Mold metabolites drive rheumatoid arthritis in mice via promotion of IFN-gamma- and IL-17-producing T cells.

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Abstract

Environmental factors have been discussed as triggers for autoimmune diseases like rheumatoid arthritis (RA). However, the role of chemical exposures in activation or exacerbation of RA is not clarified yet. Exposure of DBA/1 mice to the mold metabolites ochratoxin A (OTA) or deoxynivalenol (DON) increased the prevalence and the clinical severity of RA compared to un-exposed mice using an experimental collagen-induced arthritis model. Mycotoxin-exposed mice showed enhanced serum IgG1 and IgG2a levels and an elevated production of IL-1β and IL-6 in inflamed joints and of IFN-γ and IL-17 in splenocytes. Additionally, OTA and DON increased the release of the pro-inflammatory cytokines IL-1β, IL-6 and TNF-α in activated murine macrophages and supported the differentiation of naïve T cells into Th1 cells, while treatment of CD4+T cells with the supernatant from mycotoxin-exposed macrophages induced IL-17 production. Furthermore, exposure of mice to OTA or DON enhanced the gene expression of Stat1, Stat3 and Stat4 in the spleen while the collagen-induced increase of Socs1 and Socs3 was abolished. Our results demonstrate that mycotoxins increase the susceptibility to develop RA via an enhanced

stimulation of macrophages and promotion of Th1/Th17 cell differentiation by induction of Stat signalling pathways and down-regulation of the Socs-mediated feedback inhibition.

Beteiligte Forschungseinheiten

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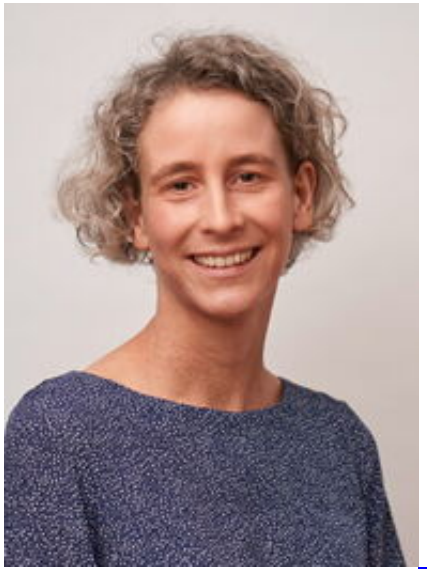

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