Background and aims Dectin-1 is a c-type lectin like receptor that signals via syk and is involved in anti-fungal immunity. Dectin-1 was found to trigger experimental inflammatory arthritis, and likely play a role in the pathogenesis of some autoimmune diseases. This study aimed to examine dectin-1 expression and function of circulating CD14+ monocytes and monocyte-derived dendritic cells (MDDCs) in patients with systemic lupus erythematosus (SLE).

Methods SLE patients with active and inactive diseases and healthy subjects were recruited. Dectin-1 agonists including curdlan, zymosan and toll-like receptor agonists Pam3CSK4 (TLR2) and LPS (TLR4) were used to stimulate monocytes and/or MDDCs. Dectin-1, ROS and phosphorylated-syk (p-Syk) were measured by flow cytometry. Cytokine profile was measured by and multi-bead immunoassay.

Results Dectin-1 expressing monocytes was significantly lower in active SLE patients compared to inactive patients and healthy controls. The absolute count of dectin-1 expressing monocytes correlated significantly and inversely with SLEDAI, anti-dsDNA antibody level and C4. Despite this, ROS production upon stimulation by dectin-1 agonists was comparable. Stimulation of dectin-1 led to activation and maturation of MDDCs. SLE MDDCs showed higher p-Syk activation compared to normal MDDCs upon dectin-1 stimulation. Curdlan-stimulated MDDCs produced higher levels of IL-1β, IL-23 and TNF-α. Adding TLR2 agonist to curdlan, SLE MDDCs produced significantly higher level of IL-1β compared to normal MDDCs.

Conclusions Active SLE patients had significantly lower circulating dectin-1-expressing monocytes which produced comparable level of ROS compared to inactive patients and healthy subjects. Dectin-1 agonists led to significantly higher Th17 promoting cytokines upon co-stimulation with TLR2 in SLE MDDCs.

349 TME173/STING IS CRUCIAL FOR LUPUS DEVELOPMENT IN FCGR2B-DEFICIENCY MICE

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Background and aims Type I interferon is one of the most critical cytokines involving in lupus pathogenesis. The activation of endosomal nucleic acid sensors leading to type I IFN production empowers the lupus phenotypes in several mouse models. The signalling of cytosolic DNA sensor also induces type I IFN production and the role in lupus disease are not clear. Stimulator of interferon genes (Sting), also known as transmembrane protein 173 (TME173) and MYS/MTA/ERIS, is a cytosolic DNA sensor which recognised cyclic di-GMP and subsequently stimulated type I interferon production. The Fcgr2b-deficient mice develop spontaneous lupus phenotypes which are splenomegaly, the presence of anti-nuclear antibodies (ANA) and fatal glomerulonephritis. The polymorphisms of FCGR2B associates with the increases of lupus susceptibility in human. The goal of the study is to identify the role of Sting in lupus mouse model.

Methods The Sting-deficient mice were bred with the Fcgr2b-deficient mice to create double deficient mice and control littermates. The mice were analysed for survival rate, autoantibodies production, severity of pathology, gene expression profiles, and immunophenotypes.

Results In the absence of Sting, the Fcgr2b-deficient mice survived longer and the level of ANA and anti-dsDNA antibody considerably reduced. The glomerulonephritis in the double-deficient mice also ameliorated. The expression of interferon inducible genes such as Cxcl10, Mx1, and Ifi5 in the kidneys of the double-deficient mice was significantly lower than the Fcgr2b-deficient mice.

Conclusions Sting-mediated signalling pathway plays the substantial role in lupus pathogenesis of the Fcgr2b-deficient mice. Blocking Sting function may be the advantage for treatment in lupus patients.
Background and aims C-type lectin domain family 16 member A (CLEC16A) has been associated with autoimmune diseases such as systemic lupus erythematosus, multiple sclerosis and type I diabetes in various genome-wide association studies. Subsequent studies revealed that mouse/human CLEC16A and its Drosophila homolog endosomal maturation defective isoform A (EMA) are involved in different aspects of autophagy, the regulated degradation of cellular components that are in excess or dysfunctional. Crosstalk between autophagy and inflammasome activity of innate immune responses has been reported and inflammasomes are activated in various autoimmune diseases. We thus sought to investigate the role of CLEC16A in inflammasome pathway in this study.

Methods Functional genetic studies of CLEC16A in NLRP3 and AIM2 inflammasomes pathways using monocyte-derived macrophages isolated from peripheral blood mononuclear cells of healthy individuals were performed. Results During induction of NLRP3 inflammasome pathway by nigericin, a knockdown of CLEC16A using specific siRNAs inhibited secretion of interleukin-1β (IL-1β), an inflammasome pathway effector. Its secretion during AIM2 inflammasome induction by intracellular dsDNA poly(dA:dT) however was not affected in the siCLEC16A group. The induction of NLRP3 mRNA level upon lipopolysaccharide stimulation was suppressed in the siCLEC16A group. No significant changes in mRNA levels was observed in other selected genes of NLRP3 inflammasome pathway, namely the adaptor protein ASC, interleukin-1 converting enzyme caspase-1 and precursor pro-IL-1β.

Conclusions These data suggest that CLEC16A regulates NLRP3 but not AIM2 inflammasome pathway and affects IL-1β secretion in part via NLRP3 level. The mechanism involved and its association with autoimmune diseases such as systemic lupus erythematosus remains to be elucidated.

Microbiome, infections, probiotics and nutritional factors in autoimmunity

Background and aims This study was performed to analyse the influence of coffee consumption on clinical outcomes in Colombian patients with systemic lupus erythematosus (SLE).

Methods A cross-sectional analytical study was conducted in 731 Colombian patients with SLE in whom coffee consumption and its frequency was assessed. Differences in clinical outcomes (i.e., cardiovascular disease, age-at-onset, organ damage, polyautoimmunity, acute activity determined by SLEDAI, and clinical remission) were determined between drinkers and non-drinkers, as well as by frequency of consumption. Association was examined by chi-square and multivariate regression analyses.

Results Sociodemographic and clinical characteristics of the patients are shown in table 1. Out of a total of 731 patients, 70% were current coffee drinkers, 57% reported daily consumption, 20% weekly consumption and 3% monthly consumption. Coffee intake was found to be associated with SLE disease activity, acute activity determined by SLEDAI, and clinical remission (Table 2). According to the frequency of intake, daily consumption was associated to reduced risk of early age-at-onset and a positive association with 6 months clinical remission (OR: 0.45, 95% CI 0.25–0.81 and OR: 1.55, 95% CI 1.07–2.25, respectively). No differences were found for organ damage, polyautoimmunity and acute SLE activity.

Conclusions In Colombian SLE patients with coffee consumption, a reduced risk of early age-at-onset and cardiovascular disease was recognised. Also, a positive association with 6 month clinical remission was found. Due to the

Abstracts

351 AUTOIMMUNE-ASSOCIATED GENE CLEC16A REGULATES NLRP3 BUT NOT AIM2 INFLAMMASOME PATHWAY IN HUMAN MACROPHAGES

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10.1136/lupus-2017-000215.351

353 COFFEE CONSUMPTION AND CLINICAL OUTCOMES IN COLOMBIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2017-000215.353