IL6 was found to be associated with severity of periodontal disease, with higher levels being found frequently in mild periodontal disease p=0.039.The condition of FDR was significantly associated with high leptin levels adjusted for presence of swollen joints, presence of *P gingivalis* and low levels of IL6 OR=2,57, 95% CI: 1.14 to 5.95. In this group, the individual with leptin at moderate levels adjusted with BMI >25, has a lower probability of presenting CRP >3 mg/L OR=0.43 95% CI: 0.20 to 0.90.

Conclusions: High levels of leptin, the presence of *P gingivalis* and swollen joints may be relevant conditions associated with the development of RA in FDR.Leptin levels and overweight can modulate the production of acute phase proteins in this group of individuals contributing to the mechanism of systemic inflammation. The clinical implications of our findings propose regulated exercise programs, oral hygiene, and weight control in FDR

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OP0172 LPS-INDUCED PERIODONTITIS PROMOTES ARTHRITIS DEVELOPMENT IN MICE

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Background: Although *in vivo* studies have demonstrated that periodontitis aggravates experimental arthritis, there are no animal models that mimic the co-occurrence of these diseases.

Objectives: To investigate the arthritogenic effect of lipopolysaccharide (LPS) in a mouse model of periodontal disease.

Methods: Periodontitis was induced in CD1 mice by injection of 0.01 or 0.05 μg of LPS in 5 μl of PBS every 48 hour into the vestibular gingiva of the second molar on the left maxilla. Untreated mice or injected with LPS at the tail were used as controls. Mice (n=10 per condition) were monitored daily and arthritis was estimated by conventional visual scoring method (scale 0–5) and recording the paw swelling with a calliper. 2 weeks after the 9th injection mice were sacrificed to collect blood, maxilla and paw samples. The left maxilla was analysed by microCT and the alveolar bone loss was assessed measuring the distance between the cementum-enamel junction (CEJ) and the alveolar bone crest (ABC) of each molar. Ultrasound (US) was performed to measure the ankle joint space. Periodontal and paw tissues were processed for histological analysis. Inflammation, vascular proliferation and bone resorption were scored (0–3) in maxilla. Inflammation, pannus formation, cartilage and bone destruction were scored (0–5) in ankle joints. CXCL1, IL-1β, IL-6 and TNF serum levels were determined by ELISA.

Results: Ankle swelling and inflammation were noted after the 5th periodontal injection of 0.05 μg of LPS, picked at day 18 and continued for the next 15 days with paw swelling and score higher than those of untreated mice (at the sacrifice $p<0.001$). 0.01 μg of LPS did not induce paw changes. Therefore, the subsequent assessments were conducted only in mice injected with 0.05 μg of LPS. The CEJ-ABC distance was greater in the inoculated (0.29±0.08 mm) than in the control (0.17±0.05 mm) mice ($p<0.001$). Histological analysis showed that LPS induced a mild vascular proliferation (score 0.8±0.42) in periodontal tissue and a substantial alveolar bone resorption (score 1.8±0.42), but not inflammation. US revealed the presence of effusion and a 1.5-fold higher joint space in the ankle of mice with periodontitis than in controls ($p<0.05$). Leukocyte infiltration (score 2.36±1.56) and synovial proliferation (score 2.09±1.54) were observed after histology in ankle joints of mice injected orally. The same sections had slight cartilage (score 1.32 ±1.21) and bone destruction (score 0.68±0.72). Animals that received LPS tail injection did not show any clinical and histological signs of arthritis. CXCL1 and TNF were higher in arthritic mice (CXCL1:2226.87±264.38 pg/ml; TNF:24.55 ±7.0 pg/ml), than in controls (CXCL1:445.97±92.09 pg/ml; TNF:3.22±1.04 pg/ml). Although there was no statistical difference, IL-1β and IL-6 were highest in LPS-mice (IL-1β:79.49±11.99 pg/ml; IL-6:196.02±40.62 pg/ml).

Conclusions: This study shows that experimental arthritis and periodontal disease can co-occur after LPS oral injection in mice. Our model may be useful to improve the understanding of the mechanisms underlying the link between periodontitis and arthritis.

Disclosure of Interest: None declared
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THURSDAY, 14 JUNE 2018

Inclusive school environment for young people with RMDs

OP0173-PARE YOUTH-R-COACH, A PROGRAM FOR YOUTH WITH A CHRONIC DISEASE

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Background: Youth-R-Coach is a project for youth (aged 15–25) with a chronic illness. It is a project set up by the Centre for Chronically Ill and Work (CCZW) in cooperation with Youth-R-Well.com, the Dutch organisation for youth with RMDs. Youth-R-Coach is based on CCZW's program for the certification of 'experience expertise'.

Objectives: Youth-R-Coach focusses on the development of experts-by-experience, and making those experiences available for others to learn from. A distinctive element is the creative aspect: the development of writing talent.

Methods: The participants reflect individually on personal experiences with their disease, as well as their personal competencies. This process is supported by a portfolio of assignments and a mentor who also has an RMD. The participants also incorporate their personal experience with the disease in a self-written book with support of a writing coach. Even though the process is an individual one, the program starts with a group of participants. There is a kick-off meeting, a weekend training and a final group meeting. In this way, the participants get to know each other and learn from each other's personal experiences with the disease. They stay in contact during the program and help each other with the portfolio and writing of their book. During the meetings, workshops are provided to teach them new skills, such as 'online coaching' and 'presenting'.

Results: Youth-R-Coach worked with a group of 7 participants who followed the program in 2016, and a group of 7 participants who started in 2017. Both groups are currently busy finalising their portfolios and books, which will be ready in May 2018.

The books are intended to make personal experiences in dealing with an RMD available for peers, for whom the books can be a source of support in dealing with the disease. The books are also interesting for a wider audience, because they provide insights into living with a chronic illness as a young person. The books are all very different. Some wrote short columns, while others wrote an entire novel. What all the books have in common is that they are all based on personal experiences of living with a chronic illness.

Developing expertise-by-experience and writing about their experiences has helped the participants to better cope with their disease, and has made them ambassadors. Some of them have been, or are still, involved in activities for patient organisations since the start of the program. For example, some have volunteered as a mentor for an RMD youth holiday camp, or given presentations based on personal experience with an RMD. Some participants will continue coaching their peers after finishing the program, and some continue writing about their personal experiences in a blog. How participants will continue to use their new-found skills is down to personal interests and competencies, but whatever they do, the program has given them useful tools for coping with and teaching others about the disease.

Conclusions: Fourteen participants (aged 18–27) developed their expertise-by-experience in dealing with an RMD and are now able to act as a coach for their peers. Their experiences in dealing with the disease will be published in self-written books and made available to a wide audience. All of the current participants had an RMD, but the project would also be useful for youths who have other chronic illnesses.

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THURSDAY, 14 JUNE 2018

The building blocks of systemic inflammation

OP0174 ALTERATION OF MEDIATORS OF VASCULAR INFLAMMATION BY ANIFROLUMAB IN THE PHASE IIB MUSE STUDY IN SLE

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Background: Cardiovascular disease remains one of the leading causes of death for patients with systemic lupus erythematosus (SLE), and the disease is

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widely known to feature premature atherosclerosis promoted by immune dysregulation. Neutrophil extracellular traps (NETs) can induce endothelial dysfunction and promote inflammatory events. Furthermore, sources of reactive oxygen species released during NET formation promote oxidised HDL, leading to deficient cholesterol efflux capacity (CEC). Type I interferons (IFNs) stimulate NET formation and inhibit vascular repair. Anifrolumab is a fully human, IgG1 κ monoclonal antibody that binds to IFNAR1 and blocks signalling of all type I IFNs. Thus, anifrolumab may decrease mechanisms of vascular damage in SLE.

Objectives: We evaluated the ability of anifrolumab to reduce *in-vivo* NET formation and improve CEC relative to standard of care (SOC) in the MUSE study.[1]

Methods: Baseline IFN gene signature (IFNGS) test status (high or low) of MUSE patients was determined as described.[1] Plasma samples from fasting patients (n=190) were obtained at days 1 and 365 of the MUSE study. Plasma MPO-, HNE- and CitH3-DNA NET complexes were quantified by ELISAs in the MUSE and healthy donor (HD) samples (n=20) as described.[2] Wilcoxon rank-sum test was used to assess differences between groups. Post-treatment samples from the placebo (n=52) and 300 mg anifrolumab (n=73) groups were compared with baseline samples. Significance of change from baseline was determined using Wilcoxon signed-rank test. CEC was tested as described.[3] Reproducibility of the CEC assay was assessed using percent coefficient of variation (CV) from the analysis of variance (ANOVA). SLE patients with defective baseline CEC were identified as those with CEC <2 standard deviations from the HD mean value in the same testing run.

Results: All three neutrophil NET complexes (NNCs) were elevated in SLE patients ($p<0.01$) and were significantly enriched in IFN test–high patients ($p<0.05$). Anifrolumab significantly decreased all three NNCs at Day 365 vs Day 1 ($p\leq0.05$), whereas in the placebo group, complexes did not change or increased. The CEC assay was reproducible (16.4% CV) across 2 days of testing for a subset of 26 baseline samples, and longitudinal changes in steroid dosage for the placebo group did not affect CEC. Greater baseline NET complex levels significantly correlated with poor baseline CEC ($p<0.05$). Anifrolumab significantly increased CEC in IFNGS test–high patients with defective CEC at baseline ($p<0.001$), whereas no significant changes occurred in the placebo group.

Conclusions: Circulating NNCs were significantly elevated in patients with moderate to severe SLE as compared with HDs. Anifrolumab decreased circulating NNCs. Although changes in steroid dosages during MUSE did not affect CEC, anifrolumab significantly improved CEC over SOC. This work supports continued assessment of anifrolumab effects on vascular inflammation and endothelial damage in SLE.

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OP0175 INTERFERON SIGNATURE MIGHT SERVE AS EARLY BIOMARKER FOR DEVELOPMENT OF LUPUS AND CORRELATES STRONGLY WITH MYXOVIRUS-RESISTANCE PROTEIN A

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Background: Incomplete systemic lupus erythematosus (iSLE) marks a group of patients with typical features of SLE, who do not meet classification criteria. Up to 55% progress to SLE, but there are no predictive markers available. Interferon (IFN) type-I is an important early mediator in SLE. The majority of SLE patients show upregulation of interferon-inducible genes. Levels of IFN-related soluble markers, which are more easily applicable, are also increased in SLE.

Objectives: To measure IFN signature and IFN-related soluble markers in iSLE patients to determine if these can serve as predictors of SLE.

Methods: Thirty iSLE patients (ANA titer ≥1:80, disease duration <5 years,≥1 ACR clinical feature), 39 SLE patients with quiescent disease (fulfilling ACR or SLICC criteria, SLEDAI ≤4) and 11 healthy controls (HC) were included. Clinical and serological data were retrieved from medical charts.

RNA was isolated from whole blood using PAXgene tubes, reversely transcribed to cDNA and quantitatively analysed by Real time PCR. IFN score was calculated based on cumulative expression of 12 IFN-related transcripts (IP-10, IFI44L, IFIT3, LY6E, MX1, SERPING1, IFITM1, IRF7, STAT1, C1QA, IFI16 and IRF9). A positive IFN-score was defined as >2 SD of the mean of the control group. Levels of IFN-related mediators, including IFN-γ induced protein 10 (IP-10) and Myxovirus-resistance protein A (MxA) were measured using ELISA.

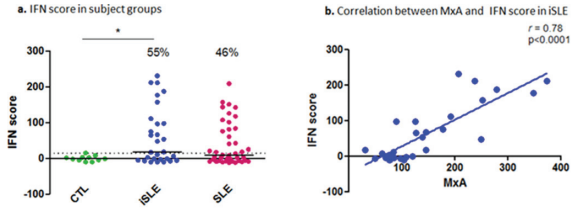
Statistical significance between groups was tested with Mann-Whitney U tests. Correlations of continuous data were calculated using Spearman's r test.

Results: Baseline characteristics are shown in table 1. An increased IFN score was present in 55% of iSLE patients (p=0.05) and 46% of SLE patients (p=0.07) (figure 1a).In iSLE, IFN score correlated positively with ESR (r=0.52, p=0.004), SSA titer (r=0.64, p=0.02) and cumulative number of ENA (r=0.57, p=0.001), and negatively with leukocyte count (r=-0.38, p=0.04), Hb (r=-0.39, p=0.04), and C4 (r=-0.47, p=0.01). SLEDAI, clinical symptoms, nor use of hydroxychloroquine were correlated with IFN score.

Abstract OP0175 – Table 1

	CTL (n=11)	iSLE (n=30)	SLE (n=39)
Female gender, n(%)	10 (91)	25 (79)	32 (82)
Age (median, range)	28 (25–65)	45 (20–83)	41 (19–76)
Disease duration, years median (range)		1.4 (0.1–4.6)	2.7 (0.5–6.8)
ACR criteria, median (range)		3 (1–3)	5 (2–9)
SLICC criteria, median (range)		3 (2–4)	5 (4–9)
SLEDAI median range)		0 (0–6)	2 (0–4)
Hydroxychloroquine use, n (%)		10 (33)	33 (85)
Immunologic features, n (%)			
ANA or SSA-pattern		30 (100)	39 (100)
Anti-dsDNA		9 (30)	33 (85)
Anti -SSA		14 (47)	12 (31)
Anti-Sm		3 (10)	6 (15)
Decreased complement		4 (13)	26 (67)

Levels of MxA correlated strongly with IFN score in both iSLE (r=0.78, p<0.0001) (figure 1b) and SLE (r=0.6, p<0.0001). IP-10 levels correlated with IFN score in iSLE (r=0.45, p=0.02), but not in SLE.



Abstract OP0175 – Figure 1 a) IFNscore in subject group, b) correlation between MxA and IFN score in iSLE

Conclusions: IFN-signature is present in 55% of patients with iSLE and correlates with ESR, autoantibody number, leukopenia, anaemia and hypocomplementemia. Interestingly, MxA levels correlated strongly with IFN-gene upregulation and thus might be a suitable and easily applicable surrogate marker for IFN type-I activity. iSLE patients with IFN upregulation might be those at most risk for disease progression; longitudinal data however should be awaited.

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