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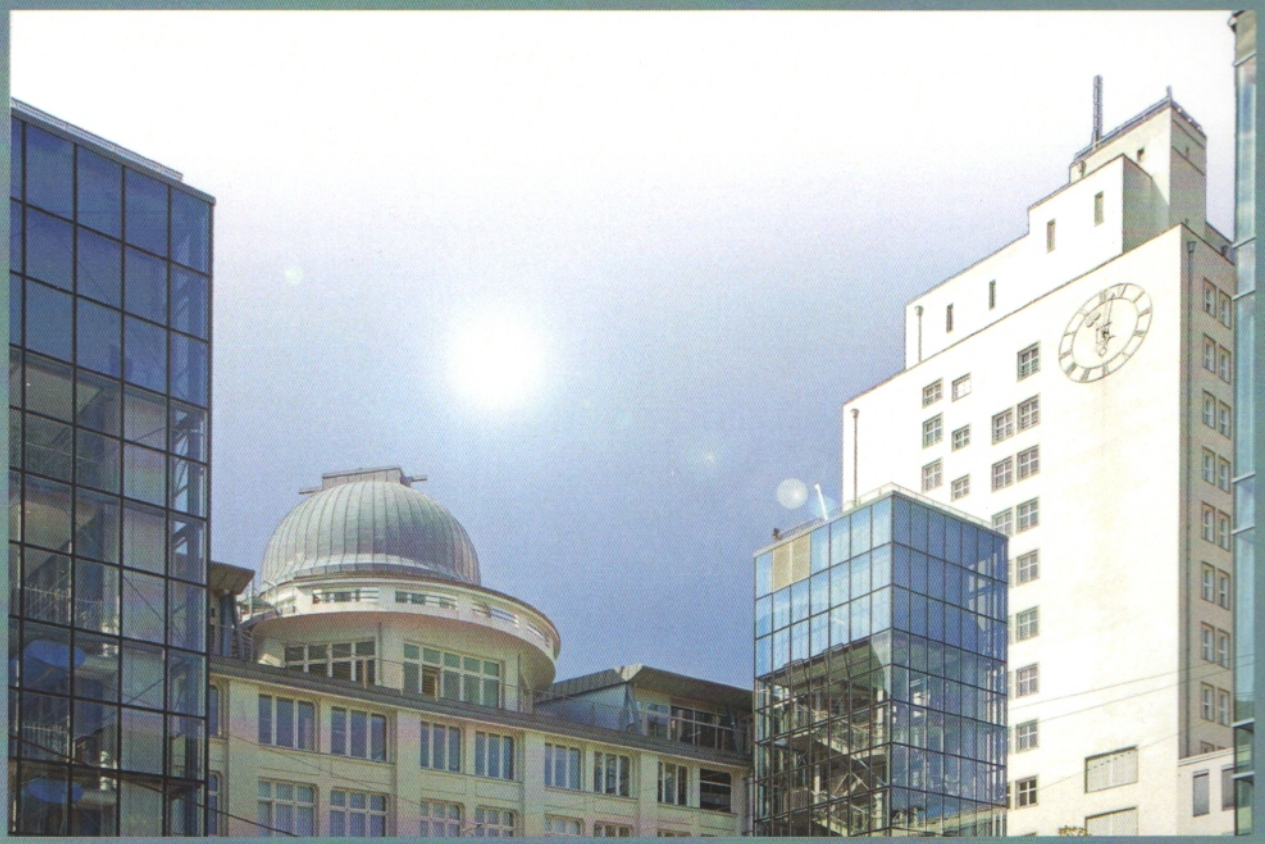

Abstracts of the 49. Wissenschaftliche Tagung der Deutschsprachigen Mykologischen Gesellschaft e.V. and 1st International Symposium of the CRC/Transregio FungiNet

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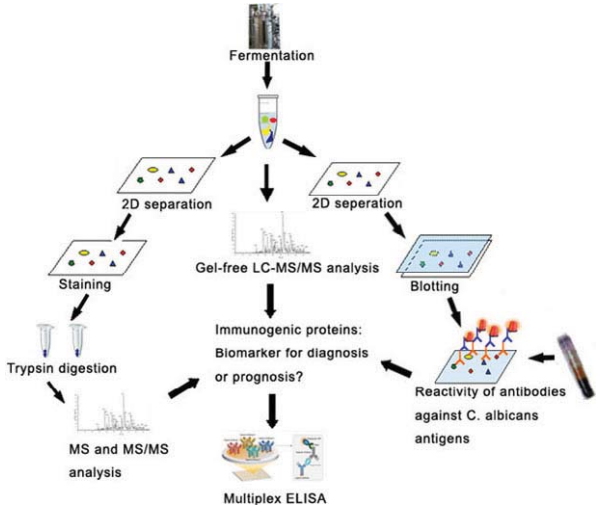

Figure

Myk08-12

Immunotoxicological concerns of mycotoxins with emphasis on permissble levels of aflatoxin B_1 and human dendritic cells

J. Mehrzad,[1] A. Bahari,[1,2] H. Dehghani,[1,2,3] M. R. Bassami[1,2,3,4] and M. Mahmoudi[1,2,3,4,5]

[1]Ferdowsi University of Mashhad, Mashhad, Iran, Islamic Republic of; [2]Ferdowsi University of Mashhad, Pathobiology, Mashhad, Iran, Islamic Republic of; [3]Ferdowsi University of Mashhad, Basic Science, Mashhad, Iran, Islamic Republic of; [4]Ferdowsi University of Mashhad, Clinical Science, Mashhad, Iran, Islamic Republic of and [5]Mashhad University of Medical Sciences, Immunology and Allergy, Mashhad, Iran, Islamic Republic of

Mycotoxins, which are toxic secondary metabolites produced by molds, are potentially harmful to human and animal health upon consumption of mycotoxin-contaminated food or feed. The contamination of agricultural products by mycotoxin-producing molds remains a serious concern for animal and human health. Despite monitoring programs and many specific regulations, humans and animals could still be exposed to mycotoxins, present at low levels in feed and food. Among these mycotoxins, aflatoxins (AFs), especially AFB_1, are the most toxic and carcinogenic to mammals. Further, AFB_1 impairs cell-mediated immunity, though the exact mechanism of this immunotoxicity is not well-known. By far the most pivotal cells in the induction of immune responses are dendritic cells (DCs). These highly specialized cells dictate T-cell activation/polarisation depending on the nature of the encountered antigens and environmental cues. To elucidate the effect of AFB_1 on the key molecules and the function of DCs, we used human monocyte-derived DCs (MDDCs) as a model system and performed cell culture, qPCR and flow cytometry assays. An environmentally relevant level of AFB_1 remarkably impaired the phagocytic capacity of MDDCs. Furthermore, as compared to untreated MDDCs, AFB_1 significantly affected on the transcription of some key functional genes in MDDCs, i.e., upregulated mRNA expression of key cytochrome P450 (CYP) families, MyD88, NF-KB, TNF-a, TLR2, TLR4, COX-2, HLA, CD16, and downregulated mRNA expression of AhR, TGF-b, CD11c and CD64 at 2–12 h post treatment. In contrast, the transcription of some other key genes, e.g., IL-10, IL-1b, AKR7A2, GSTM1, IL-6. IL-8, C5aR, CCR7, CD209 and LFA3 in post-AFB_1 treated MDDCs only slightly changed. Our results in this study indicate that an environmentally relevant level of AFB_1 impairs the phagocytosis capacity and dysregulates the key functions of MDDCs, which could mechanistically explain the observed immunotoxicity of this mycotoxin *in vivo*, and further emphasis the essentiality of reducing AFB_1 levels in agricultural commodities.

FN09-01

Manipulation of the innate immune response by Cryptococcus

R. May

University of Birmingham, Institute of Microbiology & Infection, Birmingham, United Kingdom

The two pathogenic species of Cryptococci, *Cryptococcus neoformans* and *C. gattii*, share a remarkable ability to evade the innate immune system and disseminate throughout the body. This is thought, in large part, to be the result of natural selection through environmental amoebae, since virulence traits that the fungus has evolved to survive within such predators typically work just as effectively within human phagocytes.

In this talk I will discuss our recent work in probing the cryptococcal/macrophage interaction. In particular, I will discuss what we have learned about the molecular basis of 'vomocytosis', a phenomenon that the pathogen uses to exit from phagocytic cells. In addition, we are also interested in the genetic changes that drive hypervirulent outbreaks of cryptococcosis in otherwise healthy individuals and I will attempt to 'compare and contrast' these disease situations and speculate on what they tell us about the innate immune response to fungal pathogens more generally.

FN09-02

Flipping the switch: how fungal chitin influences the immune response

J. Wagener, G. Brown and N. A. R. Gow

University of Aberdeen, Aberdeen Fungal Group, School of Medical Sciences, Aberdeen, United Kingdom

Chitin is an essential structural polysaccharide of the fungal cell wall and we recently discovered fungal chitin to trigger an anti-inflammatory immune response in myeloid cells. Activity of human chitinases was essential to release chitin particles with anti-inflammatory properties from *C. albicans*. In addition, fungal chitin induced eosinophilia *in vivo*, a typical sign for a Th2 driven allergic reaction [1].

Interestingly, high level expression of the acidic mammalian chitinase I (AMCase I) is associated with allergies and asthma. AMCase I expression, together with the ratio between Arginase I and nitric oxide synthase (iNOS) expression, serves as marker for allergy-associated alternative activated macrophages. Myeloid Arginase I has been shown to down-regulate excessive Th1-induced inflammation and further, enhances wound healing. The production of nitric oxide (NO) on the other hand, is essential for the host defence against pathogens. The balance between iNOS and Arginase I is therefore critical for host defence and immune homeostasis, and several pathogens, including fungi, can target these balance in their favour[2].

Here we report for the first time, that fungal chitin increases Arginase I protein levels in human myeloid cells, which can be blocked by the chitinase inhibitor Bisdionin C. We further show that fungal chitin shifts classical activated macrophage towards a more alternative activated phenotype. Treatment of *C. albicans* with the β-1,3-glucan synthesis inhibitor caspofungin increases fungal cell wall chitin and moreover, leads to chitin surface presentation. Caspofungin-treated *C. albicans* cells fail to induce a pro-inflammatory immune response and moreover, are shifting classical macrophages towards an alternative phenotype, as observed for fungal chitin alone.