Correlation studies revealed that disease activity (CRP, ESR, BASDAI) was associated to the alteration of a vast number of spliceosome components in the three subtypes of analyzed leukocytes. In addition, the BASFI index correlated with the expression of splicing factors ESRP1, SRSF1 and TRA2B in neutrophils. The inflammatory, atherogenic and oxidative profile of AS leukocytes was related to the expression of a number of spliceosome molecules in the three leukocyte subsets, although neutrophils exhibited the highest number of deregulated spliceosome components related to inflammation (STAT3, TNF- α , IL-1 α , IL-1 β , IL-5) and cell adhesion (ICAM-1, SELL, THBS4, CDH5). Finally, endothelial dysfunction correlated with the expression of several components of the major-spliceosome and splicing factors in monocytes and neutrophils.

Conclusions: 1) AS patients display a dysregulation of the splicing machinery components associated to disease function and activity. 2) The expression of spliceosome members in the different leukocyte subsets is related to the inflammatory, oxidative and proatherogenic profile of AS patients.

Alteration of the spliceosome may provide new biomarkers for diagnosis and clinical monitoring of AS

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FRI0431 ALTERED EXPRESSION OF CIRCULATING MICRORNAS IS RELATED TO DISEASE ACTIVITY AND STRUCTURAL DAMAGE IN ANKYLOSING SPONDYLITIS PATIENTS

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Background: Ankylosing spondylitis (AS) remains difficult to diagnose before irreversible damage to sacroiliac joint is noticeable. MicroRNAs (miRNAs) are a group of single-stranded non-coding RNAs of 20–25 nucleotides in length that can potentially regulate every aspect of cellular function. Recent studies have demonstrated that miRNAs can be detected in the circulation and serve as potential biomarkers of various inflammatory pathologies.

Objectives: To evaluate whether AS pathogenesis is related to the aberrant expression of plasma miRNAs.

Methods: The expression profile of 800 miRNAs in plasma was determined in pooled samples from AS patients and healthy donors (HDs) (n=3 each) using the nCounter technology. Next, candidate miRNAs were validated by real time RT-PCR in a cohort of AS patients and HDs (n=26 each). In parallel, the expression of validated miRNAs was examined in a cohort of 24 psoriatic arthritis (PsA) patients. To evaluate their relevance in the AS pathogenesis, an analysis was performed by using the web-based bioinformatics tool *Ingenuity Pathways Analysis* (IPA). Association and correlation studies of altered miRNAs with clinical and analytical profile of the AS patients were also performed. AS activity was defined as CRP >5 mg/L and/or BASDAI $\geq$ 4 and ESR >20 mm/h. Structural damage was evaluated by mSASSS.

Results: In discovery phase, nine miRNAs were differentially expressed (fold change $\geq$ 2) in the plasma of AS patients vs. HDs. After validation, higher expression levels of miRNA (miR)-146a-5p, miR-125a-5p, miR-151-3p and miR-22-3p, and lower of miR-150-5p and miR-451a were found in AS vs. HDs. Interestingly, higher miR-146a-5p, miR-125a-5p, miR-151-3p and miR-22-3p expression levels in AS than in PsA patients were further observed. The areas under the curve, generated to assess the accuracy of miRNAs as diagnostic biomarkers for AS, ranged from 0.717 to 0.798; the six-miRNAs signature reached 0.947. Bioinformatics analysis revealed that miRNAs targeted inflammatory and bone remodeling genes, underlying their potential role in this pathology. Indeed, correlation studies showed an association between these six miRNAs and potential target proteins associated to AS pathophysiology. In addition, miR-146a-5p, miR-146a-5p, miR-125a-5p and miR-22-3p expression was increased in active vs. non-active patients. Moreover, miR-150-5p and miR-451a expression was related to the presence of syndesmophytes in AS patients, underlying their association with structural damage.

Conclusions: 1) Several miRNAs are found differentially expressed in plasma from AS patients vs. HDs and other chronic inflammatory pathologies as PsA, indicating that these miRNAs may be considered potential biomarkers for AS diagnose. 2) The differential expression of certain miRNAs is associated to disease activity and structural damage. Overall, this study identified a six-plasma

miRNAs signature that could be attractive candidates as non-invasive biomarkers for the AS diagnosis, and may help to elucidate the disease pathogenesis.

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Spondyloarthritis - clinical aspects (other than treatment)

FRI0430 DUAL TRAJECTORIES OF DISEASE ACTIVITY AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: The ultimate goal of managing Ankylosing Spondylitis (AS) is to improve and maintain the patient's health-related quality of life (HRQoL). To reach this goal, rheumatologists target towards low disease activity, as this is the main modifiable factor. To date, there is insufficient insight into (1) the co-evolution of disease activity and HRQoL, and (2) the heterogeneity in such trajectories among patients.

Objectives: To explore the heterogeneous character of AS by identifying different temporal patterns of co-dependence between disease activity and HRQoL over 8 years follow-up.

Methods: Data from Outcome in AS International Study (OASIS; n=161) and Groningen Leeuwarden AS (GLAS; n=264) cohorts were used. All patients had an established diagnosis of AS. In GLAS, all patients started a biological. HRQoL and disease activity were measured bi-annually using ASQoL and ASDAS-CRP

Abstract FRI0430 – Table 1. Baseline characteristics of patients within each ASQoL-ASDAS trajectory

Characteristics	Trajectory 1 (N=55)	Trajectory 2 (N=105)	Trajectory 3 (N=86)	Trajectory 4 (N=124)	Trajectory 5 (N=55)	p-value
Age – yr	43.9 $\pm$ 12.4	46.0 $\pm$ 12.7	40.9 $\pm$ 10.7	47.9 $\pm$ 11.3	45.1 $\pm$ 13.7	<0.01*
Male sex (%)	46 (83.6)	71 (67.6)	62 (72.1)	83 (66.9)	29 (52.7)	0.01*
Smoking – yes (%)	16/42 (38.1)	23/85 (27.1)	26/74 (35.1)	44/98 (44.9)	20/46 (43.5)	0.13
HLA-B27 – positive (%)	50/54 (92.6)	73/103 (70.9)	72/82 (87.8)	94/119 (79.0)	44/55 (80.0)	0.01*
Symptom duration – yr	20.3 $\pm$ 10.9	21.4 $\pm$ 12.1	17.0 $\pm$ 10.9	22.2 $\pm$ 13.1	21.3 $\pm$ 12.6	0.04*
(Bridging) syndesmophytes present (%)	16/39 (41.0)	45/73 (61.6)	38/70 (54.3)	64/90 (71.1)	18/34 (52.9)	0.02*
Start biological (%)	15/54 (27.8)	41/101 (40.6)	81/86 (94.2)	85/120 (70.8)	35/55 (63.6)	<0.01*