pSS. Remarkably, depletion of NK cells during the inflammation onset prevented subsequent induction of IL-17+ CD4 (p < 0.01) and memory IgD IgM CD38+ B cells (p < 0.0001) in the SG.

Conclusion: Thus, our study provides novel innate immune cellular and molecular mechanisms contributing to pSS pathology and identifies new potential therapy targets.

REFERENCES:

Figure 1.

Acknowledgements: NIL.

Disclosure of Interests: Ildéfonso Sánchez-Cerrillo: None declared, Marta Calvet-Mirabent: None declared, Ana Triguero-Martínez: None declared, Diego Caizada Fraile: None declared, Cristina Delgado-Arèvalo: None declared, Mariel Valdivia: None declared, Maria Ramírez: None declared, Enrique Vázquez de Luí: None declared, Alberto Benguría-Filippini: None declared, Roberto Moreno: None declared, María Adrados de Llano: None declared, Hortensia de la Fuente: None declared, Ilya Tsukalov: None declared, Emilia Roy Vallejo: None declared, Almudena Ramino: None declared, Salvador Ibarra: None declared, Francisco Sánchez-Madrid: None declared, Ana Dapozo: None declared, Isidoro González-Álvaro Consultant of: Lilly and Sanofi, Santos Castañeda: None declared, Enrique Martin-Gayo Consultant declared, Salvador Iborra: None declared, Francisco Sánchez-Madrid: None declared, Enrique Vázquez de Luis: None declared, Ilya Tsukalov: None declared, Emilia Roy Vallejo: None declared, Almudena Ramino: None declared, Salvador Ibarra: None declared, Francisco Sánchez-Madrid: None declared, Ana Dapozo: None declared, Isidoro González-Álvaro Consultant of: Lilly and Sanofi, Santos Castañeda: None declared, Enrique Martin-Gayo Consultant declared, Salvador Iborra: None declared, Francisco Sánchez-Madrid: None declared.

DOI: 10.1136/annrheumdis-2023-eular.4458

POS0809

HARNESSING CELL ENERGY METABOLISM TO SUPPRESS SALIVARY GLAND INFLAMMATION IN SJÖGREN SYNDROME

Keywords: Sjögren syndrome

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Background: SG epithelial cells (SGEC) play a key role in sustaining inflammation in Sjögren Syndrome (SS), which is indeed termed an ‘autoimmune epithelitis’. However, the mechanisms responsible for the inflammatory activation of SGEC remain largely undetermined. Our line of research indicates that SGECs in SS exhibit profound changes in cell energy metabolism as indicated by TCR r expression of autophagy [1]. Inhibitions of autophagic process results in a down regulation of SGECs activation [1], thus indicating a crucial role of SGEC energy metabolism in the induction of autoimmune epithelitis.

Objectives: Aim of this study is to characterize metabolic changes occurring in SS SGECs and dissect the link between these changes and their acquired pro-inflammatory functions.

Methods: SGECs were isolated from minor SG biopsies deriving from patients with SS and sicca. Intracellular metabolomic analysis was performed on direct ex vivo isolated primary SGECs. As read out of functional activation of SS SGECs, supernatants from SGECs cultures were collected to perform ELISA test in order to evaluate the expression of the pro-inflammatory mediator IL-6.

Results: Principal component analysis (PCA) of high-throughput metabolomics analysis of sicca (n=7) and SS (n=7) SGECs revealed a separation along the component 1 axis (46.6% of variance) indicating profound differences in the intracellular metabolome (Figure 1a). Unsupervised clustering analysis of metabolites revealed profound metabolic differences between SS and (n=7) sicca (n=7) SGECs (Figure 1b). Analysis of selected metabolites confirmed a shift towards increased glycolysis and TCA cycle activation in SS SGECs (Figure 1c). Supernatant concentrations of IL-6 were higher in SS (n=21) compared to sicca (n=14) SGECs (Figure 1d).

Conclusion: SGECs from SS patients display altered cell energy metabolism with evidence of increased glycolysis and activated TCA cycle. A metabolic driven pro-inflammatory status of SS SGECs seems confirmed by increased basal expression of IL-6. Validation of our metabolomic results, along with transcriptomic and epigenetic studies, is currently ongoing in SGECs from SS and sicca to dissect the link between changes in cell energy metabolism and their acquired pro-inflammatory phenotype.

Figure 1.

Acknowledgements: NIL.

Disclosure of Interests: None Declared.

DOI: 10.1136/annrheumdis-2023-eular.3329

POS0810

T FOLLICULAR HELPER CELLS IN BLOOD MIRROR SALIVARY GLAND-INFILTRATING T CELLS IN PRIMARY SJÖGREN’S SYNDROME

Keywords: Sjögren syndrome, Adaptive immunity

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Background: Although clonal expansion of autoreactive T cells have been identified in the peripheral blood and salivary gland of primary Sjögren’s syndrome (pSS) [1], the relationship between peripheral immune environments and inflammatory processes remains unclear.

Objectives: Here, we examined which T cell subsets in blood share the same T cell receptor (TCR) repertoire with T cells infiltrated at labial salivary gland (LSG) in patients with pSS, and evaluated mechanisms of their differentiation.

Methods: 1) TCR repertoire of each effector memory T cell subset (Th1, Th17, Th1, Th2, Th17) in blood, and LSG-infiltrating T cells obtained from the same pSS patient were analyzed by TCR repertoire (n=1).

2) The proportion of each T cell subset in blood was compared between patients with pSS (n=30) and healthy controls (HC) by flow cytometry (n=20).

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