vitro, Bergenin significantly increased the expression of ABCG2 as well as activated SIRT1, which was reversed by addition of PPAR γ antagonist GW9662 and siPPAR γ .

Conclusion: These findings suggest bergenin increases uric acid excretion both in the kidney and intestines, which may be related to the upregulation of ABCG2 via SIRT1-PPAR γ pathway.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.4163

AB0054

SYNOVIAL CD163+ MACROPHAGES ARE ASSOCIATED WITH RADIOGRAPHIC JOINT DESTRUCTION IN RHEUMATOID ARTHRITIS

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Background: CD163, a hemoglobin scavenger receptor, has been identified as a marker of M2 macrophages, it can promote the release of IL-10 and carbon oxide. Researches on inflammatory diseases and tumors have suggested that CD163 plays anti-inflammatory effect and promotes tumor growth and metastasis. Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by chronic synovitis with inflammatory cells infiltration including considerable macrophages. However, little is known about the role of CD163+ macrophages in RA synovium.

Objectives: To investigate the expression and clinical significance of synovial CD163+ macrophages in RA.

Methods: Seventy-five RA patients were recruited and clinical data including disease activity, HAQ and Sharp/van der Heijde-modified Sharp score of bilateral hands and wrists were collected. Synovial tissues were obtained by needle biopsies or arthroscopy of knee joints. Eighteen osteoarthritis (OA) and seventeen orthopedic arthropathies (orth.A) patients were included as controls. All synovium were stained with H&E and immunohistochemically for CD163, CD3, CD20, CD38, CD68, and CD15. Histologic changes of synovitis in H&E stained sections were graded with Krenn's synovitis score.

Results:

1. Positive CD163 expression were found in both lining synoviocytes and sublining inflammatory cells. Both densities of lining and sublining CD163+ macrophages in RA synovium were significantly higher than that in OA or Orth.A synovium (140.47 ± 66.93 vs. 17.85 ± 7.70 vs. 19.76 ± 5.26 and 417.92 ± 249.62 vs. 27.58 ± 14.19 vs. 29.87 ± 9.33 , all $P < 0.001$, Figure 1).
2. According to Krenn's synovitis score, there were 68% RA patients showing high synovitis (score > 4). Both lining and sublining synovial CD163+ macrophages were significantly higher than those showing low synovitis (lining: 158.40 ± 62.91 vs. 122.06 ± 66.74 , sublining: 462.96 ± 62.91 vs. 371.65 ± 271.54 , both $P < 0.05$). Meanwhile, the densities of lining and sublining CD163+ macrophages were both positively correlated with Krenn's synovitis score ($r = 0.238$ and 0.343 , both $P < 0.05$).
3. For clinical relationship in RA, the density of sublining CD163+ macrophages was positively correlated with total Sharp score (mTSS) ($r = 0.399$, $P < 0.001$), joint space narrowing subscore ($r = 0.248$, $P = 0.032$) and joint erosion subscore ($r = 0.457$, $P < 0.001$). While the density of lining CD163+ macrophages was positively correlated with mTSS ($r = 0.319$, $P = 0.005$) and joint erosion subscore ($r = 0.358$, $P = 0.002$). Meanwhile, the densities of sublining and lining CD68+ macrophages were also positively correlated with mTSS ($r = 0.253$ and 0.242 , both $P < 0.05$), of which the correlation was weaker than that of CD163+ macrophages (Figure 2). There were no significant correlation between the density of CD163+ macrophages and disease activity or HAQ (all $P > 0.05$).

Conclusion: Synovial CD163+ macrophages are associated with radiographic joint destruction, which imply that CD163+ macrophages may play role in the pathogenesis of joint destruction in RA.

Figure 1. Representative immunohistochemical findings of synovial CD163 expression. (A) Synovial CD163 expression in an Orth.A patient, an OA patient and a RA patient. (B) Densities of lining and sublining CD163+ macrophages in Orth.A, OA and RA patients.

Figure 2. Spearman's rank correlation analysis for synovial macrophages and mTSS in RA. (A) Correlation between sublining CD163+ macrophages and mTSS, joint space narrowing subscore, joint erosion subscore. (B) Correlation between lining CD163+ macrophages and mTSS, joint space narrowing subscore, joint erosion subscore.

Funding: : This work was supported by National Natural Science Foundation of China (no. 81801606 and 81971527), Guangdong Natural Science Foundation (no. 2017A030313576, 2018A030313541 and 2019A1515011928).

Figures:

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.1141

AB0055

SOLUBLE TREM-1 LEVELS IN FAMILIAL MEDITERRANEAN FEVER RELATED AA-AMYLOIDOSIS

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Background: Triggering Receptor Expressed on Myeloid cells-1 (TREM-1) is a monocyte and neutrophil receptor functioning in innate immunity. TREM-1 produces proinflammatory cytokines and serves for neutrophil degranulation. TREM-1 activity is well known in the pathogenesis of sepsis; hence it can be also present in autoinflammatory diseases such as the most common monogenic one, Familial Mediterranean Fever (FMF).

Objectives: The objective of this study is to measure soluble TREM-1 (sTREM-1) activity in severe FMF cases complicated with systemic AA-Amyloidosis.

Methods: The cohort of the study includes regularly followed FMF related AA-Amyloidosis patients in a tertiary center outpatient rheumatology clinic. Soluble TREM-1 levels were measured using enzyme-linked immunosorbent assay (ELISA). In addition, demographic data, renal function tests, acute phase reactants, and medical prescription history was also noted and analyzed. None of the FMF diagnosed patients had an attack during the collection of the blood samples.

Results: The patients were categorized into 4 groups: FMF related AA-Amyloidosis patients (A(+)) FMF(+)), FMF unrelated AA-Amyloidosis (FMF(-) A(+)),

FMF patients without Amyloidosis diagnosis (FMF(+) A (-)), and healthy controls (HC). The mean ages, TREM-1, C - reactive protein (CRP), and Creatinine levels of each group are shown in Table 1. TREM-1 levels were found to be significantly higher in A(+) FMF(+) group than FMF(+) A (-), and healthy control groups ($p=0.001$ and 0.002). Nevertheless, this difference was not found in between A(+) FMF(+) and FMF(-) A(+) ($p=0.447$). In addition, the TREM-1 levels of FMF(+) A (-), and healthy control groups were not different (0.532). In A(+) FMF(+) group, 36 patients used colchicine with the mean dose of 1.9 ± 0.8 mg/day, 14 patients used anakinra, and 9 patients used canakinumab. In FMF(+) A (-) group all 20 patients used colchicine with the mean dose of 2.8 ± 0.9 mg/day, 1 patient used anakinra, and 2 patients used canakinumab.

Table 1. Clinical Features of Patients and TREM-1 levels

	A(+) FMF(+) (n= 42)	FMF(-) A(+) (n=5)	FMF(+) A (-) (n=20)	HC (n=20)
Age	43.9 $\pm$ 12.9	54.8 $\pm$ 19	35.3 $\pm$ 9.64	35.4 $\pm$ 6.57
TREM-1	735.3 $\pm$ 566.5	1247.1 $\pm$ 1349.2	414.3 $\pm$ 142.3	439.2 $\pm$ 104.6
CRP	11.1 $\pm$ 14.2	51.3 $\pm$ 98.3	25.8 $\pm$ 54	1.8 $\pm$ 1.7
Creatinine	1.6 $\pm$ 1.8	3.28 $\pm$ 4.17	0.7 $\pm$ 0.15	0.7 $\pm$ 0.15

Conclusion: In conclusion, TREM-1 is a proinflammatory marker found significantly high in AA-amyloidosis patients regardless of their FMF diagnosis. TREM-1 may be useful in AA-amyloidosis follow-up and early diagnosis since currently there is a deficit of an early diagnostic marker of amyloidosis. This study is a cross-sectional one so it is hard to reach a conclusion on the effectiveness of TREM-1 during regular FMF follow-up for the secondary prevention of amyloidosis. However, the sensitivity of TREM-1 as a marker cannot be denied in amyloidosis.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.3426

AB0056

NATURAL ANTIBODIES AGAINST PHOSPHORYLCHOLINE AND MALONDIALDEHYDE DURING THE FIRST TWO YEARS OF LIFE: IMPLICATIONS FOR RHEUMATIC DISEASE

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Background: Antibodies against phosphorylcholine (anti-PC) have potentially protective properties in both atherosclerosis and rheumatic disease. IgM anti-PC could play a role in SLE being associated with protection, also in relation to atherosclerotic plaques and vulnerable plaques in SLE¹ and being a non-responder to biologics in RA. ¹ We reported potential mechanisms by which anti-PC could be protective: 1:anti-inflammatory; 2: inhibits uptake of oxLDL in macrophages, 3: inhibits cell death. ¹ 4: anti-PC (and anti-MDA) increases clearance of human dead cells which could be of importance not especially in SLE; ² 5: anti-PC increases T regulatory cells in SLE-patients' T cells from a low level and also in atherosclerosis, with implications for both conditions. ³ Also antibodies against malondialdehyde (anti-MDA) have interesting properties

Objectives: It is not known how these antibodies develop early in life and what may cause low levels. The objective is to determine this.

Methods: Antibodies were studied by ELISA in healthy pregnant women (n=105; Born into life study) and their newborn children. Women were recruited before conception. Informed consent, questionnaires from parents and plasma sample was collected from children at birth from cord blood, at 1-year and 2 years after birth. Extracted antibodies were compared using a proteomics de novo sequencing approach.

Results: Children were born with very low levels of IgM anti-PC, while IgM anti-MDA was present at birth.. Both IgM anti-PC and anti-MDA increased during the first two years of life, but IgM anti-PC in contrast to IgM anti-MDA was still significantly lower than mothers'. IgG anti-PC decreased after 1 year, but reached similar levels as mothers' after 2 years while IgG anti-MDA reached similar levels as mothers' already after one year. Proteomics peptide sequencing analysis indicates large peptide sequence variation without specific clone expression during early stage of life compared to the adult stage for which specific peptide sequences dominated.

Conclusion: IgM anti-PC levels develop much slower than anti-MDA and are still relatively low at 2 years. We hypothesize that anti-PC is developed by a combination of pre-programming and exposure to the external world, where infectious agents may play a role. For anti-MDA pre-programming is likely to play a major role and at an earlier stage than for anti-PC.

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Disclosure of Interests: Divya Thiagarajan: None declared, Susanna Lundström: None declared, Göran Pershagen: None declared, Catharina Almqvist Malmros: None declared, Ellika Andolf: None declared, Anna Hedman: None declared, Oscar Berg: None declared, Nina Oparina: None declared, Johan Frostegård Grant/research support from: Unconditional competitive grant from Amgen, related only to PCSK9, not the topic of this abstract

DOI: 10.1136/annrheumdis-2020-eular.5311

AB0057

THE ROLE OF NON-INFLAMMATORY MACROPHAGES INITIATING AND RESOLVING THE INFLAMMATORY RESPONSE OF MONOSODIUM URATE IN MICE

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Background: Gout is the most common chronic inflammatory arthritis around the world which is associated with many conditions that affect longevity and well-being, such as metabolic syndrome, cardiovascular diseases, and renal diseases. [1]

Objectives: Gout is the most common inflammatory arthritis around the world. Innate immunity has been implicated in gout inflammation in recent years. However, the phenomena of maintenance of 'asymptomatic' hyperuricemia, the spontaneous resolution of acute gouty arthritis and non-inflammatory tophus and its association with immune regulation are still elusive. We propose that resident macrophages may be a key player in the suppression of gouty inflammation. To address this hypothesis, we used non-inflammatory macrophages to explore the role played in initiating or resolving the inflammatory response.

Methods: Bone marrow-derived macrophages (BMDM) were stimulated with monosodium rate (MSU), then analyzed the expression of RNA and protein of inflammatory cytokines, including IL-1 β , IL-18 and TNF- α . In addition, we also observe the ability of macrophage to phagocytose and hydrolyze MSU crystal.

Results: Our results indicate that MSU alone could not induce IL-1 β , IL-18, and TNF- α mRNA expression and protein production. However, when macrophages were pre-stimulated with lipopolysaccharide (LPS) or MSU, as well as in combination the production of IL-1 β and IL-18 were significantly increased. Furthermore, MSU maybe amplifies LPS-induced protein production of IL-1 β and IL-18 but not in TNF- α . A temporal delay in the correlation between mRNA expression and protein production was shown. The results also indicated that macrophages could not only phagocytize MSU crystals but may also hydrolyze MSU crystals.

Conclusion: These data indicate that MSU crystal alone is insufficient to induce pro-inflammatory cytokines production, however, when exposed to an infectious source of infection, it will amplify the inflammatory response and there is a synergistic effect between MSU and LPS. This may explain the diverse clinic phenomena of 'asymptomatic' hyperuricemia, non-inflammatory tophus and acute gouty arthritis. The high efficiency of phagocytosis and hydrolyzed MSU crystals of macrophages may explain the spontaneous regression of acute gouty arthritis. These findings may provide a new therapy for the prevention and treatment of acute gout attacks.

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