Sema3A, an Immunoregulator and Potential Biomarker for Disease Severity in Systemic Sclerosis

Introduction
Semaphorin 3A (sema3A) plays a regulatory role in immune responses, mainly affecting the activation of regulatory T cells. It has been found to correlate with disease activity in rheumatoid arthritis and systemic lupus erythematosus (SLE).

Aim
To investigate the expression of sema3A in patients with systemic sclerosis (SSc) compared to healthy controls and SLE disease controls and to correlate its expression with clinical characteristics.

Methods
27 SSc patients, 42 SLE patients and 18 healthy controls were enrolled. Serum level of sema3A was measured by ELISA and expression of sema3A on regulatory T cells was evaluated by FACS analysis. SSc patients were evaluated for demographics, clinical manifestations, routine laboratory results, nailfold videocapillaroscopy patterns, pulmonary function tests, echocardiograms, modified Rodnan skin score (mRSS) and disease activity and severity scores.

Results
Serum levels of semaphorin 3A were lower in SSc compared to healthy controls 14.38 ± 5.7 ng/ml vs. 27.14 ± 8.4 ng/ml, p < 0.0001 and similar to SLE 15.7 ± 4.3 ng/ml. The expression of semaphorin 3A on regulatory T cells was also lower in SSc compared to healthy controls 61.7 ± 15.7% vs. 88.7 ± 3.7% (p < 0.0001). Semaphorin 3A serum level inversely correlated with the duration of disease; r = -0.4, p = 0.036 and with low C4 level r = 0.66 p = 0.026. SCL-70 antibody positivity was associated with a lower semaphorin 3A level in serum (difference in mean of 3.44 p = 0.06).

Conclusion
Sema3A expression is low in SSc serum and more specifically on regulatory T cells. This may help explain the reduced activation of regulatory T cells in SSc, contributes to our understanding of the pathogenesis of the disease and may serve as a future target for treatment.

A6.15
GENETIC SIGNATURES MAY BE ASSOCIATED WITH VASCULAR PATHOLOGY IN RHEUMATOID ARTHRITIS

Background and objectives
Accelerated atherosclerosis, increased cardiovascular (CV) morbidity and mortality have been associated with rheumatoid arthritis (RA). In single SNP studies, CD40, HLADR, MTHFR, SMAD3 and possibly other alleles have been associated with cardiovascular disease (CVD) or vascular pathophysiology in RA. Endothelial dysfunction, carotid atherosclerosis and arterial stiffness that may predict the development of CVD are assessed by bracial artery flow-mediated vasodilation (FMD), common carotid intima-media thickness (cIMT) and arterial pulse-wave velocity (PWV), respectively. In this study, we wished to determine expression profiles of multiple genes that may differentiate between physiological and pathological vascular function in RA.

Patients and methods
Altogether 16 RA patients were recruited. FMD, cIMT and PWV were assessed in all patients using standard B-mode ultrasound techniques. FMD < 6%, cIMT > 0.6mm and PWV > 9 m/sec were considered abnormal. Peripheral blood mononuclear cell samples were obtained and used in microarray. The signature of those genes were determined by principal component analysis (PCA) and hierarchic clustering (GeneSpring software), which significantly differentiated patient subsets with normal vs. abnormal FMD, cIMT and PWV.

Results
Among RA patients, 11 had low (impaired) and 5 had normal FMD, 11 had high (increased) and 5 had normal cIMT and 9 had high (increased) and 7 had normal PWV. Altogether 20 genes differentiated patients with low vs. normal FMD. Altogether 33 genes separated high vs. normal PWV. Finally, 240 genes differentiated increased vs. normal cIMT.

Conclusions
Using microarray, genetic signatures may differentiate RA patients with and without vascular pathology.

A6.16
DECTIN-2 IS ESSENTIALLY INVOLVED IN INNATE IMMUNE RESPONSE OF EXPERIMENTAL ARTHRITIS

1V Stögner, T Shwets, B Niederreiter, M Koenders, WB van den Berg, I Smolen,
K Redlich, S Hayer.1Medical University of Vienna. Department of Internal Medicine III, Division of Rheumatology, Vienna, Austria; 2Radboud University Medical Center Nijmegen, Nijmegen, The Netherlands

Results
Anti-TNF treatment was highly effective in both diseases, as the mean semaphorin 3A decreased from 6.32 to 3.16 (p = 0.02) in RA, mean BASDAI decreased from 5.87 to 1.84 (p < 0.0001) in AS. In RA, AS and the mixed arthritis population (n = 43) baseline oxLDL/beta2gpI levels were 0.235 ± 0.1, 0.245 ± 0.1 and 0.238 ± 0.1, respectively. There were no significant differences between RA and AS patients. In RA, ETN/CTZ treatment resulted in non-significant decreases in complex levels after 6 months (0.214 ± 0.1) and 12 months (0.206 ± 0.1). In AS, oxLDL/beta2gpI complex levels did not change after 6 months of ETN therapy, but significantly decreased after one year (0.195 ± 0.1; p = 0.01). In the RA+AS population, anti-TNF treatment significantly decreased oxLDL/beta2gpI levels after 12 months (0.201 ± 0.1, p = 0.02). In addition, baseline oxLDL/beta2gpI complex levels positively correlated with TC (RA: r = 0.563, p = 0.002; AS: r = 0.542, p = 0.049; RA+AS: r = 0.532, p < 0.001), and LDL-C (RA: r = 0.630, p < 0.001; AS: r = 0.756, p = 0.004; RA+AS: r = 0.648, p < 0.001) in both diseases. Circulating oxLDL/beta2gpI levels did not correlate with BASDAI, BASMI or CRP.

Conclusions
In a mixed cohort of RA and AS patients, anti-TNF therapy suppressed the circulating levels of oxLDL/beta2gpI complexes, markers of atherosclerosis and vascular disease in SLE or APS. Moreover, oxLDL/beta2gpI levels correlated with TC and LDL-C in arthritides. oxLDL/beta2gpI complexes do not seem to be markers of disease activity in RA or AS.
A6.15 Genetic signatures may be associated with vascular pathology in rheumatoid arthritis

S Poliska, E Végh, A Váncsa, N Bodnár, S Szamosi, M Csumita, G Kerekes, Z Szabó, G Szucs, Š Szántó, G Zahuczky, P Soltész, L Nagy and Z Szekanecz

Ann Rheum Dis 2015 74: A61

Updated information and services can be found at:
http://ard.bmj.com/content/74/Suppl_1/A61.2

These include:
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Articles on similar topics can be found in the following collections

Epidemiology (1274)
Connective tissue disease (3922)
Degenerative joint disease (4272)
Immunology (including allergy) (4704)
Musculoskeletal syndromes (4566)
Rheumatoid arthritis (2998)
Clinical diagnostic tests (1196)
Genetics (900)
Radiology (1042)
Radiology (diagnostics) (706)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/