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 TNF α antagonism (R), as assessed by DAPSA > 14, and DAPSA $\leq$ 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 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 founded 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.

Fig. 1 Panel A: Venn Diagram; Panel B: Heatmap from Hierarchical Clustering

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 stimulus, 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

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FRI0358

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 several 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-convertors and validate the previous results in an independent cohort. 2) To determine the role of miR-21-5p in the response to methotrexate treatment (MTX) 3) To determine whether miR-21-5p modulates inflammation in psoriatic disease.

Methods: Serum & whole blood RNA samples were collected from 54 convertors and 54 non-convertors (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, psoriasis duration, and age of psoriasis onset), and 40 HC (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, TGF β 1 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 convertors compared to non-convertors (Fold change(FC)=2.16, *p*=0.002). miR-21-5p was upregulated in PsA 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*=0.003) 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-17 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), TGF β 1 (*r*= -0.45, *p*=0.04) and total active joint counts (*r*=0.40, *p*=0.016).

Conclusion: Up regulated expression levels of miR-21-5p in convertors 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 TGF β 1 is down regulated. When miR-21-5p is decreased IL-17 and IL-23 downregulate, with up regulation of TGF β 1. We have thus determined the role of miR21-5p as a potential biomarker for inflammation pathway in psoriatic disease and response to MTX possibly through modulation of CXCL10 and IL-17/IL-23 axis.

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FRI0359

KRT77 DELETIONS IN FAMILIAL INFLAMMATORY BOWEL DISEASE MAY OFFER A NOVEL LINK TO FAMILIAL SPONDYLOARTHROPATHY

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Background: Inflammatory bowel disease, either clinical or subclinical is a cardinal pathological process that is central to the spondyloarthropathy (SpA) category of disease that also includes psoriasis, psoriatic arthritis, uveitis and ankylosing spondylitis.

Objectives: To look for novel genes in familial SpA in large multigene families using a whole genome sequencing approach.

Methods: We used Whole Genome Sequencing to screen SpA family members with different disease manifestations. We screened 5 multigene SpA families (up to 8 members) with different disease manifestations.

Results: We found a 1.5MB deletion of the KRT77 gene in 3 of 7 families that segregated with SpA phenotype. Given that KRT77 is a barrier protein and given that tagging SNPs from GWAS studies do not cover the region, and given that both IBD and psoriasis are associated with barrier defects, we looked for an association with KRT77 deletion in