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 abnormalities were mainly attributed to decreased serotonin synthesis as evidenced by intact seroton metabolism (no differences were observed at its metabolite: 5-hydroxyindoleacetic 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 under the neuropathic 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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Disclosure of Interests:
None declared.

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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)

L. Chatzis1, A. Goules1, A. Tzioufas1, E. Kapsogorou1, 1School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece

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, 9 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, intermediate: FS:1.8-2.95, TS:2 and 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 levels were only marginally increased (76.47, 84.10, 55.98 and 65.30 pg/ml in SS, SSL, SC and HC, respectively; p=0.051). Among SS patients with distinct MSG lesion severity, only 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). Spearman’s Rank correlation analysis showed that both serum and saliva 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 MSGs (156.1 vs 69.64 pg/ml, p=0.0015), 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 levels were not found to significantly associate with various disease features, including GC formation, and may have a clinical utility in identifying SS patients at high risk to develop lymphoma.

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OP0042

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


1School of Medicine, University of Palermo, Mother and Child Care, Department of Health Promotion, Rheumatology Section, Internal Medicine and Medical Specialties, Palermo, Italy; 2University of Palermo, Pathology Unit, Palermo, Italy; 3University of Palermo, Mother and Child Care, Department of Health Promotion, Rheumatology Section, Internal Medicine and Medical Specialties, Palermo, Italy; 4University of Palermo, Pathology Unit, Palermo, Italy; 5University of Palermo, Mother and Child Care, Department of Health Promotion, Rheumatology Section, Internal Medicine and Medical Specialties, Palermo, Italy; 6Shanghai Bethune Hospital and Shanxi Academy of Medical Sciences, Taiyuan, China; 7Azienda Ospedaliera “Ospedali Riuniti Villa Sofia-Cervello”, Pathology Unit, Palermo, Italy

Background: Tissue-resident memory T cells (TRM), are recently identified T cell populations featuring tissue localization and expression of markers of tissue homing, CD69 and CD103. Recently, the expansion of CD6+ TRMs and their involvement in the sialadenitis was described in a murine model of SS. However, CD4+ and CD6+ TRMs’ functional relevance in SS is still not fully understood, and the TRM therapeutic targeting unexplored.

Objectives: The study aimed to address 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 (ESS) obtained by immunization of female C57BL/6 mice (n=10) with salivary glands (SG) protein extract and Freund’s complete adjuvant used to investigate the dynamic of infiltration of SG by CD4+ and CD8+ TRM, therapeutic efficacy, and the impact of CD103 blockade. For the therapeutic intervention, at 10-weeks post-immunization, the salivary gland was cannulated via Wharton’s duct, and an anti-CD103 neutralizing antibody or vehicle-injected. The mice’s saliva flow rate was assessed, and SGs were analyzed by Flow-cytometry and immunohistochemistry (IHC).

The frequency and localization of TRMs was analyzed in minor SG of sicca syndrome (nSS) and SS patients (n=39) by flow cytometry and IHC. The expression of genes involved in the tissue retention of TRMs was assessed in SS by RT-PCR.

Results: Upon the ESS progression, a significant progressive increase in CD45+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 saliva function (p<0.05) and reduced lymphocytic infiltrations 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 TNFs+ CD8+ cells. We next performed phenotypic analysis of CD45+CD103+ 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 E-cadherin glandular 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-2, 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.

Disclosure of Interests: None declared.

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OP0043

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

K. Zhao1,2, H. Xie1,2, L. Li1,2, A. Aviña3, J. Esdaile2,3, 1Simon Fraser University, Health Sciences, Burnaby, Canada; 2Arthritis Research Canada, Biostatistics, Richmond, Canada; 3The University of British Columbia, Experimental Medicine, Vancouver, Canada

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