Objectives: To investigate whether the T-cells at the normal entheses were regulatory in nature and to determine the type of regulatory T-cell as Tr1 or FOXP3 regulatory T-cell and to determine T-cell reactivity.

Methods: Healthy interspinous ligament and spinous process with matched peripheral blood were harvested from patients undergoing elective spinal surgery (n=20). Enthesal soft tissue (EST) & peri-enthesal bone (PEB) was enzymatically digested and then sorted. Tr1 and Treg phenotypes were investigated using flow cytometry. Analysis of cytokines, growth factors and chemokines was performed by qRT-PCR, ELISA and flow cytometry. TCR sequencing was performed and a search for putative T-cell reactivity was done using TCR3 database.

Results: Pro-inflammatory cytokine transcripts including IL-17A, IL-17F, IL-22, IL-23 (p19) & TNF were very low or undetectable in the Enthesis T-cells (Fig 1). Flow cytometry confirmed enthesal T-cells had a Tr1 phenotype (CD4+ LAG3+ CD49b+). Intracellular flow cytometry showed enthesal T-cells had very low FOXP3 expression, when compared to their blood counterparts. Intracellular flow cytometry and gene expression showed high basal expression of growth factors and regulatory proteins such as IL-10 & TGF β , when compared to blood T-cells. RNA-Seq data, showed 13 potential TCR clonal sequences the most common of which are predicted to be reactive viral infection was CMV present in 8 sequences and Influenza A virus present in 2 sequences.

Conclusion: The healthy human entheses has regulatory T-cells of a Tr1 phenotype rather than a FOXP3 Treg phenotype. Many clones have antigen specificity indicating reactivity to prior infection. These findings suggest that conventional enthesal T-cells have a role in entheses immune homeostasis.

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SAT0362

ASSOCIATION OF GUT DYSBIOSIS WITH STRUCTURAL DAMAGE AND ACTIVITY IN AXIAL SPONDYLOARTHRITIS PATIENTS. DATA FROM THE COSPAR REGISTRY.

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Background: The etiopathogenesis of axial spondyloarthritis (AxSpA) is multifactorial. The possible role of alteration in gut microbiome (dysbiosis) has been recently suggested. However, the association of dysbiosis with structural damage is still unknown and further studies are needed to assess its association with disease activity.

Objectives: To determine the alterations in the gut microbiota in AxSpA patients. To evaluate whether changes in the gut microbiota in AxSpA patients are associated with structural damage or disease activity.

Methods: Fifteen AxSpA patients and 15 healthy donors (HDs) were included in a cross-sectional study. Disease activity variables such as C-reactive protein and ESR were measured. Structural damage was determined by lateral X-rays of the cervical and lumbar spine to establish the mSASSS index. Axial mobility was evaluated using the BASMI index and the entheses affection was evaluated using ultrasound to obtain the MASEI index. Gut microbiota was measured using the Ion Torrent S5 platform and sequences were processed using the QIIME2. Chi-square and Mann-Whitney U were used, and correlations were determined using the Spearman Rho test. Significant differences were considered p < 0.05.

Results: Alpha diversity indicators, such as the number of observed OTUs group and the faith index, showed a greater richness in AxSpA compared to HDs (p=0.03 and p=0.01). A significant decrease in family Bacteroidaceae (p=0.006) and an increase in families Synergistaceae and Bifidobacteriaceae were found

in the microbiota of AxSpA (p=0.036, p=0.049). According to genera, Bacteroides decreased in AxSpA (p=0.006), while Dialister and Bifidobacterium increased (p=0.010 and p=0.046). Positive correlation among lumbar mSASSS (r=0.508, p=0.019) and Synergistaceae was found. This family was also increased along with the increase in entheses damage (MASEI index (r=0.656, p=0.028)) and axial mobility by the BASMI index (r=0.529, p=0.011). Correlation studies between the decrease in Bacteroidaceae and Bacteroides with disease activity measured by ASDAS (r=-0.697, p=0.025; r=-0.770, p=0.009) was also significant. Positive correlation was observed between Dialister with mSASSS (r=0.549, p=0.010) and BASMI (r=0.512, p=0.015).

Conclusion: 1) AxSpA patients had a significant alteration of the gut microbiota. 2) These alterations are associated with radiographic damage, disease activity, affection of entheses and axial mobility.

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SAT0363

DELPHINIDIN DOSE-DEPENDENTLY DIMINISHES PERIPHERAL IL-17 AND IFN- γ PRODUCING LYMPHOCYTES IN PSORIATIC ARTHRITIS

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Background: Delphinidin, a dietary anthocyanidin and powerful anti-oxidant from pigmented fruits and vegetables, has broad anti-inflammatory properties. In a human skin model of psoriasis, delphinidin reduced expression of proliferative and inflammatory markers (1).

Objectives: The rationale of our study was to assess whether delphinidin can in vitro suppress IL-17 and IFN- γ production in peripheral blood mononuclear cell (PBMC) subsets from patients with psoriatic arthritis (PsA).

Methods: PBMCs were obtained from 24 patients with PsA attending the outpatient clinic of the Department of Rheumatology/clinical Immunology at the University General Hospital of Larissa, Greece. 16 age- and sex-matched healthy volunteers were also included in the study. Delphinidin was supplemented at a concentration ranging from 1 to 50 μ g/ml, one hour prior to cell stimulation. Cell viability (Annexin V staining) and innate/adaptive lymphocyte subpopulations were assessed by flow cytometry with a panel of fluorochrome-conjugated antibodies against CD56, CD3, CD4 and CD8. Intracellular expression of IL-17 and IFN- γ was measured following PMA/ionomycin stimulation for 5 hours using standard cell permeabilization protocols and monoclonal antibodies against IL-17 and IFN- γ .

Results: Delphinidin at concentration ≥ 10 μ g/ml sharply diminished IL-17-production by CD4(+) T cells (Th17) and CD56(+)CD3(+) (NKT) cells from patients with psoriatic arthritis and normal controls (p $\leq$ 0.05). IFN- γ producing T (CD4 and CD8) cells, as well as NK and NKT cells were also dose-dependently suppressed following delphinidin pre-incubation in both patients and healthy controls. Inhibition of IFN- γ (+) cells ranged from 27 to 69% and peaked at delphinidin concentration 20-50 μ g/ml. The inhibitory effect of delphinidin on IL-17 and IFN- γ producing lymphocytes was not due to compromised cell viability, as assessed by annexin V binding.

Conclusion: Delphinidin exerts, in a dose-dependent manner, a profound in vitro inhibitory effect on T cell and NKT cell IL-17 and IFN- γ production in PsA, and therefore, it may be used as a dietary immunosuppressant, complementary to standard treatment.

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SATURDAY, 06 JUNE 2020

Spondyloarthritis - clinical aspects (other than treatment)

SAT0364

DATA TO BE COLLECTED FOR AN OPTIMAL MANAGEMENT OF AXIAL SPONDYLOARTHRITIS IN DAILY PRACTICE: PROPOSAL FROM AN EVIDENCE BASED AND CONSENSUAL APPROACHES

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Background: Standardization of clinical practice has been proven to be effective in management of chronic diseases. This is particularly true at the time where the concept of treat to target is becoming more and more important in the field of axial spondyloarthritis (ax-SpA).

Objectives: To propose a list of variables to be collected at the time of the diagnosis and over the follow-up of patients with axial spondyloarthritis (ax-SpA) for an optimal management in daily practice.

Methods: The process comprised (1) the evaluation of the interest of 51 variables proposed for the assessment of axSpA via a systematic literature research, (2) a consensus process involving 78 hospital-based or office-based rheumatologists, considering the collection of the variable in a 4 grade scale from "potentially useful" to "mandatory", (3) a consensus on optimal timeline for periodic

assessment of the selected variables on a 5 grade scale from "at each visit" to "never to be re-collected".

Results: The systematic literature research retrieved a total of 14,133 abstracts, of which 213 were included in the final qualitative synthesis. Concerning the data to be collected at the time of the diagnosis and during follow-up, we proposed to differentiate the results based on a) the way of collection of the variables (e.g. questionnaires by the patient, interview by the physician, physical examination, investigations) b) the usefulness these variables in daily practice based on the opinion of the rheumatologists " c) the optimal timeline between 2 evaluations of the variable based on the opinion of the rheumatologists. In the initial systematic review, symptoms of heart failure history of inflammatory bowel disease, psoriasis or uveitis, patient global visual analogic scale, spine radiographs, modified Schöber test, coxo-femoral rotations, swollen joint count, urine strip test, BASDAI and ASDAS global scores were considered very useful and nocturnal back pain/ morning stiffness, sacro-iliac joints radiographs and CRP were considered mandatory (Figure 1). Timeline between 2 evaluations of variables to collect in the periodic review are summarized in Figure 2.

Figure 2. Periodic review timeline of variables to collect ASDAS=Ankylosing Spondylitis Disease Activity Score, BASDAI=Bath Ankylosing Spondylitis Disease Activity Index, Spondylitis Metrology Index, CRP=C Reactive Protein, IBD = inflammatory bowel diseases, PRO = Patient Reported Outcomes

Conclusion: Using an evidence-based and an expert consensus approaches, this initiative defined a core set of variables to be collected and reported at the time of the diagnosis and during follow-up of patients with ax-SpA in daily practice.

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SAT0365

EFFECTS OF ANTI-TNF-THERAPY ON OSTEOBLASTIC ACTIVITY IN ANKYLOSING SPONDYLITIS – RESULTS FROM A PROSPECTIVE STUDY USING PET-MRI OF SIJ AND SPINE

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Background: The clinical efficacy of tumor necrosis factor inhibitors (TNFi) in patients with axial spondyloarthritis (axSpA) is well established but its effect on new bone formation is still unclear (1). Positron emission tomography (PET) using bone-seeking ¹⁸F-Fluoride [¹⁸F]F in combination with magnetic resonance imaging ([¹⁸F]F /MRI) has been shown to depict not only bone marrow edema (BME) but also shows the quantity of tracer uptake in the late phase of perfusion suggestive of remodeling and osteoblastic activity, not only in radiographic axSpA (r-axSpA) (2).

Objectives: Assess the effect of TNFi on bone remodeling processes in the axial skeleton of r-axSpA patients using [¹⁸F]F/MRI prior (baseline, BL) and 4 months after (follow-up, FU) treatment.

Figure 1. Core sets of items to collect and report in the systematic review in axial spondyloarthritis management in daily practice ASDAS=Ankylosing Spondylitis Disease Activity Score, BASDAI=Bath Ankylosing Spondylitis Disease Activity Index, BASFI=Bath Ankylosing Spondylitis Functional Index, BASMI=Bath Ankylosing Spondylitis Metrology Index, CRP=C Reactive Protein, CT=computerized tomography, FIRST=Fibromyalgia Rapid Screening Tool, HLA=Human Leukocyte Antigen, MRI=Magnetic resonance imaging, PET=positron emission tomography.