CD4+T cells were increased in fibromyalgia patients with respect to HC. However, only IL17A and IFNγ, but not IL-4 producing CD4+T lymphocytes were increased with respect fibromyalgia secondary to Sjögren. These alterations were due to an increase of T<sup>eff</sup><sub>1</sub>, IL-17A, T<sub>cyt</sub> and T<sub>H</sub> in IL-4 and T<sub>H</sub>, T<sub>cyt</sub> and T<sub>eff</sub><sub>1</sub> IFNγ producing CD4+T cells were decreased in fibromyalgia secondary to Sjögren’s with respect to fibromyalgia patients and HC. Counts of T<sub>eff</sub><sub>1</sub> TNFα producing CD4+ T cells were increased in fibromyalgia with respect fibromyalgia secondary to Sjögren. IL-10 producing CD4+T cells were normal in fibromyalgia but decreased in fibromyalgia secondary to Sjögren.

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

**References:**


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**AB0036**

**CHILDREN WITH EXTENDED OLGARTICULAR 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 fulfill 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 (n=10) and two groups of children with extended oJIA, early and established RA when compared to controls, but no significant differences were observed between children with persistent oJIA, pJIA and early and established RA patients when compared to all groups included. APRIL serum levels were significantly increased in early and established RA patients when compared to 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 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 Sjögren'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 synovium, SLE-affected skin, and SJS salivary gland samples, whereas HVEM level was affected only in the RA synovium 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:** Erdheim-Chester disease (ECD) is a rare granulomatous disease of unknown etiology. ECD is characterized by the presence of characteristic histiocytes called the “aspergilloma cells” which can be found in the bone marrow, skeletal muscles and other tissues. The disease is characterized by a spectrum of clinical manifestations which include bone pain, bone erosion, diabetes insipidus, paraproteinemia, and glomerulonephritis. The disease is typically diagnosed in middle-aged and elderly people and can be associated with a good or poor prognosis, depending on the extent of organ involvement.

**Objectives:** The aim of the study was to evaluate the immune phenotype of ECD patients using mass cytometry.

**Methods:** Peripheral blood mononuclear cells (PBMCs) were collected from ECD patients and normal controls. The expression of various immune cell markers was evaluated using mass cytometry.

**Results:** Our results demonstrated a unique immune phenotype in ECD patients compared to normal controls. The ECD group showed a significant enrichment of B cells and natural killer (NK) cells. Additionally, there was a decrease in the proportion of T helper (Th) cells and Treg cells in the ECD group. These findings suggest a dysregulation of the immune response in ECD patients.

**Conclusion:** The mass cytometry analysis revealed a distinct immune phenotype in ECD patients, which could be used as a biomarker for the diagnosis and monitoring of the disease. Further studies are needed to validate these findings and to explore the potential therapeutic implications of this immune dysregulation.
**AB0039**

**ROLE OF MESENCHYMAL STEM CELLS ISOLATED FROM DENTAL PULP (DPSCs) IN IMMUNOREGULATION PROCESSES MEDIATED BY PROGRAMMED DEATH-LIGAND 1 (PD-L1) (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-Ki and STRO-1, to obtain a pure stem cell population. Then, STRO-1+c-Ki+ 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.

**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.

**References:**

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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.