Conclusions: Higher frequency of IL-17/IFN-γ double positive TH17 cell with P-17 expression may be associated immunological and pharmacological factors for steroid resistance in LN.

Disclosure of Interest: None declared


FRI0265 ANGIogenic T CELLS in primary SJOGREN syndrome: A DOUBLE-EDGED SWORD

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Background: Angiogenic T cells (Tang) have been recently identified within colonies of endothelial progenitor cells (EPCs) as mediators of endothelial repair. Both Tang and EPCs are reduced in rheumatoid arthritis and this contributes to persistent endothelial damage and eventually increased cardiovascular risk. In primary Sjögren’s syndrome (pSS), EPCs are expanded but no data are currently available about Tang.

Objectives: Aim of this study was to assess (CD1 +CD31+CXCR4+) in peripheral blood (PB) and target organs of pSS as well as the association with EPCs (CD34 +CD133+VEGFR-2+) and clinical and serological features of the disease.

Methods: Thirty-six pSS patients and 20 sex- and age-matched healthy donors (HD) were enrolled. Phenotypic analysis of peripheral blood mononuclear cells was performed by flow cytometry using FITC, Pe, Pe-Cy7 or AlexaFluor67 labelled anti-human CD3, CD31, CXCR4, CD4, CD8, CD28, CD34, CD133, VEGFR-2, and IL-17 antibodies. Minor salivary gland (MG) biopsies from 8 pSS patients were studied and compared to samples from 12 patients with sicca symptoms and either non-specific chronic sialadenitis (NSCS) or normal parenchyma (n=6 each). MG sections were subjected to immunofluorescence staining to assess the presence of CD3 +CD31+CXCR4+Tang cells and the expression of the CXCR4-ligand CXCL12/SDF-1 chemokine.

Results: Circulating Tang were expanded in pSS compared to HD and were directly correlated to EPCs. Both Tang and EPCs directly correlated with disease activity as calculated with the EULAR Sjögren’s syndrome disease activity index (ESSDAI). Over 60% of Tang lacked CD28 revealing a senescent phenotype. Only a small proportion of Tang displayed either CD4 or CD8, the majority of Tang being therefore CD4-CD8- double negative (DN). A subset of Tang produced IL-17 and the highest proportion of IL-17-producing cells was observed among DNS. Immunofluorescence analyses revealed the exclusive presence of infiltrating Tang cells along with increased expression of CXCL12/SDF-1 in pSS MSGs compared to either NSCS or normal MSGs.

Conclusions: Circulating Tang cells are expanded in pSS, display a senescent phenotype, are mainly CD4-CD8- DN and produce IL-17. Moreover, Tang cells home to and infiltrate MSGs in pSS, presumptively through the SDF-1/CXCR4 chemotactic axis. Our study is the first to describe these pleiotropic effects together with EPCs in endothelial repair. Tang cells may contribute to disease pathogenesis.

Disclosure of Interest: None declared


FRI0266 Characterisation of the molecular profile of altered genes and pathways in monocytes of antiphospholipid syndrome patients related to their atherothrombotic status. Effects of in vivo ubiquinol supplementation

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Objectives: This study was undertaken to: 1. Characterise monocytes molecular profile of altered genes and pathways involved in the pathology of APS. 2. To evaluate the role of antiphospholipid antibodies in the regulation of these processes. 3. To investigate the short-term effects of in vivo ubiquinol (reduced coenzyme Q10 [Qred]) supplementation on the modulation of genes related to inflammation and thrombosis in this autoimmune disorder.

Methods: Monocytes from peripheral blood of 60 subjects, including 30 APS patients and 30 healthy donors (HDs) were purifed by negative immunomagnetic selection (Miltenyi). Total RNA was extracted from 6 subjects –as exploratory cohort- and microarray studies were performed in an Agilent G4112F platform (Whole Human Genome Microarray 44 k). Functional categorization of the altered gene signature and molecular pathways and networks was carried out using the Ingenuity Pathway Analysis Software (IPA). The most differentially expressed genes were validated by RT-PCR in monocytes purified from all the subjects recruited to the study. Correlation and association studies were performed with clinical and analytical variables. The effects of antiphospholipid antibodies (APL) were also evaluated by in vitro studies. The short-term effects of in vivo Qred supplementation on the monocyte gene profile were further analysed.

Results: Gene expression array identified 518 altered genes in monocytes from APS patients in relation to the control group (p<0.05 and fold change >2). IPA analysis showed that the main canonical pathways integrated by these genes were leukocyte adhesion, abnormal coagulation and extravasation signalling, interleukin and cytokine signalling, as well as oxidative stress production and antioxidant response. This analysis further identified that the most relevant diseases in which these altered genes are involved were inflammatory and cardiovascular diseases (44%), as well as reproductive (42%), neurological (11%), renal (1%) and ophthalmic diseases (2%). The alteration of several of these genes was validated by RT-PCR and protein analysis, and associated to clinical parameters of APS patients, including thrombotic recurrences and early atherosclerosis. In vitro studies

Conclusions: The CD14 +CD16+ (non-classical) monocyte subset was reduced in SLE patients with a previous history of thrombosis and circulating cytokines, were also demonstrated. Yet, SLE +APS patients with renal involvement displayed reduced proportion of circulating intermediate and non-classical monocytes, suggesting that, as in the case of SLE patients, circulating CD16+cells might have migrated to the kidney.

In APS patients we also saw enrichment of the CD14 +cohort of inflammatory subsets, associated to recurrent thrombotic events and a pathologic CIMS, pointing out that such subsets are associated with CVD. The scores of various markers related to autoimmunity, oxidative stress and prothrombotic molecules further correlated with the proportions of intermediate and non-classical monocytes.

Conclusions: Circulating CD14 +monocytes might constitute an important subpopulation of proinflammatory cells, whose frequency might identify APS, APS +SLE and SLE patients suffering thrombosis, atherosclerosis and organ involvement.

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