of autoantibodies detected at baseline did not change significantly during follow-up (median 1.5 (IQR 1-3, max. 6) to 1.0 (IQR 1-4, max. 6) ($p=0.18$)). In the patients with CSA that did not progress similar findings were made (1.0 (IQR 1-2, max. 4) at baseline and 1.0 (IQR 0-2, max. 5) after 2-years ($p=0.07$)). Increase in number of positive measurements over time took place in only few patients: in 15% of the patients that progressed to IA and in 18% from those that did not progress ($p=1.00$). Likewise, autoantibody levels did not significantly change over time, both in patients that progressed and in patients that did not progress.

Conclusion: The presence of IgM, IgG and IgA ACPA, anti-CarP and AAPA, as well as autoantibody levels, did not significantly increase over time in patients with CSA; this was similar for patients that did and did not develop clinical arthritis. These findings suggest that antibody-response maturation occurs before presenting with symptoms and also that broadening of the autoantibody response is not specific for progression from arthralgia to RA.

Disclosure of Interests: None declared

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THU0065

OXYLIPIN PROFILING DURING THE VERY EARLY PHASE OF RHEUMATOID ARTHRITIS: ASSOCIATIONS WITH DISEASE STAGE, CLINICAL FEATURES AND TREATMENT RESPONSE

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Background: traditional approaches and lipidomics support the relevance of eicosanoids in rheumatic conditions, such as rheumatoid arthritis (RA). Previous studies from our group and others have revealed altered levels of arachidonic acid in RA, pointing to a possible consumption or enhanced metabolism. However, the potential alterations of its actual metabolites are difficult to assess with conventional approaches, and new, untargeted, high-throughput technologies are needed. More importantly, whether these alterations are related to the disease course and could be found at the very early stage of the disease is unknown.

Objectives: to characterize the eicosanoid profiles during the earliest stages of RA and their potential clinical associations.

Methods: 60 very early RA patients (50 recruited at diagnosis and treatment-naïve) fulfilling 2010 ACR/EULAR criteria, 11 clinical suspect arthralgia (CSA) individuals and 28 healthy controls (HC) were recruited. Samples were collected at the moment of the diagnosis. Serum oxylipins profiles were analyzed by mass spectrometry (LC-MS/MS). Treatment-naïve patients underwent csDMARD treatment and were followed for 6 (n=49) and 12 months (n=38). Data analysis was performed in R and MetaboAnalyst.

Results: A total of 75 oxylipins, mostly derived from arachidonic (AA), eicosapentanoic (EPA) and linoleic (LA) acid, were identified. No effect was observed for age, gender or BMI. Correlation and network analyses revealed different patterns among oxylipins across RA patients, CSA and HC (Figure 1A). The 8-HETE, PGE3 and 20-HETE showed the pattern (linear increase) HC→CSA→RA ($p=1.47\cdot10^{-4}$, $5.34\cdot10^{-4}$ and $5.68\cdot10^{-4}$, respectively; and adjusted FDR<0.050) (Figure 1B). A PLS-DA (explaining 12.3% of the total variance, with a 71.0% cross-validation accuracy and permutation $p=5\cdot10^{-4}$) confirmed that oxylipins profiles differ among groups, although a certain overlap existed. A total of 22 oxylipins had VIP scores>1 (Figure 1C), which allowed the identification of two clusters (I and II). Cluster usage (I/II) differed among groups ($p=0.003$): HC (27/1), CSA (7/4) and RA (37/23). Patients exhibiting cluster II showed higher VAS global assessment ($p=0.016$) and pain ($p=0.003$) than their cluster I-counterparts. More importantly, cluster II patients were less likely to achieve DAS28 remission at 6 (12/17 vs 10/32, $p=0.008$) and 12 months (6/9 vs 9/29, $p=0.066$) upon conventional DMARD treatment compared to those showing cluster I.

OPLS-DA analyses revealed a good discrimination between CSA and HC groups, and 7 compounds (13-HODE, PGB2, 9-oxo-ODE, 12-oxo-ETE, 19,20-di-HDPA, 5-HETE and 15-HEPE) were associated with the course HC→CSA. Different precursors (2 LA, 3 AAA, 1 EPA and 1 DHA) and pathways were noted (3 LOX, 4 CYP450). Regarding RA subsets, differences were noted by seropositivity. Whereas 9 compounds were associated with the pattern HC→seronegative RA (8-HETE, PGE3, 20-HETE, 19,20-di-HDPA, PGEM, PGJ2, 12-oxo-LTB4, 14,15-EET and LTB4), a distinct set was observed for the pattern HC→seropositive RA (PGE3, 20-oh-PGE2, 5-HETE, PGE2, 12-oxo-ETE, 20-HETE, PGEM, 4-HdOHE, LTB4, 9-oxo-ODE, 12-oxo-LTB4, 8,9-EET). No differences in the major pathways were noted.

Conclusion: Oxylipin networks differ across disease stages during the very early phase of RA, and can inform on specific signatures related to the disease progression. Oxylipins can delineate profiles with clinical relevance and are able to predict treatment response.

Figure:

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THU0066

DOES PORPHYROMONAS GINGIVALLIS MODULATE GUT MICROBIOME RESULTING IN AGGRAVATION OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS?

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Background: Oral Porphyromonas gingivalis (Pg) infection in rheumatoid arthritis (RA) model revealed aggravation of arthritis, dysbiosis and higher serum LPS (1). We reported that IgA/IgG antibody against Pg-LPS ratio among the patients with RA related to disease marker levels and disease activities (2). However, there are still few reports related to Gut-Oral axis.

Objectives: Firstly, how total intestinal bacteria, well-known 5 species of gut bacteria behave in relation to disease activities and markers. Secondly, how infection by Pg aggravate RA in relation to microflora, disease activities and markers.

Methods: Eighty-seven RA patients with inadequate response to conventional synthetic DMARDs were evaluated. Age: 68.1 ± 8.7 years, female (%): 79.3, disease duration: 136 ± 91 months, DAS28-ESR: 4.68 ± 0.98 . Fecal bacteria numbers of total bacteria, Bifidobacterium, Lactobacillus, E. coli, Bacteroides and Staphylococcus were determined by PCR analysis. Fecal and serum LPS levels were measured by LAL assay. Serum endotoxin neutralizing activity (ENC) was determined along with RA disease activity and markers measurement. Infection of Pg was proofed by IgG and IgA anti-LPS antibody measurement. The statistical relationships between variables were analyzed by Spearman's non-parametric rank correlation analysis and expressed as Spearman's rank correlation coefficient "p".

Results: At first, we could neglect background effects as duration, methotrexate dose for measuring total or each bacterial number (data not shown). As shown in Figure 1, total bacteria only showed positive correlation with IL-6 levels ($p=0.230$, $p=0.034$), however inversely correlated with disease activities such as pVAS ($p=-0.223$, $p=0.038$) and Pain VAS ($p=-0.260$, $p=0.015$). While no significant relationship was observed between the numbers of each of 5 species of bacteria and the disease activities and makers except Bifidobacterium. In contrast, LPS-related markers showed positive correlation with disease activities and markers. Among LPS-related biomarker values, serum LBP levels mainly correlated with most of RA biomarker-ESR ($p=0.497$, $p<0.0001$), CRP ($p=0.697$, $p<0.0001$), MMP3 ($p=0.546$, $p<0.0001$) and so on. Fecal LPS level was shown significant positive correlation with disease activities, however almost no correlation was observed in serum LPS level. IgA anti-LPS antibody levels to Pg, resulted in inverse correlation with total bacteria ($p=-0.441$, $p<0.0001$), Lactobacillus ($p=-0.224$, $p=0.037$), Bacteroides ($p=-0.200$, $p=0.064$) and E. coli