co-expression was quantified. CD206 immunofluorescence of skin biopsies was also performed.
Macrophages were co-cultured with $8x10^4$ and $2x10^4$ fibroblasts in a collagen matrix and within a monolayer respectively.
Collagen gel contraction was quantified as a measure of fibrotic activity. CTGF and Collagen mRNA expression from gel matrices and cellular monolayers was quantified by qPCR.
Results: CD206 and $P2X_7$ expression is higher on SSc PBMC-derived macrophages (mean fluorescence 776.1 SD=409.1, 724.4 SD=455.3) compared to healthy controls (mean fluorescence 632.2 SD=73.7, 472.9 SD=25.4). There is significant correlation of CD206 expression to $P2X_7$ expression ($p<0.001$, r2=0.76) and CD206 expression is significantly correlated to Rodnan skin score ($p<0.05$, r2=0.26). $P2X_7$ expression is positively correlated to skin score. Double positive P2X7 and CD206 cells were seen in a subgroup with higher skin scores. Healthy fibroblasts co-cultured with scleroderma macrophages showed increased collagen mRNA by qPCR compared to co-culture with healthy macrophages ($p<0.01$). CTGF mRNA was positively correlated with macrophage P2X7 (r2=0.23) and CD206 (r2=0.81) expression. Preliminary work suggests contraction of collagen discs in fibroblast and macrophage co-culture is increased with SSc macrophages compared to healthy controls.
Conclusions: Data indicates a correlation between disease severity and CD206 expression by macrophages. Upregulation of CTGF and collagen expression in fibroblasts co-cultured with macrophages expressing high CD206 suggests a role for these cells in pathogenic fibrosis. The co-expression of high levels of $P2X_7$ with CD206 also indicates a possible role for the purinergic pathway in SSc fibrosis.
Future work will examine the mechanism of macrophage-fibroblast cross-talk and investigate the effect of inhibitors of CD206.
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Mucosal B cells: gatekeepers of immune function

OP0214 ACTIVATION STATUS OF MUCOSAL-ASSOCIATED INVARIANT T CELLS REFLECTS PATHOLOGY OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Mucosal-associated invariant T (MAIT) cells are innate-like lymphocytes that express a semi-invariant TCRα chain (Vα7.2-Jα33 in humans). MAIT cells are restricted by the MHC-related molecule-1 (MR1) and uniquely recognize vitamin B metabolites presented by MR1. Like other innate-like lymphocytes, MAIT cells are also activated by cytokines in the absence of exogenous antigens. Human MAIT cells are abundant and constitute approximately 5% of peripheral blood T cells, suggesting possible roles of MAIT cells in various types of immune responses.
Objectives: We aimed to investigate whether MAIT cells are involved in systemic lupus erythematous (SLE).
Methods: Peripheral blood was collected from SLE patients and healthy volunteers. Informed consent was obtained from all individuals according to institutional ethical guidelines. Disease activity was measured based on the SLE disease activity index (SLEDAI) and a SLEDAI score $\geq$5 was defined as active disease. Peripheral blood mononuclear cells (PBMC) were stained with anti-human monoclonal antibodies against CD3, γδTCR, Vα7.2TCR, CD161, CD95 (Fas) and CD69, and then analyzed by FACS. $CD19^+$B cells or $CD14^+$monocytes were isolated from PBMC of healthy controls (HC) or SLE patients by using magnetic cell sorting. MAIT cells from healthy controls were co-cultured with B cells or monocytes in the presence of MR1 ligand (MR1L), and the expression of CD69 on MAIT cells was evaluated by FACS. Cytokine levels in plasma samples and culture supernatants were measured by ELISA and Bioplex assay. PBMC were cultured in the presence of various cytokines, and CD69 expression on MAIT cells was analyzed by FACS.
Results: The frequency of MAIT cells was markedly reduced in SLE. Reduced numbers of MAIT cells were not attributable to the downregulation of surface markers, but were partially due to the enhanced cell death of MAIT cells, possibly by activation-induced cell death. The CD69 expression levels on MAIT cells in SLE correlated with disease activity. Monocytes from patients with SLE exhibited increased ability to induce MAIT cell activation, and the profound MAIT cell activating capacity of lupus monocytes was associated with enhanced IL-12 production in the culture supernatants. The plasma concentration of IL-6, IL-18 and IFNα positively correlated with the expression levels of CD69 on MAIT cells in SLE. MAIT cells were activated by cytokines including IFNα, IL-15, and IL-12 plus IL-18 in the absence of exogenous antigens.
Conclusions: These results suggest that MAIT cells reflect the pathological condition of SLE and their activated status correlates with disease activity.

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OP0215 ROLE OF INHIBITORY IGG FC RECEPTOR IIB ON B CELLS AND MONOCYTES IN YAA-RELATED MURINE LUPUS

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Background: FcγRIIB-deficient C57BL/6 (B6) mice spontaneously develop severe lupus nephritis in combination with *Yaa* locus (TLR7-duplication).
Objectives: The aim of this study is to clarify the cell type-specific roles of FcγRIIB for the pathogenesis of *Yaa*-related lupus.
Methods: We established B cell-specific ($CD19^{Cre}$.*Yaa*), myeloid-derived cell-specific ($C/EBP\alpha^{Cre}$.*Yaa*), and dendritic cell (DC)-specific ($CD11c^{Cre}$.*Yaa*) FcγRIIB-deficient mice on B6.*Yaa* background, and compared the disease features of these mice with full FcγRIIB-deficient B6.$Fc\gamma RIIB^{-/-}$.*Yaa* mice.
Results: $CD19^{Cre}$.*Yaa* mice developed milder lupus nephritis compared to B6.$Fc\gamma RIIb^{-/-}$.*Yaa* mice, indicating that FcγRIIB deficiency on only B cells is not sufficient for the development of severe disease. Surprisingly, $C/EBP\alpha^{Cre}$.*Yaa* mice developed similar mild disease as $CD19^{Cre}$.*Yaa* mice whereas $CD11c^{Cre}$.*Yaa* stayed disease free. These observations indicate that, in B6. $Fc\gamma RIIB^{-/-}$.*Yaa* mice, FcγRIIB deficiency on both B cells and myeloid cells, but not on DCs, contribute to the development of severe lupus with high autoantibody titers. Flow cytometric analysis showed that the frequency of peripheral $Gr\text{-}1^-$, but not $Gr\text{-}1^+$, monocytes was increased and correlated positively with the frequency of splenic PNA^+ activated B cells in B6.$Fc\gamma RIIB^{-/-}$.*Yaa* and C/EBPa^{Cre}.*Yaa*, but not $CD19^{Cre}$.*Yaa*, mice. This suggests a link between FcγRIIB deficiency on monocytes, the high frequency of $Gr\text{-}1^-$ monocytes and B cell activation. Transcriptome analysis of $Gr\text{-}1^+$ and $Gr\text{-}1^-$ monocytes revealed that B cell-stimulating factor-3 (BSF-3), IL-10, and IL-1β were all up-regulated in $Gr\text{-}1^-$ monocytes.
Conclusions: FcγRIIB on B cells and monocytes controls B cell activation and autoimmune responses via different but synergistic pathways in *Yaa*-related lupus nephritis.
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PsA: the options grow!

OP0216 EFFICACY AND SAFETY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, OR ADALIMUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AN INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (CSDMARDS): A RANDOMISED, PLACEBO-CONTROLLED, PHASE 3 TRIAL

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Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for treatment of psoriatic arthritis (PsA).
Objectives: To assess the efficacy and safety of tofacitinib vs placebo (PBO) in patients (pts) with active PsA.
Methods: Eligible pts in this randomised, PBO- and active-controlled, 12-month Phase 3 trial had $\geq$6-months' PsA diagnosis, fulfilled CASPAR criteria, had active arthritis ($\geq$3 tender/painful and $\geq$3 swollen joints) and active plaque psoriasis at screening, inadequate response to $\geq$1 csDMARD, and were tumour necrosis factor-inhibitor (TNFi)-naïve. 422 pts were randomised 2:2:2:1:1 to tofacitinib 5 or 10 mg twice daily (BID), adalimumab 40 mg subcutaneous injection every 2 weeks, or PBO (advancing to tofacitinib 5 or 10 mg BID at Month [M]3).