in waves 2–8 and knee pain in the same or previous wave of diagnosis were defined as having KOA (baseline). Participants with at least one body mass index (BMI) measurement and one follow-up assessment were included. Underweight/normal weight, overweight and obesity were defined using BMI <25kg/m², 25–30kg/m² and ≥30kg/m², respectively. Education, occupation (current or last occupation if retired), wealth quintiles (all individual-based) and index of multiple deprivation quintiles (area-based) were used as SEP indicators. Outcome was the first self-reported kJRS (left or right knee) in waves 3–9. Cox proportional hazards models were used to investigate the associations of obesity and SEP with kJRS, controlling for baseline covariates. Person year follow up was calculated from baseline to either a) date of self-reported kJRS, b) loss to follow-up, c) end of follow-up (wave 9).

**Results:** The analysis sample included 1499 people who reported KOA and had ≥1 BMI measure (62.3% female; mean age 66.5y (SD 9.4); 96% white; 47%/4% obese). Number of person-years included in the analysis was 8427. Over a mean follow-up of 4.7 years (SD 2.8), 144 (9.8%) reported having kJRS. Obese KOA patients were more likely to report kJRS than non-obese patients (adjHR 1.89 (95% CI 1.33, 2.68)), independent of age, gender, SEP, cardiovascular disease (self-reported) and HbA1c values (measured from collected blood samples). Education and occupation were not associated with kJRS. However, those living in the most deprived areas and with the least amount of wealth were less likely to undergo kJRS compared with the least deprived and wealthiest (HRs adjusted for age and gender 0.37 (95% CI 0.19, 0.73) and 0.55 (95% CI 0.33, 0.93), respectively). There was no evidence of interactions between obesity and SEP indicators.

**Conclusion:** Obesity increased the likelihood of undergoing kJRS in KOA patients. Therefore, reducing obesity in KOA patients may help to reduce the need for kJRS. Area-deprivation and lower wealth were associated with lower likelihood of kJRS. Taken together with findings from other studies which report associations between lower SEP and worse OA symptoms, our results suggest that there may be social inequalities in the provision of kJRS in England.

Table 1. The relationships between obesity at baseline and rates of knee joint replacement surgery over a mean of 4.7 (SD 2.8) years in follow-up in those with KOA at baseline in the English Longitudinal Study of Ageing

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Unadjusted</th>
<th>Adjusted for age and gender</th>
<th>Adjusted for age, gender, SEP, and HbA1c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>1.56</td>
<td>(1.12, 2.17)</td>
<td>1.77 (1.26, 2.50)</td>
</tr>
<tr>
<td>Non-obesity</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Obesity</td>
<td>ref</td>
<td>3.53 (1.57, 7.02)</td>
<td>3.53 (1.57, 7.02)</td>
</tr>
<tr>
<td>Overweight</td>
<td>ref</td>
<td>2.91 (1.43, 5.91)</td>
<td>2.91 (1.43, 5.91)</td>
</tr>
<tr>
<td>Underweight</td>
<td>ref</td>
<td>1.05 (1.02, 1.07)</td>
<td>1.05 (1.02, 1.07)</td>
</tr>
<tr>
<td>BMI per 1kg/m² increase</td>
<td>1.05 (1.03, 1.08)</td>
<td>1.06 (1.04, 1.09)</td>
<td>1.07 (1.04, 1.10)</td>
</tr>
</tbody>
</table>

HR, hazard ratio; CI, confidence interval; SEP, socioeconomic position; CVD, cardiovascular disease; ref, reference category; BMI, body mass index.

**Disclosure of Interests:** None declared

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**New data on pathophysiology of spondyloarthritis including psoriatic arthritis**

**POS0326**

**THE TRANSCRIPTOMIC LANDSCAPE OF ACTIVE PSORIATIC ARTHRITIS: ACTIVATED IMMUNE, EXTRACELLULAR MATRIX (ECM) TURNOVER, ABERRANT METABOLISM AND HEMOPOIETIC CELL - SKIN CROSSTALK.**

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory disease whereby activated T lymphocytes and myeloid cells interact with tissue-resident cells in the skin and joints. Gene expression studies, mainly based on the microarray platforms, have provided an initial glimpse into disease pathogenesis highlighting, among others, the role of the TNF-α and IL17 cytokine axis. Yet, the transcriptomic landscape of PsA remains largely unexplored, and the specific contribution of skin fibroblasts to disease pathogenesis remains elusive.

**Objectives:** To comprehensively characterize the gene expression profile in PsA, specifically in the blood and skin fibroblasts through next-generation RNA sequencing.

**Methods:** Peripheral blood (PB) was collected from PsA patients (n=30) after informed consent. Healthy individuals (HC) and patients with rheumatoid arthritis (RA) were used as healthy and disease controls (n=10/group) respectively. Psoriatic skin biopsies were obtained from a subset of three PsA patients and three HC. All PsA patients fulfilled the CASPAR criteria and displayed peripheral polyarthritis of moderate- to high- disease activity. Patient’s clinical and laboratory data were recorded at the time of sampling. Disease activity in PsA and RA was assessed using the Disease Activity Index for Psoriatic arthritis (DAPSA) and the Disease Activity Score-28 (DAS28), respectively. RNA from PB and skin fibroblasts was extracted, RNA libraries were prepared and sequenced. EdgeR package was used to call differentially expressed genes (DEGs). Statistical significance was set at p value<0.05 and fold-change IFCI >1.5. Functional enrichment analysis and weighted gene co-expression network analysis (WGCNA) was implemented. Inference and analysis of blood immune cells-skin fibroblasts communication were performed with CellChat.

**Results:** 8 males and 22 female patients with PsA were included with median age 49 years old and median disease duration 4 years. The median DAPSA score was 44.3 and the median DAS28 score was 5.5 for RA patients, suggesting high disease activity in both groups. We found 46 DEGs in PsA versus HC blood (303 up- and 163 down-regulated). DEGs were significantly enriched in biological pathways related to immunity (i.e. inflammatory response, TNFα signaling via NFκB, IFNα & IFNγ response, complement, IL2 signaling), metabolism (i.e. oxidative phosphorylation, adipogenesis, fatty acid metabolism) and other signaling cascades of pathophysiologic relevance (i.e. Wntb4, catenin signaling, TGFβ signaling, MTORC1 signaling). WGCNA in blood revealed four gene modules containing highly correlated genes. These modules were enriched in myeloid leukocyte mediated immunity, neutrophil-mediated immunity, ECM and collagen metabolism, TGFβ and Pdgf signaling. Next, we characterized the “PsA specific activity signature,” taking the intersection of DEGs in PsA vs. HC” and “PsA vs. RA”, which resulted in 67 DEGs enriched in response to TGF and Pdgf, ECM organization and degradation. CellChat analysis identified a higher number of interactions between blood immune cells and skin fibroblasts and increased strength of interactions in PsA compared to healthy state. Aberrant interactions between blood and skin fibroblasts in PsA were identified, among others, ligand-receptor pairs of the WNT, Notch, and GDF11 signaling pathways.

**Conclusion:** Our findings confirm the presence of an IFNα signature and complement activation in PsA. The increased cardiometabolic burden and enhanced bone remodeling are reflected by the presence of pathways related to aberrant metabolism and ECM metabolism, respectively. The myeloid cell signature in active disease supports the emerging role of monocytes/macrophages in driving inflammation in PsA, while the aberrant blood-skin fibroblast interactions suggest a novel role for these resident cells in disease pathophysiology.

**REFERENCES:**

**Disclosure of Interests:** None declared

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**POS0327**

**IRISIN: A NEW MARKER OF SUBCLINICAL ATHEROSCLEROSIS, CARDIOVASCULAR RISK AND DISEASE ACTIVITY IN AXIAL SPONDYLOARTHRITIS?**

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Background: Axial spondyloarthritis (axSpA) is an inflammatory disease with detrimental effects on the health status of the individuals affected by this condition [1]. axSpA patients also exhibit high cardiovascular (CV) risk, mainly due to accelerated atherosclerosis [2]. Interestingly, the adipokine irisin was described to play a beneficial role in several physiological and pathophysiological processes such as inflammation, angiogenesis, oxidative stress, as well as lipid and bone metabolism [3]. However, studies on the role of irisin in CV risk in the setting of axSpA or in the pathogenesis of axSpA are limited [4].

Objectives: In this study we evaluated the role of irisin as a genetic and serological biomarker of subclinical atherosclerosis and CV risk in a large cohort of patients with axSpA. We also assessed its role as a marker of axSpA susceptibility and severity.

Methods: 725 patients who fulfilled the Assessment of SpondyloArthritis international Society classification criteria for axSpA were included in this study [5]. In these patients, the presence of subclinical atherosclerosis (plaques and/or abnormal carotid intima-media thickness values) was assessed by carotid ultrasound. Four *irisin* polymorphisms (rs16835198 GT, rs3480 A/G, rs726344 G/A and rs1570569 G/T) were genotyped by TaqMan probes in all the patients and in 656 age, sex and ethnically-matched healthy controls. Additionally, serum irisin levels were determined by ELISA in all the patients. All analyses were performed using STATA v. 11.1 statistical software, adjusting for potential confounding factors. The strength of associations is indicated as odds ratios (OR) [95% confidence intervals].

Results: Low levels of serum irisin were linked to the presence of plaques (p=0.002) and with atherogenic index values indicative of an adverse lipid profile (p≤0.01). Low serum irisin levels also correlated with visual analogue scale (VAS) patient, VAS physician and Bath Ankylosing Spondylitis Profile (BASMI) values (p<0.05). Moreover, the presence of sarcorillard was related to lower serum irisin levels (p<0.001). Furthermore, the minor alleles of rs3480 (G) and rs1570569 (T) were associated with higher values of Ankylosing Spondylitis Disease Activity Score (ASDAS) in axSpA patients (p<0.01 in both cases). In this line, the frequency of the minor allele of rs3480 (G) was higher in patients with ASDAS values ≥2.1 (indicative of high disease activity) (OR: 1.46 [1.08-1.97], p=0.01), while the minor allele of rs16835198 (T) was less frequent in this group of patients (OR: 0.73 [0.57-0.92], p=0.01).

Conclusion: Low serum irisin levels could be indicators of the presence of subclinical atherosclerosis, high CV risk and more severe disease in axSpA patients. In addition, irisin may also constitute a genetic biomarker of disease activity in axSpA.

REFERENCES:

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