Methods: We collected paired PB and SF samples from HLA-B*27+ (n=5) and HLA-B*27- (n=7) patients. All patients fulfilled the CASPAR criteria. TCR beta profiling for total P/SFMC samples and T cell subsets was performed using high throughput sequencing of 5'-RACE double-bar-coded TCR beta cDNA libraries following by repertoire reconstruction with molecular barcode-based error correction [5]

Results: Clonal diversity in SF was largely restricted compared to PB, with significant enrichment of mostly expanded SF clonotypes compared to PB, suggesting antigen-driven migration and expansion of the T cells into inflamed site. Major clonal expansions of SF were private for each patient, yet SF shared significantly more clonotypes than PB independently from HLA-B*27 status. Most important, in CD8+ subsets from PB and SF we identified the previously described AS-associated T-cell clonotypes. These clonotypes were detected in SF of all HLA-B*27+ patients but not in samples from HLA-B*27- patients, suggesting the HLA-B*27 restriction of the TCR beta motif. The clonotypes were enriched in SF compared to PB, representing up to 1.6% of CD8+ SF T cells. All HLA-B*27+ patients had several variants of the TCR beta clonotypes in SF, suggesting the selection of the TCRs during disease development

Conclusion: Our results further support the supposed role of the CD8+ T cells in SpAs and suggest that similarity of clinical phenotype between AS and HLA-B*27+ PsA patients could be associated with autoimmune response to similar antigens, represented by HLA-B*27 molecule

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Rheumatoid arthritis – etiology, pathogenesis and animal models

SAT0035

IS PHARMACOLOGICAL CLINICAL REMISSION SYNONYMOUS WITH BIOLOGICAL INACTIVE DISEASE? DIFFERENTIAL GENE EXPRESSION ANALYSIS IN RHEUMATOID ARTHRITIS AND HEALTHY CONTROLS

Maria Maddalena Angioni, Daniela Perra, Enrico Mascia, Silvia Pinna, Ignazio Cangemi, Piero Mascia, Mattia Congia, Alberto Floris, Matteo Piga, Alessandro Mathieu, Alberto Cauli. *Università degli Studi ed AOU di Cagliari, Dip.to Scienze Mediche e Sanita' Pubblica, Unità di Reumatologia, Monserrato (Cagliari), Italy*

Background: Remission is an important goal of therapy in rheumatoid arthritis (RA), but data on molecular players of clinical remission and effective disease inactivation are scarce. Gene expression profiling analysis is 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) RA, and healthy controls (HCs).

Methods: From a cohort of around 1000 patients affected by RA according to ACR-EULAR 2010 criteria, we first selected 20 patients with active disease state (without biologic treatment ongoing) (A) and 20 patients with >1-year remission induced by TNFα antagonism (Etanercept) (R), as assessed by DAS28(PCR) scores, and from 20 HCs matching for age and gender ratio. Both RA 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 view the intra-condition expression profile. Here, 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.

Conclusion: Considering the amount of differentially expressed transcripts and the hierarchical clustering analysis, is evident that the drug-induced remission (R) is more similar with HCs condition, while active disease state (A) has a different profile; however "similar" profile does not mean "identical". In fact, the Gene Set Enrichment Analysis Score showed us that mRNA transcripts dysregulated in the R condition vs HCs, are involved in several biological processes regarding the immune system, response to stimulus, biological regulation, locomotion 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 disease activity.

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