Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder, characterized by a remarkable heterogeneity of clinical presentations. Glomerulonephritis (GN) remains a leading cause of morbidity and mortality in SLE, influencing long-term prognosis. The alteration of both innate and adaptive immune responses plays a pivotal role in SLE pathophysiology [1]. B lymphocytes are mainly involved in SLE through the production of autoantibodies but recent evidence suggests an effecter role of these cells in cytokine production. IL-40, a novel cytokine, is produced by B cells and involved in their homeostasis, that may participate in the pathogenesis of B-mediated autoimmune diseases, such as SLE [2].

Objectives: The purpose of this study was to evaluate the role of IL-40 in the pathogenesis of SLE, with a specific focus on renal involvement.

Methods: Peripheral blood and urine samples were collected from 10 consecutive SLE patients and 10 healthy controls; kidney biopsy specimens were obtained from 3 SLE patients and 3 controls. The concentration of IL-40 in serum and urine samples was evaluated by ELISA. IL-40 production by monocytes, B cells and T cells was assessed by flow cytometry at day 0 and after in vitro stimulation. Immunohistochemistry on kidney tissue was also performed to evaluate IL-40 expression.

Results: IL-40 levels were reduced in the serum of patients with active GN. This reduction was further observed in the serum of patients with previous GN. In the serum of active SLE patients, without renal involvement, the concentration of IL-40 did not change significantly compared to controls. Urinary levels of IL-40 showed no significant changes compared to controls. Consistently, immunohistochemistry on kidney showed the expression of IL-40 only in SLE patients (Figure 1). Flow cytometric analysis on T cells, B cells and monocytes isolated from peripheral blood of SLE patients with active GN did not show production of IL-40.

Conclusion: To the best of our knowledge this is the first demonstration of IL-40 expression at kidney level in SLE associated nephritis. These preliminary data suggest an active role of IL-40 in SLE, with specific focus on active kidney disease. Our results highlight a potential use of IL-40 as a marker of active GN, although its specific mechanism of action needs to be further elucidated.

References:

Disclosure of Interests: Chiara Rizzo: None declared. Lidia La Barbera: None declared, Marianna Lo Pizzo: None declared, Leila Mohammadnezhad: None declared, Vincenzo Luca Lentini: None declared, DENISE DONZELLA: None declared. Francesca Ciccia: Speakers bureau: Lilly, Pfizer, Novartis, Cellgene, abbvie, roche, janssen, UCB, SERENA PASANO: None declared, Giuliana Guggino Speakers bureau: Pfizer, Novartis, Cellgene, abbvie, roche, Lilly, janssen, UCB.


POS0012
GLOBAL CHARACTERIZATION OF SALIVARY GLANDS IMMUNE MICROENVIRONMENT IN PRIMARY SJÖGREN’S SYNDROME BY SINGLE-CELL SEQUENCING

N. Xiang1, X. Hao2, G. Chuang3, L. Wang1, Z. Zhou1, G. Wang1, Q. Kun2, X. Li1.1 The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Department of Rheumatology and Immunology, Hefei, China; 2University of Science and Technology of China, CAS Center for Excellence in Molecular Cell Sciences, the CAS Key Laboratory of Innate Immunity and Chronic Disease, Hefei, China

Background: Primary Sjögren’s syndrome (pSS) is a heterogeneous, chronic, complex systemic autoimmune disease. The hallmark symptom of the disease is exocrinopathy, chiefly salivary and lacrimal glands, which often results in dryness of the mouth and eyes. As of today, although a lot of genetic and epigenetic studies have reveal the complexity of pSS to a certain extent, but the knowledge of existing pSS disease heterogeneity is still limited and the immune mechanisms of salivary glands (SG) injury have been challenging to clarify.

Objectives: Single-cell RNA sequencing (scRNA-seq) is a powerful tool capable of defining cell types and states on the basis of their individual transcriptome in a given sample from health and disease. To characterize the salivary glands immune microenvironment of patients with pSS, we performed droplet-based single cell mRNA sequencing (scRNA-seq) (10X Genomics) to provide a deeper insight into the cellular and molecular characteristics of salivary glands from pSS patients.

Methods: 11 patients and 5 non-pSS controls were recruited from the The First Affiliated Hospital of USTC. The non-pSS were subjects who had experienced subjective symptoms of dryness, but no not meet any of the classification criteria of pSS. The clinical characteristics and laboratory findings of enrolled patients were also collected. After resection, salivary glands tissue samples were obtained after labial gland biopsy, rapidly digested to a single-cell suspension and subjected to scRNA-seq using the 10X platform. After rigorous quality control (QC) definition, low-quality cells were filtered. Following gene expression normalization for read depth and mitochondrial read count, we applied principle component analysis on genes variably expressed across all 72,853 cell.

Results: A total of 72,853 cells were obtained from all salivary glands samples. Our results revealed 12 major unique cell populations of salivary glands cell, including T cells, B cells, plasma cells, epithelial cells, myoepithelial cells, endothelial cells, myofibroblast, pericytes, melanocytes, fibroblast, myoid cells and a cluster of unknown cells. As expected, lymphocytes (T and B cell populations) were significant increase in the salivary glands of patients with pSS. For further subsets analysis, we identify 41 subsets, including novel subpopulations in cell types hitherto considered to be homogeneous, as well as transcription factors underlying their heterogeneity. Strikingly, we found that differentially expressed genes (DEGs) that myoepithelial cells uniquely downregulated in pSS patients were involved in regeneration, stem cell population maintenance, cell division, and epithelial cell proliferation. This indicated an impaired stem cell property and regeneration capacity of myoepithelial cells in the intrinsic pathological conditions of pSS patients which may result in the reduction of normal epithelial cells differentiation and proliferation. Our results identified three distinct endothelial subtypes according to the differentially expressed cell markers. ACKR1+ endothelial cells were expanded in the SG of pSS patients which may enhance Leukocyte transendothelial migration. A clear inter-fon response was observed in most celltypes. We also found a significantly expand PD-1+CXCR5+CD4+T peripheral helper (Tph), GZMK+CD8+T cells and a patient-specific fibroblasts in pSS patients. Cellular interaction analysis of SG revealed a strong interaction between epithelial cells and immune cells from pSS patients through CX47-MIF, MIF-TNFRSF14 and HLA-C-FOAM3C receptor/ ligand pairs. Chemokine receptors CXCR4 were broadly expressed in SG immune cells implying a potentially central role in cell trafficking.

Conclusion: This resource provides deeper insights into pSS salivary glands immune microenvironment that will be helpful in understanding of the disease heterogeneity and advancing pSS therapy.

Disclosure of Interests: None declared