any area of medical mycology. Papers will be evaluated and selected for oral presentation.
3. Dr. Kamalam Glaxo Award	Applicant must submit full length research paper in duplicate in the field of dermatomycology. Papers will be evaluated and selected for oral presentation.
4. Dr. Pankajalakshmi Venugopal - Glaxo Meritorious Award	Young scientist below the age of 35 yrs. (proof of age must be submitted). Applicants must submit curriculum vitae with list of publications and re- prints of the papers in the field of medical mycology.
5. Three (3) Best poster awards	
6. Travel Awards for Young ISHAM Members	

Last date of submission: 30th December 2024 | Mail to organisingsecretary@ismm2025.com

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