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Id3-KO mouse model of Primary Sjögren´s Syndrome shows mitochondrial alterations and signs of cellular senescence similar to pSS patients

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Primary Sjögren´s Syndrome (pSS) is systemic autoimmune disorder characterised by lymphocytic infiltrations in exocrine glands. T-cells are considered major players in pathogenesis of pSS. Previously we showed, that peripheral lymphopenia-a frequent finding in pSS- affects mostly naïve CD4+ T-cells which show senescent phenotype. The aim of this study was to investigate T-cells phenotype in Id3-KO mouse model of pSS and compare obtained data with the data from human patients. Immune cells were isolated from peripheral blood, draining lymph nodes and spleen. Flow cytometry analysis was performed to characterize CD4 and CD8 subsets (naïve T-cells, central memory T-cells, effector memory T-cells and double negative T-cells). Further staining with mitochondrion-selective fluorescent dyes MitoTracker® Green, MitoTracker® Deep Red, MitoSox Red was performed to assess mitochondrial mass, membrane potential and superoxides production, respectively. Samples were analyzed on BD FACSLytic Flow Cytometer. Agilent Seahorse XFe96 Analyzer was used to measure oxygen consumption rate in isolated total CD4+ T-cells. In Id3-KO mice, there is significant decrease in naïve cells compartment in both CD4 and CD8 T-cells in all studied tissues (blood CD4 $p=0,027$, CD8 $0,081$; lymph nodes CD4 $p=0,003$, CD8 $p<0,000001$; spleen CD4 $p<0,000001$, CD8 $p=0,000006$). These T-cells also have significantly decreased mitochondrial mass in the all phenotyped subsets (all $p<0,01$). Despite having reduced mitochondrial mass we observed that Id3 deficient T-cells produce higher amount of mitochondrial superoxides in the all phenotyped subsets, with most affected naïve CD4+ T-cells ($p=0,021$). Basal respiration was significantly decreased in Id3-KO total CD4+ T-cells ($p=0,027$). These preliminary data suggest that there are mitochondrial alterations in the immune cells of pSS mouse model. The mitochondrial alterations and significant decrease in naïve subsets indicate aged phenotype of T-cells, that is also present in pSS patients.