from AS patients participating in a previously reported in-house clinical trial [infliximab (IFX), n=15 vs. placebo (P), n=11] (2) were selected from our tissue bank. R/NR was defined as a ≥1.1 point reduction in AS Disease Activity Score (ASDAS) at week-30, or a reduction in the number of sacroiliac/vertebral MRI lesions. Expression of 96 IRG was quantified from PBMCs using custom TaqMan assays and analysed using unsupervised hierarchical clustering, Chi-Squared, and Mann-Whitney U tests.

Results: A total of 11 patients were clinical responders [IFX=7/15; P=4/11]. At week-0, patients clustered into 2 groups (C1/C2) based on expression of 14 IRG. Clinical/demographic characteristics were not significantly different between C1/C2 and groups were not biased for treatment (C1, IFX=8, P=4; C2, IFX=7, P=7, p=0.735). Improvement in ASDAS was weakly associated with C2 (C2, R=8/14, C1, R=7/12, p=0.098). Looking at IFX treated patients only (n=15), 2 cluster groups were observed (T1/T2) driven by 12 IRG. T2 was associated with a reduction in MRI lesions (T2 R=6/7, T1 R=3/8, p=0.057). Finally, paired week-0 and week-22 samples from 10 IFX-treated patients were analysed and clustered in 2 groups (H1/H2). Changes in IRG signature following treatment were observed towards segregating pre- and post- IFX treatment samples (H1, 6/8 week-0; H2, 8/12 week-22 p=?).

Conclusions: This pilot study suggests a possible association between IRG and response to IFX treatment in AS. These results now require assessment in a larger cohort in order to determine statistical and possible clinical significance, and to refine the signature further to construct potential predictive algorithms.

References:

[1] Yao Y, et al. Arthritis Rheum 2009.
[2] Marzo-Ortega H, et al. Ann Rheum Dis 2005.

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AB0113 THE RELATIONSHIP OF POLYMORPHISMS OF ANTXR2 GENE WITH ANKYLOSING SPONDYLITIS IN CHINESE HAN

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Background: ANTXR2 as the protein binding to collagen IV and laminin, may be involved in extracellular matrix adhesion. GWAS study in European had found its SNPs has relationship with ankylosing spondylitis, but these variations were not related to Chinese people.

Objectives: In this study, we would find susceptibility locus in ANTXR2 associated with ankylosing spondylitis.

Methods: After the haplotype analysis from the 1000 Genomes Project data, we chose tags SNPs validated on 254 cases and 170 matched controls through Mass Spectrometry method. The patients were diagnosed accoding to the Modified New York Criteria for Ankylosing Spondylitis (1984).

Results: In 197 Chinese people from the 1000genome database, there are 16 Haplotype blocks of ANTXR2 gene. 5 SNPs were verified (rs78740643, rs11098964, rs28688624, rs4389526 and rs7689197) by mass spectrometry. Case/control association analysis showed rs11098964 having relationship with AS (P=0.01721, OR (95% CI) = 0.4793 (0.2554–0.8621)). Dominant model of rs11098964 were significant difference from controls (P=0.0109).

Conclusions: our study found the rs11098964 also has relationship with AS. rs11098964 was protective against AS. ANTXR2 is related to susceptibility to AS

References:

[1] Ng SC, Liao Z, Yu DT, Chan ES, Zhao L, Gu J. Epidemiology of spondyloarthritis in the People's Republic of China: review of the literature and commentary. Semin Arthritis Rheum 2007;37:39–47.
[2] Reveille JD, Sims AM, Danoy P, Evans DM, Leo P, Pointon JJ, et al. Genome-wide association study of ankylosing spondylitis identifies non-MHC susceptibility loci. Nat Genet 2010;42:123–7.
[3] Momenzadeh P, Mahmoudi M, Beigy M, Garshasbi M, Vodjdanian M, Farazmand A, et al. Determination of IL1 R2, ANTXR2, CARD9, and SNAPC4 single nucleotide polymorphisms in Iranian patients with ankylosing spondylitis. Rheumatol Int 2016;36:429–35.
[4] Guo C, Xia Y, Yang Q, Qiu R, Zhao H, Liu Q. Association of the ANTXR2 gene polymorphism and ankylosing spondylitis in Chinese Han. Scand J Rheumatol 2012;41:29–32.
[5] van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361–8.
[6] Purcell S, Neale B, Todd-Brown K, Thomas L, Ferreira MA, Bender D, et al. PLINK: a tool set for whole-genome association and population-based linkage analyses. Am J Hum Genet 2007;81:559–75.
[7] Wu Z, Mou Y, Lin Z, Huang J, Wei Q, Gu J. HLA-B27 polymorphism in Han Chinese patients with ankylosing spondylitis: a distinctive disease association for B*2715 in a multiplex family. J Rheumatol 2009;36:2849–50.
[8] Goedecke V, Crane AM, Jaakkola E, Kaluza W, Laiho K, Weeks DE, et al. Interleukin 10 polymorphisms in ankylosing spondylitis. Genes Immun 2003;4:74–6.
[9] van der Paardt M, Crusius JB, Garcia-Gonzalez MA, Baudoin P, Kostense PJ, Alizadeh BZ, et al. Interleukin-1beta and interleukin-1 receptor antagonist gene polymorphisms in ankylosing spondylitis. Rheumatology (Oxford) 2002;41:1419–23.
[10] Burton PR, Clayton DG, Cardon LR, Craddock N, Deloukas P, Duncanson A, et al. Association scan of 14,500 nonsynonymous SNPs in four diseases identifies autoimmunity variants. Nat Genet 2007;39:1329–37.

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AB0114 EFFECTS OF ANTI-IL17A BLOCKADE WITH SECUKINUMAB ON SYSTEMIC AND LOCAL IMMUNE RESPONSES: A MECHANISM-OF-ACTION STUDY IN PERIPHERAL SPONDYLOARTHRITIS

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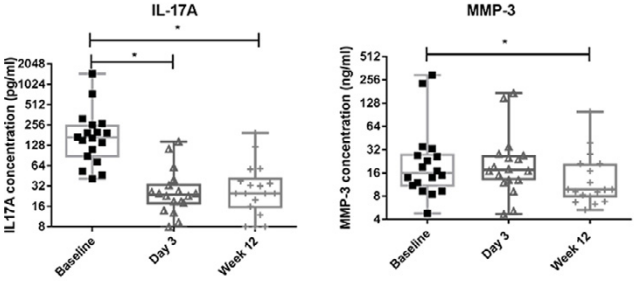
Background: IL-17A blockade is an effective therapy for ankylosing spondylitis (AS) and psoriatic arthritis (PsA), the two prototypical forms of spondyloarthritis (SpA). How IL-17A blockade affects the systemic and local immune responses in SpA remains incompletely understood.

Objectives: To assess the effect of anti-IL17A treatment with secukinumab on the systemic cytokine responses and the synovial immunopathology in SpA patients with peripheral disease (pSpA).

Methods: 20 active SpA patients were included in a 12wk open-label trial followed by 2yrs non-investigational extension. All patients received secukinumab 300mg/wk from baseline to wk4 and then every 4wks. Clinical response was measured 4wkly. TruCulture tubes with SEB and zymosan were drawn at baseline, day3, and wk12. Synovial biopsies were obtained by needle arthroscopy at baseline and wk12, analyzed by immunohistochemistry (IHC) and qPCR.

Results: The 20 pSpA patients consisted of 13 PsA, 3 undifferentiated SpA, 2 AS with peripheral arthritis, 1 reactive arthritis and 1 IBD associated pSpA. There were no SAEs in the 12wk core study. However, two SAEs occurred in the extension of the study: tonsillitis (suspected to be related to study drug) and myocardial infarction (non related), both fully recovered. Secukinumab induced a rapid and highly significant improvement in SJC (Baseline: 2,5 [IQR1–4] vs wk12: 0,5 [IQR0–1]p=0.001), TJC (6 [2–8] vs 0,5 [0–3]p<0.001); VASptglobal (46 [28–65] vs 13 [6–24]p<0.001). 18/20patients reached EULAR DAS response at wk 12 (10 good and 8 moderate responders). This was paralleled by significant improvements in other activity outcomes such as BASDAI (53 [25–63] vs 20 [9–40]p=0.001) and PASI (5,7 [4,5–7,1] vs 0,6 [0,1–1,8]p=0.001). Systemic inflammatory response revealed a decrease in CRP (3,85 [1,35–16,6] vs 2 [1,15–6,3]p=0,001) and ESR (16 [6–35] vs 6 [2,8–16,3]p=0,001), which was associated with decreased production of MMP-3, a validated biomarker of inflammation in pSpA,[1] by peripheral blood cells in the TruCulture system (see figure). With exception of a decrease in IL-17A, the TruCulture system did not reveal any impact of secukinumab on the capacity of peripheral blood cells to produce a broad panel of cytokines and chemokines upon stimulation. In contrast with this preserved systemic immune response, IHC confirmed the positive impact of 12wks of secukinumab on peripheral joint immunopathology as reflected by a significant decrease of infiltration of the synovial sublining with macrophages (2 [1–3] vs 1,5 [1–2]p=0.028) and neutrophils (1 [0,5–3,5] vs 0 [0–1]p=0.004), sensitive synovial biomarkers of treatment response in pSpA.[2] mRNA analysis of synovial biopsies before and after 12wks of secukimumab shows a decrease in IL-17A but not TNF expression.

Figure 1 - Reduction in secretion of IL-17 and MMP-3 in response to SEB in the whole blood TruCulture system after treatment with anti-IL17A.



Significance of the comparisons is determined by a paired T-Test. Concentrations shown are pg/ml (IL-17) and ng/ml MMP-3. P value <0.05 was considered significant and indicated with an (*).

Conclusions: This mechanism-of-action study indicates that IL-17A blockade with secukinumab has a profound beneficial clinical and biological impact on pSpA without compromising systemic immune responses. Further gene expression analysis will delineate which inflammatory pathways are blocked by secukinumab in the diseased target tissue.

References:

[1] van Dooren, Arthritis & Rheumatism, 2004.
[2] Kruithof, Arthritis & Rheumatism, 2005.

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AB0115 COMPARISON OF THE BACTERIAL STOOL MICROBIOTA IN ESTABLISHED PSORIATIC ARTHRITIS (PSA) AND PSORIASIS (PSC) - EXPLORATORY ANALYSIS OF PILOT DATA

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Background: Psoriatic arthritis (PsA) is a complex inflammatory condition with both genetic and environmental risk factors contributing to disease. A potential environmental risk factor, known to modify the immune system, is the intestinal microbiota. In PsA there is evidence of intestinal inflammation [1,2] and recently dysbiosis of the gut microbiota has been reported in treatment naïve PsA patients [3]. However, there is no information on the temporal stability of the microbiota over time in established PsA on treatment compared to matched PsC controls.
Objectives: To explore the temporal stability of gut microbiota composition and reveal associations with PsA compared to PsC while on stable on treatment with methotrexate.
Methods: Patients with PsA and PsC were recruited to the study if they had been on a stable dose of methotrexate for 6 months. Bacterial DNA was extracted and the V3-V4 hypervariable region of the 16S rRNA was amplified and sequenced on MiSeq. The resultant data was analysed using a bespoke bioinformatics pipeline and taxa were assigned using the Ribosomal Database Project classifier according to the SILVA119 database. The Wilcoxon rank sum test was used to assess alpha diversity indices, while permanova testing using Bray Curtis distance and DESeq2 values corrected for false-discovery rate (FDR) were used to compare beta diversity indices after removing low abundance (<0.5%) Operational Taxonomic Units (OTU). The ALDEx2 analysis package was used to assess effect size.
Results: Stool samples were available 9 PsA (n=13) and 6 PsC (n=12) individuals. Second stool samples were also obtained from the PsA (n=5) and PsC (n=4) groups.
No significant difference in the alpha diversity indices was observed between PsA and PsC. The beta diversity index showed no significant difference between the two conditions using permanova test. However, using the DESeq2-FDR analysis,

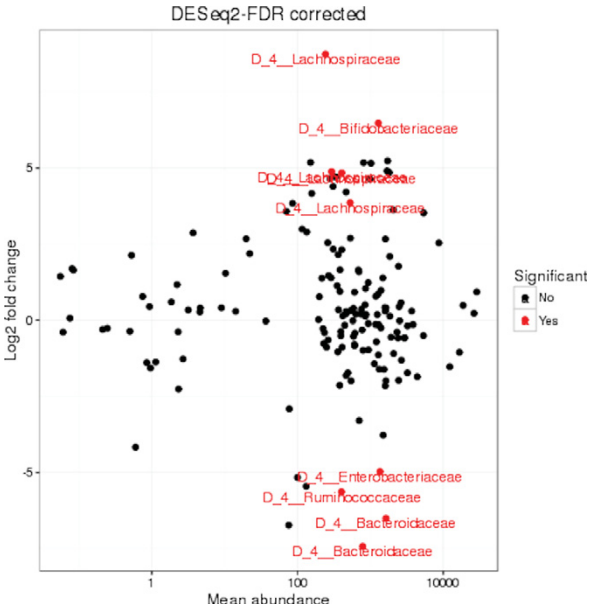

Table 1. Baseline Demographics

Demographic variables	PsA (n=9)	PsC (n=6)
Age mean (range) yrs	56.8 (40–72)	58.5 (27–79)
Gender Female (%)	2 (22)	4 (67)
Duration of Psoriasis mean (median) yrs	23.7 (26)	26.7 (30)
Type 1 Psorasis (Age at onset <40yrs) (%)	7 (77.8)	3 (50)

8 OTUs were identified which had significantly ($p<0.01$) different abundances in PsA compared to PsC. The taxa (Lachnospiraceae & Ruminococcaceae) predominantly belonged to the Firmicutes phylum, family Lachnospiraceae and Actinobacteria phylum, family Bifidobacteriaceae (Bifidobacteriaceae). The significant OTUs with DESEq2 had an effect size >1 using ALDEx2 but the BH p-value was not significant ($p<0.01$), which may be due to the small sample size. There were no significant differences in the diversity measures over time.
Conclusions: These results suggest that a gut enterotype with predominant Firmicutes/Actinobacteria composition is associated with stable/well controlled disease and is stable over time. This requires replication in a larger cohort.
References:
[1] Lindqvist, 2006.
[2] Scarpa, 2000.
[3] Scher, 2015.
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AB0116 IDENTIFYING THE AS PATIENT AT RISK: IS AORTIC ROOT DILATATION ASSOCIATED WITH HLA-B27?

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Background: Cardiac involvement is more common in *Ankylosing Spondylitis* (AS) patients with HLA-B27 genotype, especially aortic valvular regurgitation (AVR). AVR in AS is caused by aortic root dilatation and fibrotic thickening of the aortic cusps, both linked to inflammation. Inflammation of the aortic root might lead to a weakening in aortic wall strength and dilatation with AVR. Severe AVR can result in heart failure and is an indication for valve replacement or repair. The prevalence of AVR in AS is estimated at 14–18%, which is significantly higher compared to the general population. Therefore, some advocate regular echocardiographic screening of AS patients [1]. However, the cost-benefit of echocardiographic screening in AS is currently unknown and the precise effect of AS specific cardiac pathology on clinically overt cardiovascular morbidity and mortality remains to be elucidated. Hence, we should aim to identify a specific "at risk" AS population that might benefit from routine echocardiographic monitoring.
Objectives: Primary: To assess the association between the aortic root diameter in HLA-B27 positive versus HLA-B27 negative patients.
Secondary: To assess the association between the aortic root diameter with disease duration and inflammation biomarkers.
Methods: We performed a cross-sectional study in AS patients between 50–75 years who were recruited from a large rheumatology outpatient clinic. Patients underwent echocardiography, with 2D, spectral and colour flow Doppler. The aortic root was measured at sinuses of Valsalva during diastole. The aortic root diameter was corrected for body surface area (BSA). Correlation between aortic root diameter/BSA and disease duration and inflammation biomarkers were assessed.
Results: 132 Consecutive AS patients were included with a mean age of 60.5 years, of whom 110 (83%) were HLA-B27 positive. The median aortic