Phagocytosis was superior in M2 (IL10) and M2 (IL4) activated MDM than in M1 MDM. Anti-TNF agents but not TCZ or RTX induced an increase of phagocytosis in M1 MDM.
Conclusions: Anti-TNF agents upregulate M2 alternative pro-resolving markers and downregulate M1 inflammatory markers in macrophages. Our results need to be extended by transcriptional analysis and evaluated in RA patients.
References:
[1] Martinez FO and Gordon S, F1000Prime Reports 2014, 6:13.
Disclosure of Interest: Y. Degboe Grant/research support from: Société Française de Rhumatologie, B. Rauwel: None declared, M. Baron: None declared, J.-F. Boyer: None declared, A. Cantagrel: None declared, A. Constantin: None declared, J.-L. Davignon: None declared
DOI: 10.1136/annrheumdis-2017-eular.1249

SAT0007 GROUP 3 INNATE LYMPHOID CELLS NUMBERS IN PERIPHERAL BLOOD PREDICT USTEKINUMAB (STELARA) THERAPY RESPONSIVENESS IN PSORIATIC DISEASE CASES WITH SUBCLINICAL IMAGING ENTHESOPATHY

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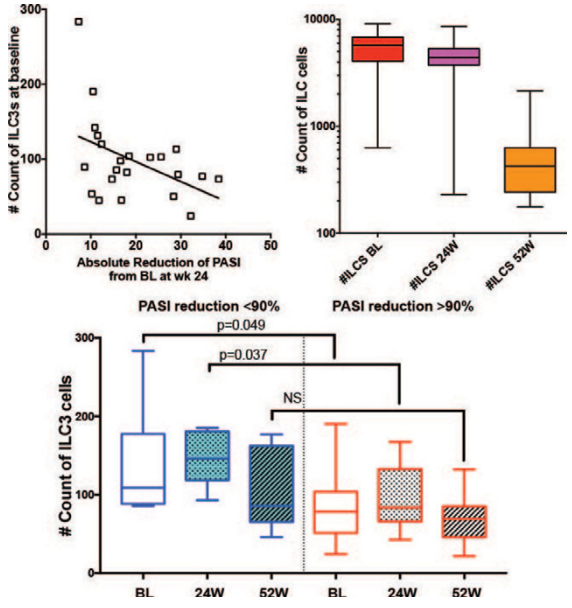
Background: Ustekinumab[1] targets the common p40 sub-unit of interleukin-12 (IL-12/interleukin-23 (IL-23). In patients treated with Ustekinumab for psoriasis where patients were selected on the basis of subclinical imaging enthesopathy, we have noted an improvement in subclinical imaging enthesopathy (Savage LJ et al submitted), raising the possibility that it may be possible to find a biomarker for predicting response to therapy in psoriatic disease. Innate lymphoid cells may be centrally involved in the pathogenesis of psoriatic skin and joints disease[2], since they express IL-23R receptor and are associated with IL-17/IL-22 production.
Objectives: This work was performed to test the hypothesis that peripheral blood ILC perturbations may be useful in defining response in psoriasis cases with imaging confirmed subclinical enthesopathy.
Methods: Peripheral blood collected at baseline (before therapy, 24weeks, 54 weeks) from patients in the MUSTEK trial (Ustekinumab in psoriasis cases who had ultrasound imaging confirmed subclinical enthesopathy) (n=23). Cellular immunophenotyping was performed density gradient separated PBMCs. Innate lymphoid cells were identified as lineage negative (CD3- TCR$\gamma\delta$- TCR$\alpha\beta$- CD19- CD14- CD11c- CD1a- CD303- FcεRI- CD34- CD123-) with positive expression of CD45, CD127. ILC2 cells were identified as Lineage- CD127+ and CRTH2 positive, while ILC3 were identified as Lineage- CD127+, CRTH2 – and CD117 (c-Kit) positive and further subdivided of NKp44+ and NKp44-. ILC1 were identified as lineage- CD127+ CD117-and CRTH2-. For data analysis we separated cases into PASI>90% or PASI <90% responders. The subclinical enthesopathy scores also fell significantly under therapy (Savage LJ data submitted)
Results: No correlation was found with total ILCs (ILC1,2, AND 3) (R=0.104, p=321, Spearman R) and therapy response. While, The absolute numbers of baseline ILC3s was inversely correlated in with the reduction in the PASI score (R -0.404, p=0308, Spearman R). The ILC3s also fell progressively under therapy. All the patients respond with reduction of PASI score mean 92.6% (range 65.8–100%), Interestingly, those patients with reduction below 90% of PASI score has a significantly higher absolute numbers of ILC3+ cells in peripheral blood at the baseline than PASI (n=6/23) than super-responder group (n=17/23)
Conclusions: Only peripheral blood ILC3s, but not other ILCs changes, correlate with the PASI score (disease activity), Furthermore, excellent responders (PASI reduction >90%) showed strong correlated with higher ILC3 population at the baseline. This may help to use ILC3 enumeration as predictive parameter for ustekinamab clinical therapeutic response and may be relevant to assessing novel biomarkers for subclincal arthropathy in psoriasis.



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[1] Kreuger et al. N Engl J Med. 2007 Feb 8; 356(6):580–92.
[2] Vallinova et al. 2014 Apr;134(4):984–91.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5347

SAT0008 DRUG THERAPY ENHANCES TOLEROGENIC PROPERTIES OF DENDRITIC CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control autoreactive T-lymphocytes, the enhancing of tolerogenic properties of DCs seems to be a new important strategy in treatment of RA. The experimental research in animals and human in vitro studies revealed the capacity of anti-rheumatic drugs to inhibit stimulating activity and to enhance tolerogenic functions of DCs. However, data concerning the in vivo influences of drug therapies on DC functions in RA patients are not available.
Objectives: The aim of our study is to investigate, whether drug therapies influence the properties of monocyte-derived DCs generated in the presence of IFNα (IFN-DCs) in RA patients, and if the effect of disease-modifying anti-rheumatic drugs differ from that of biological/pulse steroid therapy.
Methods: Thirty nine patients with RA with high and moderate activity of disease were recruited in this study. All patients fullfield ACR/EULAR criteria (2010). Nineteen patients received methotrexate, leflunomide, sulfasalazine or their combination (RA1). Twenty patients were at pulse therapy (methylprednisolone 500mg No. 3) or biological drugs (adalimumab or rituximab) (RA 2). All studies were performed after receiving informed consent. DCs were generated from blood monocytes culturing for 5 days with GM-CSF and IFN-α in the absence and presence dexamethasone, applied on third day. LPS as maturation stimuli was added on fourth day. The expression of CD14, CD83, CD 86, B7H1, HLA-DR, TLR-2 on the surface of DCs was measured by flow cytometry. The functions of DCs were evaluated by measuring cytokine production and DC allostimulatory activity in mixed lymphocyte culture.
Results: Both DC-RA1 and DC-RA2 where shown to display impaired maturation evidenced by elevated expression of CD14 and decreased number of mature (CD14-CD83+) DCs. Wherein, DCs-RA2 demonstrated several additional differences, including increased number of intermediate CD14+CD83+ cells (compared with donors DCs), higher expression of inhibitory molecule B7-H1 (PD-1L) (compare with donors DCs and DCs-RA1) and tendency to lower expression of CD86 and higher expression of TLR-2. Besides, DCs-RA2 produced higher concentrations of IL-6 and had 2-fold lower allostimulatory activity then DCs-RA1. These differences together with phenotypic changes suggested more pronounced tolerogenic properties of DCs-RA2. Despite the revealed DC differences in RA1 and RA2 patients both types of DCs preserved in vitro sensitivity to dexamethasone, that suppressed the production of TNF-α and reduced allostimulatory activity.
Conclusions: The data obtained indicate that, IFN-DCs from RA patients at drug treatments are characterized by tolerogenic properties, which are more pronounced in patients with biological or pulse steroid therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2408

SAT0009 DISTRIBUTION AND INTRACELLULAR SETTITNG OF GRANULYSIN IN WOMEN WITH KNEE OSTEOARTHRITIS

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Background: The role of the cell-mediated immune response is recently recognized in osteoarthritis (OA) (1). Granulysin (GNLY) is mediator of cellular immunity and cytotoxic molecule expressed in T and NK cells in regulatory (15 kDa) and cytotoxic (9 kDa) forms (2). Cytotoxic 9 kDa form of GNLY mediates apoptosis of eukaryotic cells (3) and might be responsible for silent unscheduled apoptosis of joint tissue cells in patients with OA without clinically recognized