contain significantly more IgD⁺CD95⁺ germinal center B cells ($P < 0.01$) with a higher expression of the costimulatory molecules CD80 and CD86 compared to WT. The vertebrae also contained more CXCR5⁺PD-1⁺FoxP3⁺CTLA4⁺ T regulatory cells and a trend towards an increase in CXCR5⁺PD-1⁺FoxP3⁺CTLA4⁺ T follicular helper cells in tmTNF tg mice. Meanwhile, B cell development in the BM of tmTNF tg hind limbs was not altered. Furthermore, BM, spleen and vertebrae from tmTNF tg mice contained significantly more IgA⁺ plasma cells compared to WT littermates. Of note, tmTNF tgxTNF-RI^{-/-} mice did not display lymphoid aggregates or HEVs in the BM, while tmTNF tgxTNF-RII^{-/-} mice did, although to a lesser extent than tmTNF tg mice.

Conclusion: tmTNF overexpression in mice results in extensive lymphoid aggregates in the BM that are often organized in ELS, which may be mediated via TNF-RI signaling. These ELS might result in an increase of IgA⁺ plasma cells in tmTNF tg mice. Ongoing studies will look further into this and may indicate whether these findings contribute to the pathology observed in these mice.

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FRI0368 VASCULAR CALCIFICATION BY INFLAMMATION COULD BE AN IMPORTANT CAUSE OF CARDIOVASCULAR DISEASE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Patients with ankylosing spondylitis (AS) have a higher risk of cardiovascular disease. Atherosclerosis is a main pathological process of cardiovascular disease and calcified plaque is a characteristic feature of atherosclerosis. Inflammation plays a potential role in vascular calcification. There is no previous study revealing the mechanism of vascular calcification in AS.

Objectives: We investigated the relationship between vascular calcification and inflammation in patients with AS.

Methods: Sixteen male patients aged over 20 years with AS were enrolled. They fulfilled the modified New York criteria and each of their ankylosing spondylitis disease activity score was more than 2.1. Sex and age matched nine healthy controls were also recruited. Mouse MOVAS (American Type Culture Collection, ATCC[®], CRL-2797TM) vascular smooth muscle cells were stabilized in maintenance medium for 24 hours. Then the amount of serum equivalent to 10% of maintenance medium from subjects was added and cells were stimulated for another 72 hours. We exchanged this medium with calcification medium every third day and cells were cultured for another 11 days. After 2 weeks, cells were stained with Alizarin Red S and the optical density (OD) was measured while being compensated by cell viability. For Western blotting, cells were stabilized for 24 hours and stimulated for another 72 hours through the same procedure as that of Alizarin Red S staining. Then we measured the level of protein expression in PPAR-gamma, beta-catenin, TNF- α , interleukin (IL)-23, and MMP7.

Results: The level of OD of MOVAS cells treated with serum from AS patients (19.503 ± 6.422 , mean $\pm$ SD) was significantly higher than that from controls (12.724 ± 5.746) ($P=0.027$, Mann-Whitney test). The level of MMP7 expression of MOVAS cells treated with serum from AS patients (1.921 ± 0.702) was significantly higher than that from controls (0.779 ± 0.191) ($P=0.000$, Mann-Whitney test). The level of beta-catenin expression of MOVAS cells treated with serum from AS patients (1.292 ± 0.356) was significantly higher than that from controls (0.887 ± 0.310) ($P=0.025$). There was negative correlation between PPAR-gamma and TNF- α ($\rho=-0.762$, $p=0.028$, Spearman rank correlation coefficient), and between PPAR-gamma and IL-23 ($\rho=-0.601$, $p=0.039$); positive correlation between MMP7 and TNF- α ($\rho=0.833$, $p=0.010$), and between MMP7 and IL-23 ($\rho=0.797$, $p=0.002$).

Conclusion:

1. Serum from AS patients showed increased calcification of vascular smooth muscle cells than serum from controls.
2. The level of vascular calcification marker from vascular smooth muscle cells treated with serum from AS patients was significantly higher than that from controls.
3. There were negative relationship between inflammatory markers and inhibitory marker of vascular calcification but positive relationship between inflammatory markers and stimulatory marker of vascular calcification.

These findings suggest that vascular calcification by inflammation could be an important cause of cardiovascular disease in AS patients.

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FRI0369 TOWARDS MORE PRECISE ESTIMATES OF THE FAMILIAL AGGREGATION AND HERITABILITY OF ANKYLOSING SPONDYLITIS – A SWEDISH NESTED CASE-CONTROL STUDY

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Background: Ankylosing spondylitis (AS) is known to have strong familial aggregation, but studies quantifying the familial risk are few and have reached varying results. Familial risks reported from population-based studies range from 17 to 94 in first-degree relatives of AS cases.^{1,2} The heritability (i.e., the proportion of variance in AS liability explained by genetic variation) has been reported to >90%, based on very small studies of twins.³

Objectives: To assess the familial aggregation and heritability of AS among all Swedish AS patients, and to investigate if risks vary by type of first-degree relative or sex.

Methods: We identified all patients with an ICD-10 code of AS in the Swedish National Patient Register (NPR) between 1 January 2001 and 31 December 2016. To increase validity, index patients were required to have two or more visits listing an AS diagnosis, and at least one of the visits being to a specialist in rheumatology or internal medicine. Each index patient was matched on sex and birth year to 50 general population controls from the Total Population Register. First-degree relatives of index patients and controls were identified through the Multi-generation register. Their disease status was ascertained from the NPR in a similar manner as for index patients. Familial risks of AS among first-degree relatives were calculated as odds ratios (ORs) with conditional logistic regression. Based on the familial risks, the corresponding heritability was calculated for a range of plausible prevalence estimates.

Results: We identified 13 795 patients that met the inclusion criteria. Of their siblings, parents, and children, 3.6, 2.3, and 2.1% respectively also had AS. The overall familial OR when having one affected relative was 19.4 (95% CI 18.1-20.8). The estimates were similar for relatives of different kinds (see table), but having more than one affected relative resulted in a higher risk (OR 68.0 (95% CI 51.3-90.1)). Heritability, estimated from sibling risk, was 77%. There were no clear-cut differences between the sexes, but women tended to have an elevated familial risk if the affected relative was female, and slightly lower heritability compared to males. These estimates can be considered as an upper limit of heritability, as shared environmental factors have not been taken into account in calculations.

Conclusion: Familial risks of AS were similar between different types of first-degree relatives, and no significant gender difference was seen on the heritability scale. Although high compared to most other diseases, the familial risks and heritability were lower than previous reports from other countries, though in line with earlier Swedish findings using in part the same data source. The heritability proposed here might still be an overestimate of the true influence of genetics on disease risk. Thus, efforts should also be directed at identifying other risk factors for AS that are not of genetic origin.

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Table. Familial risks and heritability of AS by type of first-degree relative (FDR) and sex

	Overall	Male-male	Male-female	Female-male	Female-female
Relative with AS	Familial risk, odds ratio (95% CI)				
Sibling	19.5 (16.9 - 22.4)	19.9 (16.1 - 24.7)	20.9 (16.0 - 27.4)	20.5 (16.0 - 26.5)	21.0 (13.3 - 33.2)
Parent	19.1 (17.2 - 21.3)	18.3 (15.5 - 21.6)	20.8 (16.3 - 26.4)	14.1 (11.3 - 17.5)	34.2 (26.1 - 44.9)
Child	20.6 (18.2 - 23.3)	20.5 (16.8 - 25.1)	16.0 (12.2 - 21.0)	19.9 (15.0 - 26.4)	26.2 (18.5 - 37.2)
Any FDR	19.4 (18.1 - 20.8)	19.0 (17.2 - 21.1)	18.2 (15.9 - 21.0)	17.7 (15.4 - 20.3)	26.9 (22.0 - 32.9)
>1 relative	68.0 (51.3 - 90.1)				
	Heritability (95% CI)				
Siblings	0.77 (0.73 - 0.80)	0.80 (0.74 - 0.85)	0.73 (0.67 - 0.78)	0.77 (0.72 - 0.83)	0.71 (0.61 - 0.81)

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FRI0370 ACCELERATED EXTRACELLULAR MATRIX REMODELING IN PSORIATIC ARTHRITIS & VALUE OF ECM-RELATED BIOMARKERS

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Background: With our increasing understanding of cross-talk between the immune system (immune cells, cytokines) and extracellular matrix (ECM) of the affected tissues, ECM destruction and turnover has gained a lot of attention in inflammatory arthritis. ECM mainly consists of interstitial matrix (rich in type I and III collagens) and basement membrane (mainly composed of type IV collagen), both of which are affected in inflammatory arthritis. We hypothesize that inflammatory milieu in Psoriatic Arthritis (PsA) leads to accelerated ECM destruction and remodeling, and the release of ECM metabolites into circulation, that can be measured in serum as biomarkers of tissue remodeling and may give insight to pathological process at the tissue level.

Objectives: This prospective study aimed to use serological biomarkers for evaluation of the extent of damage to, and changes in turnover of ECM in patients with PsA and to investigate their relation to inflammatory biomarkers and disease activity.

Methods: Patients with PsA (n=145) fulfilling the CASPAR criteria and above 18 years of age with any disease activity were recruited through outpatient department in Aalborg University Hospital, Denmark. Exclusion criteria were pregnancy, treatment with biological DMARD, or with oral corticosteroids and other comorbidities. Clinical disease parameters were recorded, and blood samples were collected at baseline and 24 weeks follow-up. Inflammation-related ECM remodelling was measured by serological biomarkers of type I, III and IV collagen formation (Pro-C1, Pro-C3 and Pro-C4, respectively) and MMP-mediated degradation (C1M, C3M and C4M respectively). The chronic inflammation was measured by CRPM (MMP degraded metabolite of CRP). All biomarkers were measured by competitive ELISAs and levels were compared to the reference levels of healthy individuals. The biomarker data was log₂ transformed for normalization and standard parametric statistical methods were applied.

Biomarkers (ng/ml)	PsA patients			Reference values*			Statistics	
	Mean	SD	n	Mean	SD	n	Difference	P Value
C1M	50.00	32.18	145	24.8	10.8	29	25.2	<0.0001
C3M	10.94	3.15	145	9.69	2.59	127	1.25	0.0004
C4M2	29.57	10.51	145	21.33	5.64	89	8.24	<0.0001
Pro-C1	79.20	38.85	145	104.77	54.17	119	-25.57	<0.0001
Pro-C3	11.49	3.56	145	11.28	3.56	111	0.21	ns
Pro-C4	304.07	120.17	145	204.88	63.54	127	99.19	<0.0001

Table 1. Comparison of ECM turnover biomarkers in PsA patients (at baseline) and healthy individuals (*internal laboratory data)

	Log ₂ ΔC1M	Log ₂ ΔC3M	Log ₂ ΔC4M	Log ₂ ΔPro-C1	Log ₂ ΔPro-C3	Log ₂ ΔPro-C4
ΔCRP	0.621±	0.53±	0.341±	-0.062	0.098	0.267±
Log ₂ ΔCRPM	0.436±	0.615±	0.415±	0.097	0.208	0.393±
ΔASDAS	0.202*	0.21*	0.207*	0.042	0.104	0.204*
ΔBASDAI	0.032	0.102	0.148	0.03	0.057	0.117
ΔBASMI	0.015	0.005	0.107	-0.015	-0.061	0.175*
ΔPASI	-0.076	-0.033	-0.001	-0.09	-0.053	0.008
ΔLEI	-0.024	0.027	0.246*	0.108	-0.043	0.094
ΔSPARCC	0	0.152	0.163	0.018	-0.049	0.174
ΔSJC	-0.015	-0.144	0.153	-0.011	0.019	0.062
ΔTJC	-0.039	0.037	0.062	0.006	-0.006	0.077
ΔVAS-Pain	0.07	0.104	0.138	0.075	0.087	0.198*

Results: We found that there was an increase in the degradation of interstitial matrix (represented by C1M and C3M) which was uncompensated with either decreased (Pro-C1) or unaltered (Pro-C3) formation in patients with PsA as compared to healthy individuals. On the contrary, there was a compensated increase in basement membrane remodeling in patients with PsA as represented by increase in both C4M and Pro-C4 in comparison to healthy individuals (Table 1). Interestingly, there was a strong correlation between baseline C4M and Pro-C4 (r=0.703, p<0.0001), and 24-week changes in both biomarkers (r=0.468, p<0.0001) pointing towards coupling between the two processes which was either lost or was weak in case of interstitial collagens. As baseline values and changes in C1M, C3M, C4M and Pro-C4 showed a strong correlation with changes in inflammatory biomarkers, we believe that ECM remodeling in PsA is, at least partly, driven by inflammation. Furthermore, baseline values and changes in these ECM turnover biomarkers correlated positively with changes in composite disease activity scores (Table 2) that may indicate their clinical importance as potential diagnostic or disease activity markers.

Conclusion: Chronic inflammation underlying PsA pathology results in an increased amount of ECM turnover that correlates with clinical progression and can be measured by serological biomarkers.

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FRI0371 ALTERED EXPRESSION OF LNCRNA NR_003542 AND NR_026756 IN ANKYLOSING SPONDYLITIS MIGHT BE ASSOCIATED WITH THE DISEASE ACTIVITY

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Background: lncRNAs have been recognized as powerful regulators of numerous genes and pathways in the pathogenesis of inflammatory and autoimmune diseases, including SLE, RA, T1DM, MS, autoimmune thyroid disease, Sjögren's syndrome psoriasis, and Crohn's disease[1]. The role of lncRNAs in the pathogenesis of Ankylosing Spondylitis (AS) is just beginning to be investigated

Objectives: To determine whether the altered expression of lncRNA NR_003542 and NR_026756 in peripheral blood of AS patients could provide insights into the pathogenesis of AS.

Methods: Peripheral blood mononuclear cells (PBMCs) lncRNA NR_003542 and NR_026756 expression were measured in 30 active AS (AAS) group, 30 inactive AS (IAS) group and 30 healthy control (HC) subjects. Clinical characteristics of the subjects are summarized in Table1.

Results: 1. Clinical and laboratory characteristics of the three groups (Table 1)