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 PRR ligands was performed for an additional 24 h. Surprisingly, pre-incubation 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-glucans can induce strong priming of the production of proinflammatory cytokines through a Dectin-1/CR3/Raf-1 mediated pathway, an effect that may play an important role in resistance to re-infection and for the future design of novel vaccines.

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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 pathogenic fungi. In vivo, while Dectin-2-deficient mice were more susceptible to NBRC1385 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 production was partially suppressed in Dectin-2 deficient mice when stimulated with hyphae form of *C. albicans*, cytokine secretion was significantly suppressed in Dectin-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.

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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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Hepatitis B virus infection is a global health problem. Accumulating evidences show that inadequate immune responses to HBV are responsible for its persistence. 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 inhibit 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 significantly inhibit TLR9 mediated IFN-α production in healthy donors' PBMCs where monocytes were involved. We also found that monocytes strengthened HBsAg's inhibitory effect on purified pDCs and when more monocytes were co-cultured with pDCs, the inhibitory effect become more significant. In further research, we found that cytokines secreted by monocytes were responsible for the inhibitory effects by trans-well experiment. In addition, we found that HBsAg inhibited IFN-α production through upregulating 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.

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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 responsible for IFN-β expression after infection with the intracellular pathogen *Listeria monocytogenes* by using a genetic approach. By means of newly established reporter mice, maximum of IFN-β expression was observed at 24 h post infection in spleen and, surprisingly, 48 h post infection in colonized cervical and inguinal lymph nodes. Colonization 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 LysM 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.

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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 commensal 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 synergistic 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* (10^7/ml), heat- killed *C. albicans* (10^5/ml), or the combination and cytokine levels were determined in supernatants by ELISA.

Results: Both *B. fragilis* (10^7/ml) and *C. albicans* (10^5/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 pathophysiology of bacterial–fungal mixed abscesses, as well as during co-colonization of the intestinal mucosa with these two microorganisms.

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PS2-107

Effector proteins from *Yersinia pseudotuberculosis* influence cytokines 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