FRI0165

MICRORNAS DYSREGULATION IN MONOCYTES AND T CD4 LYMPHOCYTES FROM PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: MicroRNAs have been shown to play a crucial role during innate or adaptive immune response. Dysregulation of miRNAs has been described in several autoimmune or rheumatic diseases including rheumatoid arthritis, inflammatory bowel disease or psoriasis. In spondyloarthritis (SpA), only few studies on miR expression have been reported with highly diverse methodologies and involving small samples of patients.

Objectives: Because T CD4 lymphocytes and monocytes are important cells in SpA pathophysiology, we wanted to assess the miR expression profile in these two cell types sorted from axial SpA (AxSpA) patients.

Methods: Eighty one AxSpA patients were included in this study. Among these patients, 74 fulfilled the ASAS classification criteria (imaging arm) with sacro-iliitis on X-rays (n=56) or objective signs of inflammation on MRI (n=18). Two independent cohorts of 22 and 59 SpA patients were compared to 17 and 38 age and sex-matched controls. Both SpA patients and controls were recruited from October 2014 to July 2017 in the department of rheumatology at Cochin Hospital in Paris, France. All SpA patients had an active disease despite NSAIDs intake (mean BASDAI score of 49±19 and mean ASDAS score of 3±0.9), were free of any biologic treatment and were eligible for a TNF-blocker treatment. Seventy-seven percent were HLA-B27 positive. T lymphocytes and monocytes were isolated from PBMC by direct isolation with magnetic microbeads (CD4 +and CD14+). Three-hundred seventy two miRs were screened by q-RT-PCR on the exploratory cohort and only MiRs showing a significant differential expression in the first cohort were analysed in the validation cohort. An unpaired T-test was used for comparison of miR expression level.

Results: In the exploratory cohort, 51 (CD14+) and 70 miRs (CD4+) were found to be differentially expressed between patients and controls. Among these, 15 miRs (in CD14+), and 12 miRs (in CD4+) were also found dysregulated in the validation cohort. These validated miRNAs were found to play a key role in physiological pathways such as NFkB or TGFb, Wnt signalling and monocyte differentiation that have been involved in the pathophysiology of the disease. Neither clinical subphenotypes nor biological parameters were associated with different profiles of miR expression after adjusting for multiple tests. We found a negative correlation between miR-146a-5p level and BASDAI (r=-0.28, p=0.011) and ASDAS (r=-0.38, p=5.9 10⁻⁴) in monocytes.

Conclusions: We found a dysregulation of miR expression in monocytes and T CD4 lymphocytes from patients with axial spondyloarthritis, whose consequences could contribute to the pathophysiology of the disease and be of interest for therapeutic perspective. Moreover, identifying biomarkers with the potential of diagnostic signature should help the clinician in daily practice.

Disclosure of Interest: None declared

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FRI0168

PHENOTYPIC, FUNCTIONAL AND MOLECULAR CHARACTERISATION OF IL-17+CD8+ T CELLS IN HUMAN HEALTH AND PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a spondyloarthritis affecting the joint and skin. The genetic association with HLA Class I and the clinical efficacy of IL-17A inhibitors in the treatment of PsA suggest a potential role for IL-17 +CD8+T cells in PsA pathogenesis. This concept is supported by our previous data showing that IL-17 +CD8+T cell frequencies are increased in the synovial fluid (SF) vs the peripheral blood (PB) of patients with PsA¹. We hypothesise that IL-17 +CD8+T cells are pro-inflammatory contributors to PsA pathogenesis.

Objectives: To perform molecular, phenotypic and functional characterisation of IL-17 +CD8+T cells.

Methods: Healthy donor PB CD8 +T cells were cultured for 3 days with anti-CD3/CD28 mAb, IL-1β and IL-23 to induce IL-17 +CD8+T cells *in vitro*, whilst PB and SF mononuclear cells were isolated from patients with PsA and stimulated *ex vivo* with PMA/ionomycin. Cytokine secretion assays were used to sort IL-17 +CD8+T cells, from which RNA was extracted for RNA-sequencing of PsA PB and SF cytokine-secreting T cells. 24 hour supernatants were generated from cultured sorted cells for cytokine analysis (Luminex) or culture with fibroblasts (IL-6 and IL-8 secretion measured by ELISA).

Results : *In vitro*-generated IL-17 +CD8+T cells produced significant levels of IL-17A, IL-17F, IFN-γ, TNF-α, IL-22 and GM-CSF (10–9000 pg/ml range), but little IL-10. Flow cytometry showed that *in vitro*-generated IL-17 +CD8+T cells co-expressed IFN-γ (median 80%), TNF-α (40%) and GM-CSF (35%) at comparable frequencies to *ex vivo* PsA synovial IL-17 +CD8+T cells (70%, 50%, 55% respectively). Whilst only 5% of PsA SF IL-17 +CD8+T cells co-expressed the MAIT cell marker Vα7.2, 50% of *in vitro*-generated IL-17 +CD8+T cells co-expressed Vα7.2. The cytokine profile of *in vitro*-generated Vα7.2+and Vα7.2- IL-17 +CD8+T cell supernatants was however comparable, sharing the cytokine profile of total IL-17 +CD8+T cells. Functionally, *in vitro*-generated sorted IL-17 +CD8+T cell culture supernatants enhanced IL-6 and IL-8 production by synovial tissue fibroblasts from patients with PsA compared to IL-17- counterparts, thus exhibiting pro-inflammatory capacity; we will also determine if this response is IL-17 and/or TNF-mediated. Additionally, the majority of synovial IL-17 +CD8+T cells co-expressed cytotoxic molecule Granzyme B, which may contribute to PsA pathogenesis. Finally, RNA-sequencing revealed that IL-17 +CD8+T cells from PsA synovial fluid displayed a distinct transcriptomic signature compared to PB IL-17 +CD8+T cells as well as to synovial Th17 or Tc1 cells.

Conclusions : *In vitro*-generated and *ex vivo*-derived synovial IL-17 +CD8+T cells display a type 17 profile, as evidenced by flow cytometry and Luminex. In contrast to *ex vivo* PsA synovial IL-17 +CD8+T cells, 50% of *in vitro* IL-17 +CD8 +T cells co-express Vα7.2; however, both Vα7.2+and Vα7.2- subsets share a similar cytokine profile. Functionally, IL-17 +CD8+T cells exhibit pro-inflammatory potential, upregulating IL-6 and IL-8 production via fibroblasts. Analysis of our RNA-sequencing data will further reveal the molecular profile of human IL-17 +CD8+T cells, and how they may contribute to joint inflammation in PsA.

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FRIDAY, 15 JUNE 2018

Spondyloarthritis – clinical aspects (other than treatment)

FRI0169

FIRST VALIDATION OF CONSENSUS DEFINITIONS FOR MRI LESIONS IN THE SACROILIAC JOINT BY THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS) MRI GROUP

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Background: The diversity of MRI lesions in the sacroiliac joints of patients with axial spondyloarthritis (axSpA) has only recently been appreciated and consistent terminology, descriptions, and definitions have not yet been internationally accepted. The ASAS MRI group has generated updated consensus lesion definitions (ASAS_MRI_def[®]) and these now require validation in multi-reader exercises to support widespread adoption for clinical practice and research.

Objectives: To assess the reliability of detection of active and structural lesions as defined by (ASAS_MRI_def[®]) on MRI images from the ASAS Classification Cohort (ASAS-CC) in a multireader ASAS exercise.

Methods: ASAS_MRI_def[®] were recorded in an eCRF that comprises global assessment (lesion present/absent) and detailed scoring (SPARCC SIJ inflammation, SPARCC SIJ structural). MRI images were available in a variety of formats (DICOM (n=175), JPEG(n=71), DICOM film(n=32)) and sequences, axial and semicoronal orientations, from 278 of the 495 cases who had MRI performed in the ASAS-CC. Image quality was considered sufficient to record global data by 6 central readers in all cases. An additional reader assessed only images in DICOM format (n=175). Detailed SPARCC scoring data was based only on assessment of images in DICOM format. Detection of lesions assessed as

present/absent by global assessment was analysed using kappa. Reliability of detailed scoring was analysed by intraclass correlation coefficient (ICC).

Results: Reliability of detection of active and structural lesions was comparable and somewhat better when DICOM images were evaluated (table 1). The most frequently detected active lesion, subchondral inflammation, was detected to a comparable degree of reliability as the most frequently detected structural lesion, erosion. Fat metaplasia in the joint space (backfill) and ankylosis were also reliably detected despite low frequency of occurrence in this cohort. Mean ICC for detailed scores were BME-0.84, Erosion-0.55, Fatty lesion (any)–0.61, Fatty lesion (>1 cm depth)–0.55, Sclerosis-0.73, Fat metaplasia in joint space-0.36, Ankylosis-0.97, Bone bud-0.07.

Abstract FRI0169 – Table 1. Kappa values for detection of MRI lesions in the SIJ of patients in the ASAS-CC

*Based on all images (n =278).	**Based on DICOM images (n =175).	
	Mean of all reader pairs (95% CI)*	Mean of all reader pairs (95% CI)**
Active lesions typical of axSpA	0.73 (0.64-0.81)	0.70 (0.58-0.82)
Active lesions typical of axSpA (confidence ≥3) (1-4 scale)	0.77 (0.68-0.86)	0.80 (0.69-0.92)
ASAS positive MRI	0.74 (0.65-0.82)	0.73 (0.61-0.84)
ASAS positive MRI (confidence ≥3) (1-4 scale)	0.76 (0.67-0.85)	0.79 (0.67-0.90)
Structural lesions typical of axSpA	0.64 (0.53-0.74)	0.71 (0.59-0.83)
Structural lesions typical of axSpA (confidence ≥3) (1-4 scale)	0.61 (0.49-0.74)	0.75 (0.62-0.88)
Subchondral inflammation	0.66 (0.57-0.75)	0.60 (0.49-0.72)
Inflammation in Erosion cavity	0.29 (0.11-0.47)	0.37 (0.15-0.58)
Capsulitis	0.37 (0.12-0.62)	0.55 (0.18-0.90)
Joint fluid	0.35 (0.21-0.50)	0.41 (0.23-0.59)
Enthesitis	0.21 (0.04-0.39)	0.23 (0.03-0.45)
Sclerosis	0.42 (0.30-0.55)	0.48 (0.33-0.63)
Erosion	0.59 (0.47-0.70)	0.61 (0.47-0.75)
Fatty lesion (any)	0.61 (0.50-0.73)	0.61 (0.46-0.76)
Fatty lesion >1cm	0.57 (0.41-0.73)	0.66 (0.47-0.84)
Fat metaplasia in joint space	0.47 (0.27-0.67)	0.50 (0.26-0.74)
Bone bud	0.14 (-0.03-0.31)	0.11 (-0.06-0.29)
Ankylosis	0.54 (0.22-0.86)	0.58 (0.25-0.89)

*Based on all images (n=278); **Based on DICOM images (n=175)

Conclusions: The reliability of the ASAS_MRI_defⁿ was substantial for the most frequently detected lesions.

Disclosure of Interest: None declared

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FRI0170 CONSENSUS DEFINITIONS FOR MRI LESIONS IN THE SACROILIAC JOINTS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: FIRST ANALYSIS FROM THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS) CLASSIFICATION COHORT

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Background: A broad spectrum of MRI lesions has been described in the sacroiliac joint (SIJ) of patients with axial spondyloarthritis and a recent consensus from the ASAS MRI group has culminated in updated lesion definitions (ASAS_MRI_defⁿ). There has been no central reader evaluation of MRI scans from the ASAS Classification Cohort (ASAS-CC)¹ to determine the spectrum of MRI lesions in the SIJ in this cohort, to compare the frequencies of different lesion types, and to compare detection of lesions between central and ASAS-CC local site readers

Objectives: To determine the spectrum and compare the frequencies of active and structural lesions on MRI images from the ASAS-CC according to the consensus ASAS_MRI_defⁿ update.

Methods: ASAS_MRI_defⁿ were recorded in an eCRF that comprises global assessment (lesion present/absent) and detailed scoring (SPARCC SIJ inflammation, SPARCC SIJ structural). For global assessment, wording of lesions defining active and structural lesions typical of axSpA was the same as in the original ASAS-CC eCRF permitting comparisons between central and local site readers. MRI images were available in a variety of formats (DICOM (n=175), JPEG(n=71), DICOM film(n=32)) and sequences, axial and semicoronal orientations, from 278 of the 495 cases who had MRI performed in the ASAS-CC. Image quality was considered sufficient to record global data by 6 central readers in all cases. An additional reader assessed only images in DICOM format (n=175). Detailed SPARCC scoring data was based only on assessment of images in DICOM format. Comparison of active and structural lesion frequencies was assessed descriptively according to individual and majority of central readers data. Detection of active

lesions typical of axSpA in all available images from the ASAS-CC was compared between central and local readers.

Results: The percentage of cases with active lesions typical of axSpA recorded by central readers (28.4% by majority read) was lower than the 40% reported by local site readers in the ASAS-CC (table 1). This was similar to the frequency of structural lesions typical of axSpA (28.6% by majority read) (table 2). 11.2% had subchondral inflammation but not active lesions typical of axSpA but only 0.3% had active lesions typical of axSpA without subchondral inflammation. Erosion was the most frequently observed structural lesion (25.2%) followed by fatty lesion (19.8%). Results were very similar when only data from the 175 DICOM cases was analysed.

Abstract FRI0170 – Table 1. Frequencies of active MRI lesions in the SIJ in the ASAS-CC

Variable	Mean% (Range) of cases*	Number (%) of cases*
Active lesions typical of axSpA	31.5 (24.5-38.5)	79 (28.4%)
Active lesions typical of axSpA and level of confidence ≥3 (scale of 1-4)	22.4 (18.0-27.3)	58 (20.9%)
Active lesions typical of axSpA and meets ASAS definition for positive MRI	30.0 (22.6-37.4)	71 (25.5%)
Meets ASAS definition for positive MRI and level of confidence ≥3 (scale of 1-4)	23.1 (18.3-30.2)	58 (20.9%)
Subchondral inflammation	43.5 (38.5-51.1)	110 (39.6%)
Site of erosion cavity inflammation	8.9 (5.8-12.6)	10 (3.6%)
Capsulitis	4.0 (1.8-7.2)	6 (2.2%)
Joint fluid	14.1 (6.8-20.5)	11 (4.0%)
Enthesitis	7.5 (1.8-12.2)	6 (2.2%)

(*Individual data from 6 readers; majority reader (≥4) data).

Abstract FRI0170 – Table 2. Frequencies of structural MRI lesions in the SIJ in the ASAS-CC

Variable	Mean% (Range) of cases*	Number (%) of cases*
Structural lesions typical of axSpA	31.4 (23.5-39.9)	68 (28.6%)
Structural lesions typical of axSpA and level of confidence ≥3 (scale of 1-4)	20.8 (14.0-29.4)	46 (19.3%)
Subchondral sclerosis	24.2 (10.1-39.1)	36 (15.1%)
Erosion	27.9 (23.1-32.8)	60 (25.2%)
Fatty lesion (any)	23.5 (18.1-29.8)	47 (19.8%)
Fatty lesion (>1cm)	11.7 (8.0-15.6)	22 (9.2%)
Bone bud (yes)	2.1 (0.4-3.8)	1 (0.4%)
Fat metaplasia in joint space (yes)	8.1 (4.2-10.5)	11 (4.6%)
Ankylosis	1.1 (0.8-3.8)	5 (2.1%)

(*6 readers; majority reader (≥4) data).

Conclusions: In this first central reader analysis of MRI images from the ASAS-CC we demonstrate similar frequencies of active and structural lesions typical of axSpA, erosion as a common lesion, some degree of false positive subchondral inflammation, and a lower frequency of active lesions typical of axSpA than noted by local site readers.

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[1] Rudwaleit, et al. Ann Rheum Dis 2009;68:777–831.

Disclosure of Interest: None declared

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FRI0171 WHICH IMAGING OUTCOMES FOR AXSPA ARE MOST SENSITIVE TO CHANGE? A 5-YEAR ANALYSIS OF THE DESIR COHORT

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Background: Several imaging outcomes have become available to assess inflammation and structural damage over time in patients with axial spondyloarthritis (axSpA). However, no formal comparison of their sensitivity to change has been made in the early phases of the disease.

Objectives: We aimed to compare the sensitivity to change of different MRI and radiographic scoring methods in patients with early axSpA.

Methods: Patients from the DESIR cohort fulfilling the ASAS axSpA criteria were included. Radiographs and MRI of the sacroiliac joints and spine were obtained at baseline, 1 year, 2 years and 5 years. Each film was scored by 2 or 3 readers in 3 'reading-waves' (wave 1: baseline; wave 2: baseline, 1 year, 2 years; wave 3: baseline, 2 years, 5 years). Outcomes measuring inflammation and structural damage both on MRI and radiographs in the spine and SIJ were assessed (table 1). The analysis of change captured over time was performed using generalised estimating equations (GEE) longitudinal models separately for each outcome, taking into account data from all readers and waves ('integrated analysis'). To allow