

ISHAM Working Group on *Aspergillus terreus*

The *A. terreus* working group consists of a diverse group of mycologists, clinicians and molecular biologists. This unique consortium will work towards the common goal of augmenting existing knowledge on the biology, genetic diversity, population dynamics, clinical epidemiology, virulence and antifungal susceptibilities of the emerging fungal pathogen *A. terreus*. The working group will sustain a communication network through which the members can exchange research idea and thoughts freely and will also function as a portal for the group to meet and exchange research data.

Objectives:

1. Explore the genetic diversity and population dynamics of *A. terreus*. Under this aim, we propose to:
 - a) develop a comprehensive culture repository comprising both clinical and environmental isolates of *A. terreus* and other isolates in section *Terrei*,
 - b) design a multilocus sequence typing scheme (MLST) for species identification in Section *Terrei*,
 - c) using the repository and the MLST scheme, generate data on the genetic diversity and population dynamics of *A. terreus*,
 - d) establish a new typing method based on the polymorphism of tandem repeats in *A. terreus*,
 - e) recognize and validly publish new species.
2. Understand the epidemiology of *A. terreus* by
 - a) Developing a microsatellite marker panel for strain discrimination and use test this panel on several environmental and clinical isolates of *A. terreus* to understand the molecular epidemiology of this organism
 - b) Elucidating the clinical epidemiology of *A. terreus*
3. Investigate amphotericin B resistance in *A. terreus*
4. Study immune response and virulence potential of *A. terreus*
5. To set up animal models to establish in vivo and in vitro correlation

MEMBERS AND RESPONSIBILITIES:

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Epidemiology of *A. terreus*; collection of clinical samples

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Exo-metabolomics on *Aspergillus terreus* and related species

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Maintain *A. terreus* repository. Design and validate the MLST scheme

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Scanning electron microscopic studies of drug-fungal interaction

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Extrolite profiling of *A. terreus*

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Design and validate typing assays for *A. terreus* and sibling species using microsatellite markers and/or AFLP

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Virulence potential of *A. terreus*

Cornelia Lass-Flörl, convenor
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Antifungal susceptibility testing
Gerhard Blum (together with C. Lass-Flörl)
Emina Jukic (together with C. Lass-Flörl)
Animal models, MICs, proteome map

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Virulence potential of *A. terreus*

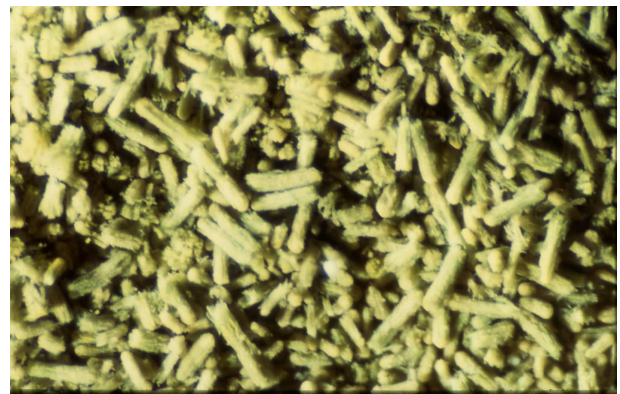
6. To create an *A. terreus* proteome map
7. Database
A web-based data base will be built up and made accessible for all participants for studies.
8. Prepare a genomic bank for *A. terreus* which will be use for the identification and characterization of some putative virulence factors of the fungus (e.g. anti-oxidant systems, proteases, etc.).
9. Exo-metabolomics on *Aspergillus terreus* and related species.

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Phylogenetic analysis

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Contribute to *A. terreus* repository

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Innate immunity

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Contribute to *A. terreus* repository



ISHAM Working Group for *Aspergillus terreus* Publications

- Lass-Flörl C, Grif K, Kontoyiannis DP. Molecular typing of *A. terreus* isolates collected in Houston, Texas and Innsbruck, Austria: evidence of great genetic diversity. *J Clin Microbiol.* 2007 Aug;45(8):2686-90. Epub 2007 Jun 20.
- Perkhofer S, Blum G, Speth C, Mayr A, Dierich MP, Lass Flörl C. *Eur J Clin Microbiol Infect Dis.* 2007 Jun;26(6):413-7. Influence of amphotericin B and amphotericin B colloidal dispersion on the functions of human phagocytes in defence against *Aspergillus* species.
- Lass-Flörl C, Alastruey-Izquierdo A, Cuenca-Estrella M, Perkhofer S, Rodriguez-Tudela JL. In Vitro Activities of Various Antifungal Drugs against *Aspergillus terreus*: Global Assessment using EUCAST Methodology. *Antimicrob Agents Chemother.* 2008 Dec 8; 53(2): 794-795.
- Blum G, Perkhofer S, Grif K, Mayr A, Kropshofer G, Nachbaur D, Kafka-Ritsch R, Dierich MP, Lass-Flörl C. A 1-year *Aspergillus terreus* surveillance study at the University Hospital of Innsbruck: molecular typing of environmental and clinical isolates. *Clin Microbiol Infect.* 2008 Dec;14(12):1146-51.
- Blum G, Perkhofer S, Haas H, Schrettl M, Würzner R, Dierich MP, Lass-Flörl C. Potential basis for amphotericin **B** resistance in *Aspergillus terreus*. *Antimicrob Agents Chemother.* 2008 Apr;52(4):1553-5.
- Elad D., Lahav D., Blum S. (2008) Transuterine transmission of *Aspergillus terreus* in a case of disseminated canine aspergillosis. *Medical Mycology.* 46:175-178. 2005; 6/128.
- Deak E, Wilson SD, White E, Carr JH, Balajee SA. *Aspergillus terreus* accessory conidia are unique in surface architecture, cell wall composition and germination kinetics. *PLoS One.* 2009 Oct 30; 4(10):e7673.
- Baddley JW, Marr KA, Andes DR, Walsh TJ, Kauffman CA, Kontoyiannis DP, Ito JI, Balajee SA, Pappas PG, Moser SA. Patterns of susceptibility of *Aspergillus* isolates recovered from patients enrolled in the Transplant-Associated Infection Surveillance Network. *J Clin Microbiol.* 2009 Oct;47(10):3271-5. Epub 2009 Aug 19.
- Balajee SA, Baddley JW, Peterson SW, Nickle D, Varga J, Boey A, Lass-Flörl C, Frisvad JC, Samson RA; ISHAM Working Group on *A. terreus*. *Aspergillus alabamensis*, a new clinically relevant species in the section Terrei. *Eukaryot Cell.* 2009 May;8(5):713-22. Epub 2009 Mar 20.
- Balajee SA. *Aspergillus terreus* complex. *Med Mycol.* 2009;47 Suppl 1:S42-6. Epub 2009 Mar 17.
- Ben-Ami R, Lamaris GA, Lewis RE, Kontoyiannis DP. Interstrain variability in the virulence of *Aspergillus fumigatus* and *Aspergillus terreus* in a Toll-deficient *Drosophila* fly model of invasive aspergillosis. *Med Mycol.* 2009 Jul 29:1-9. [Epub ahead of print]
- Deak E, Nelson M, Hernández-Rodríguez Y, Gade L, Baddley JW, Momany M, Steele C, Balajee SA. *Aspergillus terreus* accessory conidia induce inflammatory responses during infection in a pulmonary model of aspergillosis possibly due to early and sustained β -glucan display. *Virulence* 2011 May 1; 2(3).
- Samson RA, Peterson SW, Frisvad JC, Varga J (2011) New species in *Aspergillus* section Terrei. *Studies in Mycology* (in

press).

Conference Presentations:

- Molecular phylogeny of *Aspergillus terreus*. Balajee SA. Oral presentation at the meeting an "*Aspergillus* systematics in the genomic era". 2007.
- The *A. terreus* complex. Balajee SA. Oral presentation. Joint meeting of the Netherlands Society for Medical Mycology. 2007.
- Caspofungin (CAS) mediated beta-glucan (BG) unmasking and enhancement of human neutrophil (PMN) activity against *Aspergillus* spp. GA Lamarinis, RE Lewis, G Chamilos, G May, II Raad, DP Kontoyiannis. The University of Texas MD Anderson Cancer Ctr, TX. Poster presentation at ICAAC 2007.
- Epidemiology of *Aspergillus terreus* Infection in Transplant Recipients from Transplant Associated Infection Surveillance Network (TRANSNET). J. W. Baddley, K. A. Marr, D. R. Andes, D. P. Kontoyiannis, T.F Patterson, E.J. Anaissie, T.J. Walsh, B. D. Alexander, M. Schuster, R. A. Oster, and P. G. Pappas. IDSA. 2007.
- A one year *Aspergillus terreus* surveillance study at the University Hospital Innsbruck: molecular typing of environmental and clinical isolates. Lass Florl et al.
- Evaluation of liposomal dose-escalation and de-escalation strategies in a neutropenic murine model of aspergillus terreus pneumonia. Russell E. Lewis, Nathan D. Albert, Guangling Liao, and Dimitrios P. Kontoyiannis. Abstract, Advance Against Aspergillosis, Rome Italy, 2010.