Background: Early diagnosis of axial Spondyloarthritis (axSpA) represents a major clinical challenge nowadays. Increasing evidence has determined that early diagnosis, prompt treatment initiation and early achievement of remission are the best predictors of long-term clinical, functional and radiographic outcomes. New tools to support the diagnosis are needed.

Objectives: This study aims to identify differentially expressed genes that may improve the current clinical diagnosis approach for early axSpA.

Methods: A cross-sectional study was conducted on 50 participants, 25 patients with axSpA (according to ASAS criteria) and 25 Healthy Controls, matched by gender, age and levels of physical activity. Peripheral blood samples were collected and RNA-Seq technology was performed. Normalization of raw data, and identification of differentially expressed genes was obtained using edgeR and limma approaches. Gene Set Enrichment Analysis (GSEA) and Functional Enrichment analysis using Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) annotations were also performed. A number of Differently Expressed Genes were highlighted.

Results: 311 genes were identified as being significantly differentially expressed between patients and controls. In details, 129 downregulated (7 genes have fold change more than 1) and 182 upregulated genes (3 genes have fold change more than 1) are highlighted. These genes are mostly involved in Myogenes, Innate Immune Signalling and JAK/STAT pathways. Several genes with functions of skeletal muscle development and muscle contraction were identified.

Conclusion: The evidence disclosed that regulation of muscle development and contraction may be also engaged in pathophysiology mechanisms of axSpA. These new cues open new perspectives for diagnosis and therapeutic approaches in axSpA.

Acknowledgments: To all patients and healthy people who participate in MySpA study.

Disclosure of Interests: Atlas Mashayekhi Sardoo: None declared, Daniel Sobral: None declared, Lucia Domingues: None declared, Santiago Rodriguez-Manica Speakers bureau: Jansse, MSD, Novartis, Rita Pinheiro Torres: None declared, Agna Neto: None declared, Patricia Alves: None declared, Julii Costa: None declared, Anna Mara: None declared, Jair Francisco: Vitoria, Fernando Pimentel dos Santos Speakers bureau: Novartis, Pfizer, Biogen, Vitoria.

DOI: 10.1136/annrheumdis-2020-eular.5331

THU0022

DIFFERENTIAL DNA METHYLATION AS A PREDICTOR OF TOCILIZUMAB RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Tocilizumab (TCZ) is a biological disease-modifying antirheumatic drug that blocks IL-6 signalling and is effective in ameliorating disease activity in rheumatoid arthritis (RA). However, approximately 50% of patients do not respond adequately to TCZ and some patients report adverse events. Considering there is growing evidence that DNA methylation is implicated in RA susceptibility and response to some biologics (1, 2), we investigated DNA methylation as a candidate biomarker for response to TCZ in RA.

Objectives: To identify different DNA methylation signatures in whole blood associated with TCZ response in patients with RA.

Methods: Epigenome-wide DNA methylation patterns were measured using the Infinium EPIC BeadChip (Illumina) in whole blood-derived DNA samples from patients with RA. DNA was extracted from blood samples taken pre-treatment and following 3 months on therapy, and response was determined at 6 months using the Clinical Disease Activity Index (CDAI). Patients who had good response (n=10) or poor response (n=10) to TCZ by 6 months were selected. Samples from secondary poor responders (n=10) (patients who had an improvement of CDAI and were in remission at 3 months, followed by a worsening of CDAI at 6 months) were also analysed. Differentially methylated positions and regions (DMPs/DMRs) were identified using linear regression, adjusting for gender, age, cell composition, smoking status, and glucocorticoid use. Gene Set Enrichment Analysis (GSEA) was used to identify significant pathways associated with response and Functional Epigenetic Module analysis of interactome hotspots in regions of differential methylation.

Results: 20 DMPs were significantly associated with response status at 6 months in the pre-treatment samples. Another 21 DMPs were associated with response in the 3 month samples. Within good responders, 10 DMPs showed significant change in methylation level between pre-treatment and the 3 month samples (unadjusted P-value <10^-6). One DMP, cg03121467, was significantly methyalted in good responders compared to poor responders in the pre-treatment samples. This DMP is close to EPB41L4A and thought to have a role in β-cat- enin signalling. GSEA of DMRs in non- and secondary non- responders identified histone acetyltransferase pathways and included the KAT7A gene, which is a repressor of NF-κB. Additional analysis of interaction hotspots of differential methylation identified significant interactions with STAMBP and PTPN12 associated with response status.

Conclusion: These preliminary results provide evidence that DNA methylation patterns may predict response to TCZ. Validation of these findings in other larger data sets is required.

References:

THU0023

DETAILED PROFILE OF CO-OCCURRENCE OF RELAPSING POLYCHONDRITIS AND AUTOIMMUNE THYROID DISEASE

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Background: Relapsing polychondritis (RP) is a rare inflammatory disease, which is characterized by recurrent inflammation and destruction of cartilage tissues. RP also has the profile of autoimmune disease and is often complicated by other autoimmune diseases. Autoimmune thyroid disease (AITD) is one of the most common autoimmune diseases, which consists of Graves’ disease (GD) and Hashimoto’s thyroiditis (HT). While RP is reported to be complicated with AITD1, there has been no study on detailed profile of co-occurrence of RP and AITD.

Objectives: We aimed to reveal whether there is common (statistically significant) co-occurrence of RP and AITD. We also analyzed clinical and genetic pro- files characterizing the co-occurrence.

Methods: We recruited 117 patients with RP and checked their medical records in order to obtain the information about complication of AITD and clinical features. In addition, we genotyped Human Leucocyte Antigen (HLA) A, B, Cw, DRB1, DQB1 and DPB1 alleles for 88 of the 117 patients. Co-occurrence ratio was compared with prevalence of AITD in the Japanese population. Associations of co-occurrence of AITD with clinical manifestations or HLA alleles were analyzed among the patients.