CD4+T cells were increased in fibromyalgia patients with respect to HC. However, only IL17A and IFN γ , but not IL-4 producing CD4+T lymphocytes were increased with respect fibromyalgia secondary to Sjogren. These alterations were due to an increment of T $_{EM}$ IL-17A, T $_{CM}$ and T $_{EM}$ IL-4 and T $_{N}$ T $_{CM}$ and T $_{EM}$ IFN γ producing CD4+T cell subsets in fibromyalgia patients. Furthermore, IFN γ producing CD4+T cells were decreased in fibromyalgia secondary to Sjogren's with respect to fibromyalgia patients and HC. Counts of T $_{N}$ TNF α producing CD4+T cells were increased in fibromyalgia with respect fibromyalgia secondary to Sjogren. IL-10 producing CD4+T cells were normal in fibromyalgia but decreased in fibromyalgia secondary to Sjogren.

Conclusion: Fibromyalgia patients show an abnormal circulating activation stages of CD4+T cells, as well as, express unusual elevated counts of CD4+T cells producing IL-17A, IL-4 and IFN γ . These alterations could differentiate two different pathologic and inflammatory behaviors of the T cell compartment between fibromyalgia and fibromyalgia secondary to Sjogren patients.

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AB0036

CHILDREN WITH EXTENDED OLIGOARTICULAR AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS HAVE A CYTOKINE PATTERN FAVOURING B CELL ACTIVATION IN CIRCULATION

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children. The majority of polyarticular JIA (pJIA) and a large fraction of extended oligoarticular JIA (oJIA) patients fulfil classification criteria for rheumatoid arthritis (RA) in adulthood. B-cells play several important roles in RA pathogenesis, but it is still unclear if the pattern of B-cell involvement in pJIA and extended oJIA follows what has been described for adults with RA.

Objectives: The main goal of this study was to determine the concentration of cytokines potentially relevant for B-cell activation in serum from children with pJIA and extended oJIA when compared to children with persistent oJIA, adult JIA, early and established RA.

Methods: Serum samples were collected from children with extended oJIA (n=8), persistent oJIA (n=6), pJIA (n=6), adult JIA (n=8), untreated early RA (<1 year of disease duration, n=12), established RA patients treated with synthetic disease-modifying anti-rheumatic drugs (DMARDs) (n=10) and two groups of age- and sex-matched healthy donors (children, n=6 and adults, n=10). A proliferation-inducing ligand (APRIL), B-cell activating factor (BAFF), interleukin (IL)-6 and IL-21 serum levels were measured by enzyme-linked immunosorbent assay (ELISA).

Results: Children with extended oJIA, early and established RA patients had significantly higher BAFF serum levels when compared to controls, but no significant differences were observed in children with persistent oJIA, pJIA and adult JIA when compared to all groups included. APRIL serum levels were significantly increased in early and established RA patients when compared to both controls and children with persistent oJIA. No significant differences were found in APRIL concentrations between children with JIA, adult JIA and controls. IL-6 serum levels were significantly increased in children with extended oJIA, pJIA, early and established RA when compared to controls, but no significant differences were found in children with persistent oJIA and adult JIA patients. IL-21 serum levels were significantly increased in early RA when compared to controls, but no significant differences were observed between any of the other groups included.

Conclusion: The similarity in B-cell cytokine pattern found between extended oJIA, pJIA, early and established RA patients, contrarily to what was observed in persistent oJIA, suggests an early B-cell involvement in the pathogenesis of extended oJIA and pJIA as described for RA.

Disclosure of Interests: None declared

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AB0037

EXPRESSION OF NEGATIVE CHECKPOINT MOLECULES BTLA AND HVEM IS DYSREGULATED IN AUTOIMMUNE DISEASES

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Background: Immune checkpoint blockade with agents targeting CTLA4 and PD-1/PD-L1 alone or in combination has demonstrated exceptional efficacy in multiple cancer types by "unleashing" the cytotoxic action of quiescent, tumor-infiltrating T cells. However, the therapeutic action of these immunotherapies goes hand in hand with the loss of immune tolerance and appearance of immune-related adverse events such as colitis, arthralgia and inflammatory arthritis in responsive patients. Therefore, immune checkpoint molecules have been proposed as targets for the treatment of autoimmune diseases.

Objectives: Herein, we interrogate the potential of BTLA/HVEM axis as a target for restoring immune homeostasis in rheumatoid arthritis (RA), Systemic Lupus Erythematosus (SLE) and Sjogren's Syndrome (SjS) by examining their expression patterns in autoimmune disease tissues.

Methods: Message and protein expression of BTLA and HVEM were examined in RA and SLE synovial tissues, SLE cutaneous lesions, SjS salivary glands and peripheral blood samples of autoimmune disease by RNA sequencing and flow cytometry.

Results: Tissue dysregulation of the BTLA-HVEM axis was observed: Increased BTLA RNA level in RA synovium, SLE-affected skin, and SjS salivary gland samples, whereas HVEM level was affected only in the RA synovium when compared to unaffected tissues. Detailed immunophenotyping of B, T, and myeloid cell populations in RA, SLE, SjS and healthy control PBMCs revealed differential modulation of the BTLA+ or HVEM+ immune cell subsets in a disease-context dependent manner. SjS patients showed an overall decrease in memory B cells and most of the BTLA+ B cell subsets while a decrease in HVEM+ B cells was observed only in SLE PBMC samples and not RA and SLE samples. Immunophenotyping with a T cell panel exhibited decreased BTLA and HVEM expression on T cell subsets in SjS and SLE but not in RA patients. In addition, protein levels of HVEM were differentially decreased in SLE myeloid cell subsets. Finally, we demonstrate tissue-specific surface expression patterns of BTLA in RA and SLE samples: higher surface BTLA levels on RA and SLE PBMC B cells than matched tissue-derived B cells.

Conclusion: Our results demonstrate a dysregulation of the BTLA/HVEM axis in either lesional tissue or peripheral blood in an autoimmune disease context-dependent manner. These results also indicate the potential of targeting BTLA-HVEM axis for the treatment of multiple autoimmune diseases.

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AB0038

IMMUNE PHENOTYPING OF ERDHEIM-CHESTER DISEASE THROUGH MASS CYTOMETRY

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Background: The understanding of Erdheim-Chester Disease (ECD) pathogenesis has been greatly improved these past few years with the discovery of activating MAPK pathway mutations in most of ECD patients. However, the inflammatory phenotype of ECD remains widely unknown.

Objectives: We aimed to explore the inflammatory phenotype of Erdheim-Chester disease (ECD) using mass cytometry.

Methods: We analyzed peripheral blood mononuclear cells from 13 ECD patients and 11 healthy donors (HD) using mass cytometry with 29 metal-conjugated antibodies.

Results: Compared to HD, untreated ECD patients had increased proportion of classical monocytes (90.8 [87.1-96.5] vs 81.6 [76.2-87.5] %, $p=0.02$) and decreased proportion of non-classical monocytes (4.7 [3.4-9.7] vs 11.8 [6.6-17.2] %, $p=0.047$). Untreated ECD patients had more circulating Th17 cells compared to HD (3.3 [3-5.3] vs 1.3 [0.4-2.3] %, $p=0.015$) and ECD patients treated with BRAF or MEK inhibitors (3.3 [3-5.3] vs 1.9 [0.6-2.4] %, $p=0.005$). Moreover Treg cells were lower in ECD patients than HD, with an increased Th17/Treg ratio (1.37 [0.74-1.9] vs 0.34 [0.19-0.43], $p=0.0004$). There was no difference regarding Th1 cells, Th2 cells, B cells, NK cells and circulating dendritic cells.

Conclusion: ECD monocyte profile seems similar to what have been described in CMML. Inflammation observed in ECD may be driven through Th17 cells, and might be targeted with specific treatment.

Disclosure of Interests: None declared

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AB0039 **ROLE OF MESENCHYMAL STEM CELLS ISOLATED FROM DENTAL PULP (DPSCs) IN IMMUNOREGULATION PROCESSES MEDIATED BY PROGRAMMED DEATH-LIGAND 1 (PD-L1)**

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Background: Stem cells isolated from dental pulp (DPSCs) are characterized by a high rate of proliferation, low immunogenicity and a high ability to differentiate in different lineages (i.e. osteogenic, chondrogenic, adipogenic, myogenic and neural commitment). Their multipotency can be attributed to the peculiar embryological origin from the neural crest. DPSCs represent a promising stem cell resource since they hold a low ethical impact and can be easily isolated through routine dental procedures. These cells own immuno-modulatory properties, exerted through the activation of different mechanisms, including the Fas / FasL pathway, as well as through the release of soluble factors. Currently, other molecular mechanisms are under consideration such as PD-1 / PD-L1 (Programmed Death 1 and its Ligand) which are supposed to be involved in the induction and / or maintenance of immune tolerance.

Objectives: The aim of this research was to investigate whether the stimulation of PD-L1 in DPSCs can affect the immunomodulatory effects of these stem cells on peripheral blood mononuclear cells (PBMCs). Furthermore, the expression of PD-L1 was also assayed after the induction of osteogenic differentiation of DPSCs in order to evaluate a possible application of DPSCs in autoimmune inflammatory osteo-erosive diseases.

Methods: Immuno-selection was performed on DPSCs, isolated from waste material, against the stemness markers c-Kit and STRO-1, to obtain a pure stem cell population. Then, STRO-1+/c-Kit+ DPSCs, were co-cultured either directly and indirectly with peripheral blood mononuclear cells (PBMCs) from healthy adult donors, previously activated by anti-CD3 and anti-CD28 antibodies. Co-cultures of PBMCs with amniotic fluid stem cells (AFSCs) and bone marrow mesenchymal stem cells (BM-MSCs) were also set up. The expression of PD-1 in PBMCs as well as of PD-L1 in DPSCs, AFSCs, BM-MSCs and PBMCs, was evaluated by Western Blot (WB) and immunofluorescence (IF) analyses, before and after osteogenic differentiation. Osteogenic differentiation of DPSCs, after 30 days of induction, was verified by IF and WB, of osteopontin, osteocalcin and RUNX2 markers. Interleukin-2 (IL-2) expression levels in PBMCs were analyzed by Real-Time PCR analysis.

Results: Our data highlight that, after direct and indirect co-culture with activated PBMCs, PD-L1 expression was up-regulated not only in DPSCs, but also in BM-MSCs and AFSCs (Figure 1), thus suggesting that 1) this is a common ability of mesenchymal stem cells and 2) this event can be also mediated by soluble factors release. Moreover, when evaluating the effects of DPSCs co-culture on PBMCs an increased expression of cleaved caspase 3 was observed, together

with a decreased expression of IL-2 - a growth factor essential for the proliferation and survival of T cells (Figure 2). These findings showed how DPSCs can modulate the immune system by PD-L1 up-regulation. On the other hand, it is noteworthy that, after reaching osteogenic commitment, DPSCs down-regulated the expression of PD-L1, allowing to hypothesize that PD-L1 expression is strictly related to the maintenance of stemness.

Figure 1.

Figure 2.

Conclusion: Taken together, our findings suggest that the expression of PD-L1 in DPSCs is involved in the modulation of immune response and pave the way for further investigations on the role of PD-1/PD-L1 pathway in controlling inflammation and immune response when applied to the treatment of autoimmune inflammatory diseases.

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AB0040 **IMPAIRED REGULATORY T CELL FUNCTIONS IN PATIENTS WITH PSORIASIS ARTHRITIS ELIGIBLE TO SWITCH TO ANTI-IL-17 TREATMENT**

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Background: A dysbalance between Th17 and regulatory T cells (Treg) has been suggested for several T cell-mediated autoimmune disorders. Inhibitors of IL-17 are successfully used for treatment of psoriasis arthritis (PsA). However, so far reconstitution of Treg functions has not been studied in detail in PsA eligible for switching to anti-IL-17 treatment.

Objectives: The project aims to analyze the reconstitution and maintenance of regulatory T cell (Treg) function after inhibition of inflammatory Th17-inducing pathways mediated by IL-1, IL-6, IL-17 and TNFalpha in a longitudinal manner.

Methods: Therefore, Treg derived from 12 PsA patients switching to Th17 inhibition and healthy controls were phenotypically characterized by flow cytometry.