indicating that microglia cells may carry out the antigen presentation process seen in transcriptomic data. Low levels of serotonin and noradrenaline were observed at both 3 and 6 months of age in lupus mice; these aberrancies were mainly attributed to decreased serotonin synthesis as evidenced by intact seroton metabolism (no differences were observed at its metabolite: 5-hydroxy-
doleacetic acid). Analysis of the remaining regions of the brain combined with studies of metabolic activities of various brain regions by PET-CT scanning is in progress.

Conclusion: Immune cell trafficking from the periphery combined with marked inflammatory response in the hippocampus underlie the neuropsychiatric phenotype in NZB/W murine lupus. Our data indicate increased expression of activated myeloid cells -including microglia- in the hippocampus of lupus mice culminating in increased antigen presentation and decreased neurotransmitter levels.

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OP0041

SALIVA AND SERUM LEVELS OF CXCL13: ASSOCIATION WITH THE SEVERITY OF SALIVARY GLAND LESIONS AND LYMPHOMA IN PATIENTS WITH SJÖGREN’S SYNDROME (SS)

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Background: CXCL13 has been implicated in the formation of ectopic germinal centers (GC) in minor salivary gland (MSG) inflammatory lesions of SS patients. Recent studies suggest that serum CXCL13 levels associate with disease severity and risk for non-Hodgkin lymphoma (NHL) development.

Objectives: To validate the clinical utility of CXCL13 by investigating potential associations of saliva and serum CXCL13 levels with various histopathologic (including severity of MSG autoimmune infiltrates and GC formation), serologic and clinical features of the disease, as well as NHL.

Methods: CXCL13 levels were measured by a commercially available ELISA (sensitivity: 1 pg/ml; Abcam, Cambridge, UK) in paired serum and saliva specimens from 25 SS patients (9 with NHL; SSL), 9 sicca controls (SC; sicca-complaining individuals with no infiltrates in diagnostic MSG biopsy and negative autoantibody profile) and 6 healthy controls (HC). From the 16 SS patients without evidence of NHL, 5 had mild, 6 intermediate and 5 severe lesions at MSGs, as arbitrarily defined by focus (FS) and Tarpley (TS) biopsy scores (mild: FS:1-1.7, TS:1-1.7, intermediate: FS:1.8-2.95, TS:2-3.0; severe: FS:3.0-11, TS: 3-4). Furthermore, the organization of the MSG infiltrates to GCs has been evaluated in 23 patients revealing 10 with GCs.

Results: Kruskal-Wallis analysis revealed that serum CXCL13 levels were significantly increased in SS patients without or with NHL (median: 94.83 pg/ml and 96.70 pg/ml, respectively), compared to SC and HC (35.44 and 40.92 pg/ml, respectively; p<0.05), whereas saliva CXCL13 levels were only marginally increased (78.47, 84.10, 55.98 and 65.30 pg/ml in SS, SSSL, SC and HC, respectively; p=0.051). Among SS patients with distinct MSG lesion severity, those with severe lesions were found to express significantly higher serum CXCL13 levels (149.3 pg/ml) from SC and HC (p=0.0051 and 0.0166, respectively). Mann-Whitney test revealed that serum CXCL13 levels correlated with SG biopsy focus score (r: 0.6889, p=0.0001 and r: 0.4222, p=0.01, respectively). Mann-Whitney test revealed that serum CXCL13 levels were significantly elevated in patients with GCs at MSG lesions (156.1 vs 69.64 pg/ml, p=0.00015), rheumatoid factor (105.0 vs 53.72 pg/ml, p=0.015) and marginally with anti-Ro/La antibodies (121.8 vs 65.05 pg/ml, p=0.06) compared to those without. Furthermore, CXCL13 levels were significantly increased in SS patients at high risk to develop NHL compared to low risk (149.3 vs 71.54 pg/ml, respectively; p=0.0275). Saliva CXCL13 levels were not found to be associated with the studied features.

Conclusion: Serum and to a lesser extend saliva CXCL13 levels are increased in SS and SSL patients and associate with the degree of MSG infiltration, as assessed by focus score. Serum, but not saliva, CXCL13 associates with various disease features, including GC formation, and may have a clinical utility in identifying SS patients at high risk to develop lymphoma.

Disclosure of Interests: None declared

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OP0042

BLOCKING OF CD103+ TISSUE RESIDENT MEMORY T CELLS (TRM) AS A THERAPEUTIC STRATEGY IN SJÖGREN’S SYNDROME


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Objectives: To study the role of CD4+ and CD8+ TRMs in the pathogenesis of SS and to explore the therapeutic targeting of the tissue residency marker of TRM CD103.

Methods: An animal model of experimental SS was used. CD4+ and CD8+ TRMs were detected using the CD45RO+CD103+ marker. A significant increase in the frequency of CD103+ TRMs was observed in the salivary glands of the SS model. CD45RO+CD103+ TRMs were significantly reduced after anti-CD103 treatment.

Results: Upon the ESS progression, a significant progressive increase in CD45RO+CD103+ cells frequency was observed from 5wk to 20wk post-immunization (p=0.001), where the CD8+ were the most abundant, followed by CD4+. Consistently, CD103+CD8+ T cells were detected within the lymphocytic infiltration of SG from ESS mice. Sorted purified SG CD10+CD3+CD8+ T cells showed higher Granzyme B, TNF-alpha expression compared to CD103-CD3+CD8+ at both mRNA and protein levels. Notably, ESS mice treated with anti-CD103 showed improvement in salivary function (p<0.05) and reduced lymphocytic infiltration measured as focus score (FS) (p<0.01) and area-fraction (p<0.01). Consistently, anti-CD103 treatment consistently reduced CD103+ cells and IFN-gamma-, Granzyme B+ and TNFa+ CD8+ cells. We next performed phenotypic analysis of CD45RO+CD103+ in immune cells in the SG of pSS patients observing an increase in both with CD8+CD103+CD69+ and CD4+CD103+CD69+ (p<0.05). Finally, IHC showed that the expansion of TRMs in pSS salivary glands was accompanied by a down-regulation of CD69 expression and their migration outside the epithelium in the context of inflammatory infiltrates. SG of patients with pSS showed a significant up-regulation of BLIMP1, KLF-L and S1PR1 and down-regulation of ITGB2, CXCL9 and CXCL10, and IL-15 involved in the tissue recruitment and long-term survival of TRMs were significantly modulated in pSS salivary glands.

Conclusion: TRM are expanded and activated in the SG of pSS and ESS, participating in the organization of tissue inflammation. Although the mechanisms behind this expansion are still not fully understood, CD103 could be a valuable novel therapeutic target to prevent lymphocytic infiltrations and glandular destruction in Sjogren syndrome.

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OP0043

INCREASED RISK OF SEVERE INFECTIONS AND MORTALITY IN PATIENTS WITH NEWLY DIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSUS: A POPULATION-BASED STUDY

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Background: Systemic lupus erythematosus (SLE) is a chronic disease with a broad spectrum of autoantibodies and clinical manifestations. As much as 45%...