disease inactivation are scarce. Gene expression profiling analysis could be useful to elucidate the pathogenic mechanisms of diseases, and differential gene expression analysis between diverse disease conditions produces gene signatures characteristic of the state or disease being studied.

Objectives: Our aim was to compare the transcriptional profiles of patients with clinically active versus inactive (remission state) PsA (peripheral joint subset), and healthy controls (HCs).

Methods: From a cohort of around 300 patients affected by PsA according to CASPAR criteria, we first selected 20 patients (peripheral arthritis subset) with active disease state (without biologic treatment ongoing) (A) and 20 patients with >1-year remission induced by TNFα antagonism (R), as assessed by DAPSA > 14, and DAPSA ≤ 4 scores respectively, and from 20 HCs matching for age and gender ratio. Both PsA groups were not on corticosteroid treatment. RNA from peripheral blood was extracted from 20 HCs matching for age and gender ratio. Both PsA groups were not on corticosteroid treatment. RNA from peripheral blood was extracted and, following quality analysis by Agilent Bioanalyzer, each condition has been profiled using RNAs pools in biological duplicates by distinct Affymetrix Human GeneChip HTA 2.0, for a total of 6 arrays. Data analysis was performed using the commercial software Partek Genomics Suite, V 6.6. To identify a transcript as differentially expressed, a value of fold change 1.5 and p-value 0.05 has been set.

Results: The Venn diagram shows all comparative groups (A vs R, A vs HC, R vs HC) with their relative amount of transcripts differentially expressed, generated using abovementioned parameters, and the relationship between sets (fig1, panel A). Using the list of transcripts differentially expressed in at least one of the aforementioned comparison, a hierarchical clustering was carried out to highlight the intra-condition expression profile. We have identified (arbitrarily) 4 clusters of transcripts with analogous transcriptional profile and to each of them a color code has been assigned (Heatmap in Fig1, panel B). For these clusters and for all lists of transcripts differentially expressed found by our comparative study, we carried out the Gene Set Enrichment Analysis by Gene Ontology (GO), in order to identify how molecular functions, cellular components or biological processes occurs more frequently than expected in a reference list of transcripts.

Conclusion: Observing the amount of differentially expressed transcripts, is evident that while active disease state (A) has a clear-cut different profile, the drug-induced remission (R) is more similar with HCs condition. However, in the hierarchical clustering this trend of similarity does not appear in all clusters of transcripts, as shown particularly in the red, orange and green clusters. Again, the Gene Set Enrichment Analysis Score showed us that mRNA transcripts dysregulated in the R condition vs HCs, are involved in several biological processes related to immune system, development, response to stimuli, localization and others. Our next step will be to validate, by Real Time PCR in a large cohort of patients, the most interesting dysregulated genes covering biological functions eventually sustaining subclinical activity in PsA.

Disclosure of Interests: None declared


FR10358 ROLE OF MiRNA-21-5PAS A POTENTIAL BIOMARKER FOR THE INFLAMMATION PATHWAY IN PSORIATIC DISEASE AND RESPONSE TO METHOTREXATE TREATMENT

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Background: Psoriatic arthritis (PsA) is an inflammatory arthritis occurring in patients with psoriasis. Several studies have shown links between altered miRNA expression with the pathogenesis of some autoimmune disorders. We previously demonstrated that miR-21-5p was upregulated in PsA compared to psoriasis without arthritis (PsC) and healthy controls (HC) and is thus a potential biomarker for PsA.

Objectives: 1) To determine whether miR-21-5p is differentially expressed in PsC patients who convert to PsA vs non-converters and validate the previous results in an independent cohort. 2) To determine the role of miR-215p in the response to methotrexate treatment (MTX) 3) To determine whether the inflammatory response to psoriasis is antagonised in PsA patients.

Methods: Serum & whole blood RNA samples were collected from 54 converters and 54 non-converters (matched for age, sex, psoriasis duration), 40 patients with early PsA (<2 years’ disease duration and not receiving biologic therapy), 40 patients with PsC (>10 years disease duration, not receiving biologic therapy, and matched to PsA patients on age, sex, and disease duration, but not on biologic treatment given age of psoriatic onset), and 54 non-convertors (matched to patients based on age, sex). RNA was extracted using the Tempus Spin RNA Isolation Kit. miR-21-5p was validated using droplet digital PCR (ddPCR). Serum IL-17, CXCL10, IL-23, TGFβ1 were measured by commercially available ELISA kits. Mann-Whitney test, Kruskal-Wallis test, Wilcoxon signed rank test and Spearman correlations were performed.

Results: The expression of miR-21-5p was significantly higher in converters compared to non-convertors (Fold change(FC)=2.16, p=0.002). miR-21-5p was upregulated in PsA as compared to PsC (FC=2.32, p=0.001) and HC (FC=15.7, p<0.0001) in the validation cohort. miR-21-5p was significantly down regulated 24 weeks post-MTX treatment in 30 PsA patients (FC<1.9, p<0.008), which correlated with swollen (r=0.49, p=0.033) and tender joint counts (r=0.41, p=0.02) supporting a possible role in inflammation pathway in PsA patients. IL-17 levels in PsA & PsC were significantly higher from HC (p<0.03), but not different between PsA & PsC. IL-23 levels were down regulated post MTX treatment and correlated with miR-21-5p (r=0.56, p<0.001), CXCL10 levels (r=0.48, p=0.01), IL-23 levels (r=0.43, p=0.02), TGFβ1 (r= -0.45, p=0.016).

Conclusion: Up regulated expression levels of miR-21-5p in converters and in PsA patients suggests a role as a potential biomarker for PsA. In the presence of upregulated miR-21-5p, IL-17 and IL-23 are upregulated while TGFβ1 is down regulated. When miR-21-5p is decreased IL-17 and IL-23 downregulated, with up regulation of TGFβ1. We have therefore examined the role of miR21-5p as a potential biomarker for inflammation pathway in PsA patients and response to MTX possibly through modulation of CXCL10 and IL-17/L123 axis.

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ANALYSIS OF BLOOD MONOCYTE TRANSCRIPTOMES AND BONE MARROW SAMPLES OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS.

Objectives: To assess and compare gene expression profiles of neutrophils, MAIT, γδ T, CD4+ and CD8+ T cells from AxSpA patients.

Methods: We recruited 5 healthy donors and 10 patients with a diagnosis of AxSpA according to the ASAS criteria. We compared the gene expression profiles of 5 sorted cell populations: 3 innate cell populations (neutrophils, MAIT and γδ T cells) and 2 adaptive cell populations (CD4+ T and CD8+ T) after cell stimulation by PMA + A23187 (calcium ionophore) + j1.3 glucan (extracted from Aspergillus fumigatus hyphae). Published data suggested that neutrophils stimulation by Aspergillus fumigatus induces IL-17A production by these cells(4). For each of these cell populations, cytokine production and the expression of a panel of 755 genes (Autoimmune discovery panel from Nanostring including 43 genes for which a polymorphism was associated with AxSpA) were assessed. Patient and control groups were compared with a Mann-Whitney test and comparison of cell populations was performed by a multigroup comparison.

Results: There was no significant difference between patients and controls regarding gene expression profile of neutrophils, γδ T, CD4+ T and CD8+ T. We observed that 34 genes were differentially expressed between patients and controls in MAIT cells (p = 0.03, q = 0.1). In particular, T cell activation genes (TBX21, AHR, ZAP70) and cell interaction genes (ITAG6, CTNNB1, ICAM2, ITGB2, SELL) were decreased in AxSpA patients. Among AxSpA patients, MAIT cells were those significantly showing the highest level of IL-17A expression. IL23R and RORC were also more expressed by MAIT compared to other cell populations. IL-17A expression was very low in neutrophils but we observed that 18 out of the 43 AS associated genes were mainly expressed by neutrophils (p