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 TMEM173/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 (TMEM173) and MPYS/MITA/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 *Irf5* 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.

350 TOLL-LIKE RECEPTOR 7 SIGNALLING DRIVES TRANSITIONAL B CELLS EXPANSION AND AUTOANTIBODY PRODUCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and aims Toll-like receptor 7 (TLR7) has been implicated in B cells activation and the generation of pathogenic autoantibodies. Newly-formed transitional (TR) B cells are enriched in autoreactive specificities and are increased in some SLE patients. This study was undertaken to examine a possible link between the TR B cells expansion/activation and *TLR7* levels in SLE.

Methods PBMCs were collected from SLE patients and healthy donors and analysed for the expression of *TLR7*, *TLR9* and IFN-responsive genes by RT-PCR. The frequencies of B cell populations were analysed by flow cytometry. BAFF titers were analysed by ELISA. *TLR7* variant rs3853839(C/G) was detected by Taqman 5'-allele discrimination assay. TR B cells were primed with IFNα and stimulated with *TLR7* ligands *in vitro*.

Results High expression levels of *TLR7* in SLE patients positively correlated with IFN signature and disease activity, but not with BAFF titers. SLE patients with high levels of *TLR7* ($TLR7^{hi}$ group) showed an expansion of $CD19^{+}CD38^{high}CD24^{high}CD10^{+}$ TR B cells. Overall, frequencies of TR B cells positively correlated with the levels of *TLR7*, but not *TLR9*. SLE patients, carrying a risk G allele, had increased *TLR7* expression and TR cell frequencies, compared to non-risk allele carriers. $TLR7^{hi}$ SLE patients showed increased autoantibody titers and skewing towards Sm/RNP antigens. Upon IFNα priming, TR B cells up-regulated *TLR7* and differentiated into plasmablasts in response to TLR7-ligand stimulation.

Conclusions Our findings suggest that dysregulation of TLR7 in SLE might drive the expansion and promote the activation of TR B cells, which might be a source of autoantibodies.