maintenance of chronic inflammation. Consequently, NIK may be an attractive therapeutic target.
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OP0169 A COMBINATION OF PROTEINS AS MEASURED WITHIN THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE AT PRESENTATION OF RA IDENTIFIES A GROUP OF ACPA-NEGATIVE RA PATIENTS WITH HIGH LIKELIHOOD OF DEVELOPING DMARD-FREE SUSTAINED REMISSION

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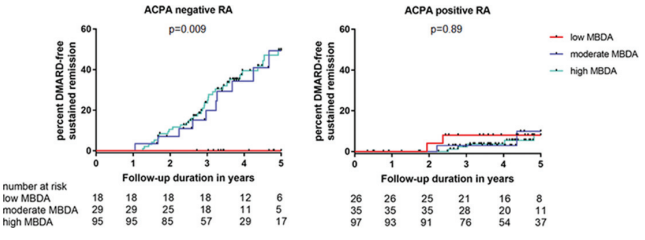
Background: Rheumatoid arthritis (RA) typically requires lifelong treatment. However, some RA patients achieve sustained disease-modifying antirheumatic drug (DMARD)-free remission, which is a proxy for cure of RA that has become increasingly achievable, as reported previously. DMARD-free sustained remission has been reported mostly in autoantibody-negative RA, yet the underlying mechanism is unknown. The multi-biomarker disease activity (MBDA) score combines 12 serum biomarkers and is developed to measure RA disease activity. We hypothesise that the subgroup of RA patients that is most likely to achieve DMARD-free sustained remission is identifiable at disease presentation by cytokines such as those combined in the MBDA score.
Objectives: To evaluate whether the MBDA score or its component cytokines at the presentation of RA are associated with ability to later achieve DMARD-free sustained remission.
Methods: 300 patients with RA (by the 1987 and/or 2010 criteria) who had been consecutively enrolled in the Leiden Early Arthritis Clinic between 2010 and 2015 were studied. At time of diagnosis, before DMARD treatment was started, the MBDA score, with a scale of 1–100, was determined from the serum concentrations of 12 biomarkers (VCAM-1, EGF, VEGF-A, IL-6, TNF-RI, MMP-1, MMP-3, YKL-40, Leptin, Resistin, CRP, SAA) with a pre-specified, validated algorithm. Patients were categorised as having a low (<30), moderate[30–44] or high (>44) MBDA score. DMARD-free sustained remission was defined as the absence of synovitis (by physical examination) that sustained after discontinuation of all DMARD therapy (including biologics and systemic and intra-articular corticosteroids) for the entire follow-up period, but had to extend to at least one year after DMARD withdrawal. Analyses were stratified for ACPA and restricted to 5 years follow-up as thereafter the number of patients became small. The median follow-up duration of all patients was 4.3 years.
Results: A total of 54 RA patients (18%) had achieved DMARD-free sustained remission. For the total group of RA patients, baseline MBDA category (p=0.03) and ACPA-negativity (p<0.001) were associated with achieving DMARD-free sustained remission. For ACPA-positive RA patients, the MBDA category at baseline was not associated with achieving DMARD-free sustained remission (p=0.89, figure 1). By contrast, among ACPA-negative RA patients, none of those with low MBDA score achieved DMARD-free sustained remission during 5 years follow-up, whereas the estimated rate of remission was 50% for those with moderate or high MBDA scores (p=0.009, figure 1). Of the 12 biomarkers in the MBDA test, only SAA showed a significant difference between ACPA-negative patients with and without DMARD-free sustained remission (p=0.01).



Conclusions: ACPA-negative RA patients who achieved DMARD-free sustained remission were characterised by moderate to high MBDA scores at disease presentation. This is the first evidence that a cytokine profile at disease onset can identify a subgroup of ACPA-negative RA patients with a high likelihood of maintaining clinical remission after treatment withdrawal.

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OP0170 HUMAN IL-38 REDUCES JOINT INFLAMMATION IN A MOUSE MODEL OF GOUTY ARTHRITIS

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Background: Interleukin-38 (IL-38) is the last member of the IL-1 family of cytokines to be fully investigated for its functions. IL-38 is proposed as an anti-inflammatory cytokine in various auto-inflammatory diseases, such as psoriasis and rheumatoid arthritis. For example, IL-38 knockout mice have exacerbated autoantibody-induced arthritis. Current understanding of the capacity of IL-38 in gout, a prototype IL-1β driven auto-inflammatory disease, is unknown.
Objectives: We hypothesised that *in vivo* treatment with human recombinant IL-38 results in a reduction in join inflammation in a mouse model of gouty arthritis.
Methods: We treated C57/Bl6 mice with 1 μg recombinant IL-38 (3–152 AA) intraperitoneally at 24, 12 and 2 hours before induction of gouty arthritis with intra-articular injection of albumin-opsonized monosodium urate crystals (300 μg) and palmitic acid (200 μM) in 10 μL PBS. Joint inflammation was scored after 4 hours. The synovial lining was cultured in RPMI for 2 hours to allow cytokines to be secreted, and cytokines in the synovium were extracted with Triton-X 100 to obtain total cytokines (membrane and intracellular). In the synovial culture fluid and extract, IL-1β, IL-6 and KC were measured by ELISA. Data
Results: Mice treated with recombinant IL-38 exhibited significantly reduced joint swelling and redness on a three-point macroscopic inflammation scale: Vehicle-treated 1.5±0.25 vs IL-38 Treated 0.75+0.25 (n=10, p<0.0001, Mann Whitney-U test). The 2 hour synovial membrane culture fluid contained significantly lower levels of IL–1β (1207±480 vs 379±184 pg/mL, p<0.05), IL-6 (10783±2490 vs 5321±2935 pg/mL, p<0.05) and KC (4390±931 vs 1081±750 pg/mL, p<0.05). In extract of the synovial membrane, there is a reduction in IL–1β (1505±397 vs 624 ±509 pg/mL, p<0.05), IL-6 (11059±2299 vs 3597±2509 pg/mL, p<0.01) and KC (1505±397 vs 624±509 pg/mL, p<0.05).
Conclusions: Human recombinant IL-38 reduces swelling and redness of the joint, and pro-inflammatory cytokines secreted by and contained in the synovial membrane in a mouse model of gouty arthritis. These data reveal that recombinant IL-38 has therapeutic benefit in an IL–1β mediated model of inflammation.
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OP0171 LEPTIN LEVELS, OVERWEIGHT AND P GINGIVALIS PRESENCE CONTRIBUTE TO THE MECHANISM OF SYSTEMIC INFLAMMATION IN FIRST-DEGREE RELATIVES OF RHEUMATOID ARTHRITIS INDIVIDUALS

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Background: Association studies in rheumatoid arthritis (RA) have been focused in the pre-clinical phases of the disease in first-degree relatives (FDR). Data has shown that obesity, ACPA and the periodontal condition may modulate the severity and the clinical presentation of RA
Objectives: To investigate the levels of adipokines in FDR and establish their association with the state of rheumatic and periodontal condition
Methods: 124 FDR individuals and 124 healthy controls matched by age and gender were included. Rheumatologic (clinical and serological markers) and periodontal assessment was performed. It was quantified the adiponectin, leptin, IL6 levels. HLA-DRB1 was determined. Serum markers of RA (rheumatoid factor, erythrocyte sedimentation rate, C reactive protein (CRP), and APCA. *P gingivalis* and IgG1/IgG2 *P gingivalis* were measured. Radiographs of hands and feet were evaluated the Sharp-van der Heijde score. An association analysis was made to evaluate the relationship between adipokines and periodontal, rheumatologic conditions using X2 test, and logistic regression model was performed to confirm this associations
Results: In FDR group, 71.77% were women with a mean age of 39.24±12.22 years. 37.09% had overweight and 4.83% had obesity. Among the controls, 70.97% were women, with an average age of 39.31±12.30 years. 27.41% had overweight and 4.83% had obesity. Leptin levels were found in 37.66% vs 18.42% in controls(p=0.002). In FDR, 60.48% had periodontal disease of which 62.66% moderate, *P gingivalis* in 62.10%. In controls, 55.64% had periodontal disease, of which 63.76% moderate with 42.74% *P gingivalis* positive (p=0.002). In the FDR, radiography of hands and feet showed in 25.28% of them had some alteration, 68.18% had ≥1 erosion, 45.45% had ≥1 joint space narrowing and in 6.89% juxtaarticular osteopenia. An association of leptin levels with the low economic level was found p=0.006 and high levels of leptin in individuals with BMI ≥30 p=0.031.