low concentrations of culture medium or fungal ligands for 24 h, followed by a wash-out period of 7 days. After this period, a second stimulation of cytokine production with various PRX ligands was performed for an additional 24 h. Surprisingly, pre-incu-
ba
cation of primary PBMCs or monocytes with C. albicans induced either tolerance or priming, depending on the concentration of fungal ligands in the system. While a high concentration of ligands induced cross-tolerance, low amounts of C. albicans strongly primed production of the proinflammatory cytokines TNF and IL-6 induced by both CLRs and TLRs, a dose-dependent response reminiscent of antigen-dependent adaptive immune responses. The priming effects of C. albicans were reproduced with purified beta-glucans, but not mannans. The mechanism of priming induced by beta-glucans required the alternative beta-glucan receptor complement receptor 3 (CR3) and the non-canonical Raf1 pathway. Strikingly, the beta-glucan receptor Dectin-1 also seemed to mediate the priming but in a Syk kinase independent pathway. Initial data suggest an important role of epigenetic changes at the level of histone acetylation/ methylation as an important molecular mechanism through which the beta-glucan receptors induced the priming effects on gene transcription. In conclusion, beta-glu-
cans can induce strong priming of the production of proinflammatory cytokines through a Dectin-1/CR3/Raf1 mediated pathway, an effect that may play an important role in resistance to re-infection and for the future design of novel vaccines.


PS2-103

The roles of Dectin-1/2 in the host defense against fungal infection
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Dectin-1 and Dectin-2 are type II transmembrane proteins of the C-type lectin family with single carbohydrate recognition domains (CRDs) in their extracellular region. To elucidate their function, we produced Dectin-1- and Dectin-2-deficient mice and determined the roles of these molecules in the host defense against patho-
genic fungi. In vivo, while Dectin-2-deficient mice were more susceptible to NRB1C385 strain of Candida albicans (C. albicans), Dectin-1-deficient mice showed normal response to this fungus. Th17 cell differentiation was markedly decreased when naïve T cells were cultured with culture supernatant obtained from Dectin-2-
deficient DCs with C. albicans stimulation, it was indicated that Dectin-2 is mainly involved in the Th17 cell differentiation by candida infection. In vitro, cytokine pro-
duction was partially suppressed in Dectin-2-deficient mice when stimulated with hyphae form of C. albicans, cytokine secretion was significantly suppressed in Dep-
tin-1/Dectin-2 double deficient mice. Thus, Dectin-1 and Dectin-2 are required for the immune responses to some fungal infections as a protective immunity and these molecules may synergistically contribute to this host innate immune response.


PS2-104

HBsAg inhibits IFN-α production in plasmacytoid dendritic cells via inducing TNF-α and IL-10 production in monocytes
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HBsAg inhibits IFN-α production in plasmacytoid dendritic cells (pDCs) are professional IFN-α-producing cells that play important roles in antiviral immune response. However, evidence shows that pDCs in chronic hepatitis B (CHB) patients was impaired, but the mechanisms underlying pDCs’ impairment are not fully elucidated. Previously, we and others have reported that HBsAg could inhib-
bit Cpg-A induced IFN-α production in healthy donors’ PBMCs and pDCs. Here we showed that serum purified or CHO cells expressed-HBsAg pretreatment could signifi-
cantly inhibit IFN-α production through upregul-
ating TNF-α and IL-10 expression, which are known as pDCs’ inhibitor. HBsAg induced monocytes TNF-α and IL-10 production in a dose dependent manner. Besides, HBsAg, TNF-α and IL-10 were all shown to down-regulate TLR9 expression on pDCs, which maybe reasonable mechanism for inhibiting IFN-α production. Our observations help to understand the lack of strong antiviral immunity in CHB patients.


PS2-105

Production of IFN-β during Listeria monocytogenes infection is restricted to the monocyte/macrophage lineage
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The family of type I interferons (IFN), which consists of several IFN-α and one IFN-
β, are produced not only after stimulation by viruses, but also after infection with non-viral pathogens. In the course of bacterial infections, these cytokines could be beneficial or detrimental. IFN-β is the primary member of type I IFN that initiates a cascade of IFN-α production. Here we addressed the question which cells are respon-
sible for IFN-β expression after infection with the intracellular pathogen Listeria mon-
ocytogenes by using a genetic approach. By means of newly established reporter mice, maximum of IFN-β expression was observed at 2 h post infection in spleen an-
surprisingly, 48 h post infection in colonized cervical and inguinal lymph nodes. Colon-
i zation of lymph nodes was independent of the type I IFN signaling, as well as bacterial dose and strain. Using cell specific reporter function and conditional deletions we could define cells expressing Ly5m as the major IFN-β producers, with cells formerly defined as Tip-DCs being the highest. Neutrophilic granulocytes, dendritic cells and plasmacytoid dendritic cells did not significantly contribute to type I IFN production.


PS2-106

Bacteroides fragilis inhibits Candida albicans induced IL-17
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Background: Bacteroides fragilis and Candida albicans are both part of the commen-
sal intestinal flora. When B. fragilis spreads to normally sterile parts of the body it is a potent inducer of abscess formation. These abscesses are often polymicrobial and syn-
egergistic effects in promoting larger abscesses and bacterial persistence have been observed for bacterial co-infections. In contrast, the presence of fungi in abscesses and the effect of fungal and microbial co-infections on the host immune response, has been poorly studied. The aim of this study was to assess the modulatory effect of B. fragilis on the C. albicans induced cytokine profile.

Methods: Peripheral blood mononuclear cells (PBMCs) from healthy volunteers were stimulated with heat- killed B. fragilis (107/ml), heat- killed C. albicans (109/ml), or the combination and cytokine levels were determined in supernatants by ELISA.

Results: Both B. fragilis (109/ml) and C. albicans (109/ml) are potent inducers of IL-8 and IL-6, with a moderate IL-1β and TNFα production, while induction of IL-23, IFNγ and IL-10 is low. In contrast to B. fragilis, C. albicans is a potent inducer of IL-17. Co-
incubation of Bacteroides fragilis and C. albicans resulted in a significant decrease of IL-
17 secretion by PBMCs, whereas co-incubation had an additive effect on most other cytokines. B. fragilis inhibited IL-17 production even if added to the cells two hours after stimulation with C. albicans. B. fragilis induced these effects through Toll-like receptor 2 (TLR2), and the TLR2 stimulus Pam3Cys had similar inhibitory effects on C. albicans-induced IL-17 secretion.

Conclusion: B. fragilis inhibits C. albicans induced IL-17 secretion through TLR2-
mediated signaling. This finding may have important consequences for the patho-
physiology of bacterial–fungal mixed abscesses, as well as during co-colonization of the intestinal mucosa with these two microorganisms.


PS2-107

Effector proteins from Yersinia pseudotuberculosis influence cytokine expression in T lymphocytes subpopulations
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Y. pseudotuberculosis is an enteropathogen that causes gastrointestinal disorders. The resolution of the infection is linked to activation of CD4+ Th1 cells that produce cytokines such as IFN-γ and IL-2. All the pathogenic Yersinia spp. contain an extra-
chromosomal 70-kb plasmid, which encodes the Yops (Yersinia outer proteins). The effector proteins can inhibit the host immune response by interfering in the T cells activation. In this study, the possible role of the Y. pseudotuberculosis infection and Yops virulence factors in the response of T lymphocytes was investigated. Spleen cells