

**Conclusion:** sICAM-1 and CXCL13 are elevated in RA patients and correlated with disease activity. sICAM-1 is an independent predictor of TNFi response in csDMARDs refractory RA patients.

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## 7. Spondyloarthritis - etiology, pathogenesis and animal models

AB0113

### ANTIBODIES AGAINST HELICOBACTER PYLORI ANTIGENS IN PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS

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**Background:** Psoriasis (Ps) and Psoriatic Arthritis (PsA) are inflammatory diseases of unknown etiology. *Helicobacter pylori* (Hp) infection has been hypothesized as one of the microbial agents that can lead to development of immune-mediated psoriatic disease, but the nature of the specific Hp antigens involved remains unclear.

**Objectives:** To assess antigen specific antibody responses against immunodominant Hp antigens in patients with psoriatic diseases.

**Methods:** Ninety-one patients with Ps (35 females; median age 51.9, age range 25-87), 47 patients with PsA (25 females; median age 52.9, age range 25-87) and 60 demographically matched healthy controls (HC) were studied. Reactivity to Hp-specific antigens were tested by Western immunoblotting (in combination with line immunoassay for anti-CagA and anti-VagA antibody testing) (Euroimmun AG, Lübeck, Germany).

**Results:** Positivity against Hp was comparable between PsA (38.3%), Ps (39.6%) and HCs (50%). Anti-p66-UreB, anti-p54-flagelin and anti-p29-UreA abs were more frequent in psoriatic patients compared to healthy controls (p66: 94.4% in Ps vs 69.7% in HC, p=0.017; p54: 66.7% in Ps vs 33.3% in HC, p=0.012; p29 72.2% in Ps vs 45.5% in HC, p=0.044) and anti-p29-UreA abs were detected in higher frequency in PsA patients compared to HC (94.4% vs 45.5%, p=0.002). Reactivities against the remaining Hp antigens were comparable between Ps and PsA patients and HC.

**Conclusion:** Antibody responses against p66-UreB, p29-UreA, and p54-flagelin are more prevalent in patients with psoriatic disease, suggesting their potential involvement in PsA and Ps.

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AB0114

### IL12P40/IL23P40 BLOCKADE WITH USTEKINUMAB DECREASES THE INFLAMMATORY INFILTRATE AND MODULATES MOLECULAR PATHWAYS IN THE SYNOVIUM OF PSORIATIC ARTHRITIS PATIENTS

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**Background:** Psoriatic arthritis (PsA) is a chronic inflammatory joint disease within the spondyloarthritis (SpA) spectrum. TNF and IL17/IL23 pathways play a

key role in SpA pathogenesis. Blocking of IL12p40/IL23p40 has been shown to effectively reduce disease activity in PsA [1,2]. It is however incompletely understood how IL12p40/IL23p40 blockade affects local inflammatory processes.

**Objectives:** To investigate the cellular and molecular pathways affected by IL12p40/IL23p40 blockade with ustekinumab in PsA patients (pts).

**Methods:** Eleven male PsA pts with at least 1 inflamed knee or ankle joint, who were scheduled to start ustekinumab treatment, were included in a 24-week single-center open-label study. All pts received ustekinumab 45 mg/sc according to standard care at week (W) 0, 4 and 16. Besides clinical outcomes, needle arthroscopic synovial tissue (ST) biopsy samples were obtained from an inflamed knee or ankle joint at baseline (BL), W12 and W24. ST samples were analyzed by immunohistochemistry (IHC), RNA sequencing and real-time quantitative polymerase chain reaction (qPCR) analysis.

**Results:** Paired BL and W12, and paired BL, W12 and W24 ST samples were available of 9 and 6 pts, respectively. Two pts only underwent BL ST sampling (pt refusal; withdrawal after the W12 clinical visit). Two pts were excluded after W12 because of treatment adjustments. Of 1 pt no ST was obtained at W24 due to technical difficulties. Eight pts finished 24 weeks of clinical follow-up. No serious adverse events were observed. At W12 6/11 pts met ACR20, 2/11 met ACR50 and 1/11 met ACR70 improvement criteria, at W24 this was 3/8, 2/8 and 1/8 pts, respectively. Significant improvements between BL and W12 and/or W24 were seen in clinical (TJC, PASI, BASDAI) and serological markers (CRP and ESR), Table 1. IHC showed a significant decrease in sublining macrophages, a sensitive biomarker of an inflammatory response in peripheral SpA, of BL 2[1-3] vs W12 1.5[0-2] p=0.020, but not W24 1[0.5-2.5]ns. Other synovial infiltrating cells were not significantly decreased. Significant downregulation of MMP3 (p=0.047) and IL-23p19 (p=0.046), but not IL6, TNF or IL12p40 were seen with qPCR analysis at W12. RNA seq analysis showed 178 significantly differentially expressed genes between BL and W12 (FDR 0.1). Gene ontology and KEGG terms enrichment analyses identified overrepresentation of MAPK and PI3K-Akt signalling pathways among the down-regulated genes and WNT signalling pathway among the up-regulated genes. Gene expression was confirmed by qPCR analysis.

**Table 1.**

	Baseline (n=11)	Week 12 (n=11)	Week 24 (n=8)	p-value*	p-value**
TJC	1 (0-5)	1 (1-2)	0 (0-0.75)	0.168	0.034
SJC	2 (1-3)	2 (1-3)	1.5 (1-2)	0.394	0.715
VAS patient global	28 (16-55)	22 (12-46)	45 (2.8-50.5)	0.423	0.779
PASI	3.2 (1.2-7.4)	0.8 (0-1.8)	0 (0-2.4)	0.028	0.046
BASDAI	3.2 (2.4-4.7)	1.9 (1-3.8)	2.1 (0.4-4.2)	0.008	0.161
CRP (mg/L)	8.5 (1.7-16.4)	1.6 (0.6-3)	1.0 (0.6-7.0)	0.008	0.012
ESR (mm/hr)	20 (8-35)	6 (2-17)	8 (2-20.5)	0.008	0.017

TJC/SJC tender/swollen joint count; VAS visual analogue scale; PASI psoriasis area severity index; BASDAI Bath Ankylosing Spondylitis Disease Activity Index; CRP C-reactive protein; ESR erythrocyte sedimentation rate;

All values are presented as median (IQR) p-value for the comparison of baseline and week 12 (\*) or week 24 (\*\*)

**Conclusion:** Ustekinumab treatment reduced synovial inflammation and modulated specific molecular pathways, however inflammation was not completely resolved. Future studies comparing histological and gene expression data between different treatments targeting IL17/IL23 axis will show which changes are treatment-specific and which reflect downregulation of local inflammation.

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AB0115

### SECUKINUMAB THERAPY DOES NOT AFFECT NEUTROPHIL HOST DEFENCE IN PSORIATIC ARTHRITIS

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**Background:** Biologic therapies have revolutionised therapy in inflammatory diseases such as psoriatic arthritis (PsA), driving major improvements in outcomes. Th17 cells appear to play a key role in the pathogenesis of PsA, and IL-17 can trigger the release of chemoattractants such as CXCL8 and CCL20, leading to the further infiltration of other immune cells including neutrophils. Infiltrating activated neutrophils can themselves generate a range of chemoattractants which may amplify and sustain the inflammatory response. Therapeutic targeting of IL-17 with biologics such as secukinumab offers great benefit in PsA by blocking this inflammatory cycle: however the interaction of this agent with neutrophils, key components of host defence as well as potential mediators of this disease, is not known.

**Objectives:** This study aimed to measure key aspects of neutrophil function to determine: a) changes in the functions of circulating neutrophils in PsA patients pre-therapy, compared to age- and sex-matched healthy controls and b) if these functions changed in PsA patients 12-weeks post-secukinumab therapy.

**Methods:** Neutrophils were isolated from venous blood of 16 PsA patients and 10 healthy controls. Key neutrophil functions were measured at baseline and 12 weeks: reactive oxygen species (ROS) production, apoptosis (+/- TNF and GM-CSF), phagocytosis, receptor expression and chemotaxis. Changes in gene expression pre- and 12-weeks post-therapy (n=5 PsA) were measured using RNAseq.

**Results:** PsARC response was observed in 70.6% of participants on secukinumab therapy at 12 weeks. There were no significant differences in ROS production, phagocytosis or chemotaxis in PsA patients at baseline (compared to healthy controls) or during therapy. Chemotaxis towards IL-8 in PsA patients at baseline was decreased compared to that of healthy controls, but this difference did not reach statistical significance. Surface levels of activation markers CD11b/CD18 and CD63 were increased in PsA patients at 12-weeks compared to baseline, while surface levels of CD16 decreased. RNA-seq analysis indicated down-regulation of pathways mediated by IL-17A, oncostatin M, TWEAK (TNFSF12) and CCL2 during therapy, but up-regulated expression of pathways involving *de novo* protein biosynthesis.

**Conclusion:** Therapy with secukinumab in PsA did not significantly affect neutrophil host defence functions. The changes that were seen in circulating neutrophils indicate selective up- and down-regulation of functions that may reflect potential alterations in local or systemic cytokines, and/or an increase in the circulating pool of activated neutrophils that are no longer recruited into sites of inflammation because of the down-regulation of the local IL-17/CXCL8 signalling network.

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#### AB0116 DECREASED SERUM LEVEL OF IRISIN IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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**Background:** Irisin, exercise-mediated myokine, is one of the most recently discovered hormones. Irisin has been shown to play multifunctional roles including anti-inflammation by suppressing secretion of NF- $\kappa$ B, TNF- $\alpha$ , IL-6, and other pro-inflammatory cytokines from macrophages and adipocytes [1]. Thus, several attempts have been made to investigate irisin in chronic inflammatory rheumatic diseases. And recent evidences show that serum irisin concentration is lower in patients with osteoarthritis, rheumatoid arthritis, and behcet disease than healthy individuals [2-4]. Furthermore, one study showed that serum irisin level was negatively correlated with radiographic severity of knee osteoarthritis [2]. However, no previous study has investigated irisin in patients with ankylosing spondylitis (AS).

**Objectives:** To assess the serum level of irisin, and evaluate the possible relationship of irisin with disease activity in patients with AS.

**Methods:** Male patients with AS fulfilled the modified New York criteria (n=119), and healthy male controls (n=30) were enrolled. Serum irisin level was measured by ELISA (Cusabio, CSB-EQ027943HU). Disease activity was assessed by acute phase reactants, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), and modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Clinical characteristics

and serum irisin level of the AS group were compared with those of the control group using Student t-test for normally distributed continuous measures and Mann-Whitney U test for non-normally distributed continuous measures. To evaluate the correlations of serum Irisin level and AS disease activity, Spearman's correlation test was used. AS patients were grouped into the high BASDAI group (BASDAI  $\geq 4$ , n=45) and the Low BASDAI group (BASDAI  $< 4$ , n=74). And serum irisin level was also compared between two groups.

**Results:** AS group had lower serum irisin concentration compared with healthy control group (60.50 [23.68-131.15] vs. 124.69 [79.58-192.90], p=0.013), while age and body mass index were not significantly different between groups. There was no significant correlation between irisin level and disease activities. However, High BASDAI group showed significantly lower irisin level than low BASDAI group (44.64 [18.13-85.89] vs. 65.68 [31.81-165.31], p=0.011).

**Conclusion:** AS patients have lower serum irisin concentrations than healthy controls. AS patients with severe symptoms tend to have lower serum level of irisin than those with less severe symptoms.

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#### AB0117 HLA B27\*SUBTYPES FREQUENCIES IN COLOMBIAN PATIENTS WITH SPONDYLOARTHRITIS AND HEALTHY SUBJECTS TYPED IN HIGH-RESOLUTION TECHNIQUE

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**Background:** HLA-B\*27 has been identified as a susceptibility and prognostic factor associated to axial spondyloarthritis. HLA-B\*27 allele has been described to be present in about 90% of patients with ankylosing spondylitis, and with a different frequency in patients with other subtypes of SpA. In contrast, this allele has been observed to be present only in 7-8% in general population. A remarkable heterogeneity in HLA-B\*27 alleles has been reported. They have been determined at DNA sequence and some subtypes have been associated increasing the risk to develop the disease

**Objectives:** To establish the frequencies of HLA-B27 subtypes in a group of Colombian patients with SpA and healthy population

**Methods:** In total, 61 Blood samples from Colombian mestizo individuals with SpA according to ASAS classification-criteria were evaluated by Sequencing Technology: Illumina Sequencing/PacBio Sequencing with analysis of the second and third exon. Results reported with six digits (including null alleles). In total, 294 results of peripheral blood from healthy individuals without joint symptoms were analyzed. Frequencies were obtained for demographic and genetic variables. Ethic Committee approval code 2018-020/2017-023

**Results:** The SpA group had a mean age of 45.88  $\pm$  11.67, 62.3% of them were male, 6.6% reported current smoking and 37.7% reported smoking sometime in life. In total, 67.2% had inflammatory back pain, 14.8% had dactylitis, 63.9% enthesitis and 57.4% arthritis. Thirty patients were HLA-B\*27 positive with a genotypic frequency of 50.8% and an allelic frequency of 24.6%. In this group of patients, the mean age was 43.5  $\pm$  11.8, 76.6% were male, 86.7% of them were subtype B\*27:05:02g and 13.3% presented the B27:02:01g. None of the SpA patients had both B\*27 alleles.

On the other hand, the healthy individuals were men in 51.0% and the mean age was 37 $\pm$ 15.4 years. Ten subjects were positive for the HLA-B\*27 allele with a genotypic frequency of 3.4% and an allelic frequency of 1.7%. In this group of individuals 50.0% were male gender with a mean age of 38.4 $\pm$ 17.9. No individuals were found to have the two alleles or homozygous for the B\*27 allele. In all of them the subtype B\*27:05:02g was observed in high-resolution sequencing