MORPHOLOGICAL HEART CHANGES IN ANIMALS WITH TOLL-LIKE RECEPTOR 7 (TLR7) IS UPREGULATED ON SUPPRESSION OF ENDOPLASMIC RETICULUM STRESS

Methods: A20 gene expression was knocked out in KRT14+ cells, namely ductal and myoepithelial cells. Whole pilocarpine-stimulated saliva was collected from A20−/− mice and wildtype (WT) littermate controls at 10, 20 and 30 weeks of age. Submandibular SGs were harvested at all time points for histological examination and qPCR.

Results: In submandibular SGs of A20−/− mice at 30 weeks of age, 10% of all cells were CD45+ leukocytes and 3% were CD3+ T cells, both significantly more than controls. B cell proportion increased over time in A20−/− mice, but was not significantly different to controls. CD45+ cells formed immune foci (>50 CD45+ cells together) localized to striated ducts, present at significantly greater frequencies than control mice. CD45+ cells, T cells and occasional B cells in A20−/− mice also invaded striated ducts. Expression of the pro-inflammatory cytokine chemokines IFNγ, TNFα, IL-6, CXCL10 and CXCL13 was also significantly greater in A20−/− mice. Functionally, both volume and mucin 10 content of whole stimulated saliva from A20−/− mice was significantly reduced compared to controls.

Conclusions: We present a model for epithelial cell involvement in pSS SG pathology development. We confirm that saliva production defects, foci formation and striated duct invasion can be triggered solely by immune activated epithelial cells.

REFERENCES:

Disclosure of Interest: None declared

AB0177
TOLL-LIKE RECEPTOR 7 (TLR7) IS UPREGULATED ON PERIPHERAL B CELLS AND ASSOCIATED WITH DISEASE ACTIVITY AND DAMAGE IN PRIMARY SJÖGREN SYNDROME

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Objectives: Primary Sjögren Syndrome (pSS) is characterised by activation of B cells, increased production of RNA-antibodies and elevated proportion of transitional B cell. Toll-like receptors 7 (TLR7) have been reportedly promoting the effects above in some murine models of SS. We took up this study to identify if TLR7 expression is associated with disease activity and the role of TLR7 in pSS.

Methods: 21 pSS patients and 12 healthy controls (HCs) were selected. The mRNA expression of TLR7 was determined by real-time PCR on peripheral B cells of both pSS patients and HCs. We measured serum concentrations by ELISA, and the BAFF-R, TACI and BCM expression was analysed on each B cell subset (CD27+CD24+CD38low/transitional B cell; CD27+CD24+CD38high/naive B cell) by flow cytometry. The results were compared among patients with different degree of disease activity and damage to HCs.

Results: The expression level of TLR7 mRNA were elevated in pSS patients compared with HCs (p<0.004), and correlated with the SDDI (SS disease activity index) (r=0.803; p=0.009) and the SSDI (SS damage index) (r=0.881; p=0.002). Serum BAFF concentrations increased in pSS patients compared with HCs (p=0.041), but not correlated with TLR7 expression. TACI expression in pSS patients in total B cells and traditional B cells compared to HCs were elevated and are both associated with TLR7 expression (r=0.763; p=0.048, r=0.820, p=0.004, respectively). A lower BAFFR expression was seen in transitional B cell compared to HCs (p=0.018). BCM expression was of no significance.

Conclusions: Increased TLR7 expression on peripheral B cells were associated with disease activity and damage, suggesting that TLR7 may play a role in the development in pSS. Increased serum BAFF concentration and TACI expression were associated with TLR7 expression, indicating that BAFF may regulate TLR7 expression through TACI according to previous studies. TLR7 may be a potential treatment target of pSS and worth of further study.

Disclosure of Interest: None declared

AB0178
SUPPRESSION OF ENDOPLASMIC RETICULUM STRESS THROUGH 4-PBA IMPROVES THE MANIFESTATIONS OF MURINE LUPUS THROUGH MODULATING REGULATORY T CELLS

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Background: Impaired function of regulatory T cells (Treg) contributes to the pathogenesis of systemic lupus erythematosus (SLE). It has been reported that the aberrant responses of T lymphocytes to endoplasmic reticulum (ER) stress in patients with SLE.

Objectives: In the present study, we investigated whether ER stress inhibition through 4-phenylbutyric acid (4-PBA) ameliorates lupus manifestation on