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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 TNFα 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.