are associated with reduced therapeutic efficacy as compared to RA patients with normal body composition. The unfavourable effect of body weight on disease activity was paralleled by a favourable, protective effect on joint destruction. This uncoupling is not fully elucidated yet, and should be further investigated.

Disclosure of Interest: None declared

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OP0151 DOCOSAHEXAENOIC ACID TREATMENT OF RHEUMATOID ARTHRITIS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSS-OVER STUDY

T. Neumann^{1,2}, C. Dawczynski^{3,4}, M. Dittrich⁵, K. Goetze⁶, A. Welzel¹, P. Oelzner¹, S. Voelker⁷, A.M. Schaible⁷, F. Troisi⁷, L. Thomas⁷, S. Pace⁷, A. Koeberle⁷, O. Werz⁷, P. Schlattmann⁸, S. Lorkowski^{3,4}, G. Jahreis^{3,4}.

¹Department of Internal Medicine III, Jena University Hospital, Jena, Germany;

²Department of Rheumatology, Kantonsspital St. Gallen, St. Gallen, Switzerland;

³Competence Cluster for Nutrition and Cardiovascular Health (nutriCARD);

⁴Department of Nutritional Biochemistry and Physiology, Institute of Nutrition;

⁵Department of Nutritional Physiology, Institute of Nutrition, Friedrich Schiller University of Jena;

⁶Department of Rheumatology, Jena University Hospital;

⁷Department of Pharmaceutical/Medical Chemistry; ⁸Department of Medical Statistics, Informatics and Documentation, Friedrich Schiller University of Jena, Jena, Germany

Background: Epidemiological studies and clinical investigations indicate a beneficial impact of long-chain n-3 polyunsaturated fatty acids (n-3 PUFA) on the inflammatory activity of rheumatoid arthritis (RA). However, the knowledge about the physiological effects of the individual compounds eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) is limited.

Objectives: In our pilot study presented here, we investigated the clinical benefit of daily intake of foods enriched with microalgae oil as source of DHA in RA patients. In particular, the influence on disease activity and changes in the profile of pro-inflammatory/non-resolving and anti-inflammatory/pro-resolving lipid mediators was examined.

Methods: This is a randomized, double-blind, cross-over study on 38 patients (32 females/6 males) with active RA (DAS28 $\geq$ 2.4). They were allocated to consume foods enriched with microalgae oil from *Schizochytrium* sp. (2.1 g DHA/day) or sunflower oil (placebo) for 10 weeks while maintaining stable immunosuppressive treatment.

Results: Thirty-two patients finished the study but seven patients were excluded from analysis because their DHA increase in erythrocyte lipids (EL) was less than 25% after 10 weeks of intervention indicating insufficient adherence to the intervention. Supplementation of DHA led to a decline in tender joints (TJ68) 8.4 $\pm$ 5.6 to 6.0 $\pm$ 5.0 (p=0.03), swollen joints (SJ66) 5.6 $\pm$ 3.5 to 3.9 $\pm$ 3.5 (p=0.07) and DAS28 4.3 $\pm$ 1.0 to 3.9 $\pm$ 1.2 (p=0.07). Joint counts in the placebo arm remained stable (TJ68) 6.7 $\pm$ 4.9 to 8.8 $\pm$ 8.0 (p=0.12), swollen joints (SJ66) 3.5 $\pm$ 3.0 to 4.2 $\pm$ 3.7 (p=0.40) and DAS28 4.0 $\pm$ 0.9 to 4.1 $\pm$ 1.2 (p=0.45). Ultrasound score (US-7) remained stable (15.1 $\pm$ 9.5 to 12.4 $\pm$ 7.0; p=0.160) while it increased in the placebo arm (11.4 $\pm$ 7.0 to 14.0 $\pm$ 8.8; p=0.03).

The amount of n-3 PUFA in erythrocyte increased in supplemented patients (7.0 $\pm$ 1.2% to 10.6 $\pm$ 1.4%; p<0.001) and the ratios of arachidonic acid (AA)/EPA (18.5 $\pm$ 6.3 to 12.6 $\pm$ 5.5; p<0.001) and AA/DHA (3.8 $\pm$ 1.0 to 1.8 $\pm$ 0.6; p<0.001) dropped significantly. Fatty acid distribution in erythrocyte lipids (n-3 PUFA, AA/EPA and AA/DHA) remained stable in the control arm.

Conclusions: The study shows that microalgae DHA supplements can ameliorate disease activity in patients with active RA along with a shift in the balance of AA- and DHA-derived lipid mediators towards an anti-inflammatory/pro-resolving state.

Disclosure of Interest: None declared

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OP0152 A LONGITUDINAL STUDY OF THE EFFECTS OF DISEASE ACTIVITY ON RENAL FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS UTILIZING LINEAR MIXED EFFECT MODELS - ANSWER COHORT STUDY -

A. Onishi¹, K. Akashi¹, M. Hashimoto², M. Furu², W. Yamamoto², M. Katayama³, R. Hara⁴, T. Fujimura⁵, S. Yoshida⁵, K. Nagai⁵, T. Hirano⁶, K. Ebina⁷, Y. Son⁸, H. Amuro⁸, H. Yamada¹, Y. Ichise¹, D. Waki¹, I. Naka¹, K. Tsuda¹, T. Okano¹, S. Takahashi¹, S. Sendo¹, Y. Ueda¹, Y. Kogata¹, J. Saegusa¹, A. Morinobu¹. ¹Department of Rheumatology, Kobe University Hospital, Kobe; ²Department of the Control for Rheumatic diseases, Graduate School of Medicine, Kyoto University, Kyoto; ³Department of Rheumatology and Clinical Immunology, Osaka Red Cross Hospital, Osaka; ⁴The Center for Rheumatic Diseases, Nara Medical University, Nara; ⁵Department of Internal Medicine (I), Osaka Medical College; ⁶Department of Respiratory Medicine, Allergy and Rheumatic Disease, Graduate School of Medicine, Osaka University; ⁷Department of Orthopaedic Surgery, Osaka University, Graduate School of Medicine; ⁸First Department of Internal Medicine, Kansai Medical University, Osaka, Japan

Background: Patients with RA have higher risk of developing chronic kidney disease compared to the general population. Although some causes of renal

impairment in RA include nephrotoxic medications, amyloidosis, and glomerulonephritis, specific causes are not determined among most patients with RA. While experimental researches showed inflammatory process per se might also contribute to renal dysfunction, the results of previous clinical studies that assessed the effects of disease activity or C-reactive protein on renal function were inconsistent. This inconsistency might be attributable to their cross-sectional design, small sample size, and assessment of association between only baseline characteristics and renal outcomes without consideration for the fact that disease activity and medications had changed over time.

Objectives: To identify the effects of disease activity on renal function in RA in a multi-center cohort study.

Methods: RA patients with a sampling interval of less than 150 days were enrolled because wide sampling intervals could not take into consideration changes in disease activity and medications during their follow-up. An estimated glomerular filtration rate (eGFR) was calculated using an equation approved by the Japanese Society of Nephrology and used as an outcome variable. Linear mixed effect models were used to evaluate the renal trajectories of patients. Time from baseline (months), disease activity, and their interaction were included as fixed effects while participant identification number and time from baseline were included as random factors. Age, sex, disease duration, RF, ACPA, NSAIDs, and DMARDs that were known as a cause of renal impairment, such as tacrolimus, iguratimod, and tofacitinib, were included as covariates.

Results: A total of 25661 samples (mean sampling interval: 2.0 months) from 2104 patients was included. Patients with lower DAS28-CRP had worse renal function at inclusion, but a significantly better longitudinal trajectory on eGFR (0.0079 ml/min/1.73m² per month, P=0.025). Although all RA patients had naturally progressive renal impairment as they got older, patients who achieved remission or low disease activity had slower renal impairment rate of -0.068 ml/min/1.73m² per month compared to patients with moderate or high disease activity (-0.084 ml/min/1.73m² per month; P=0.037). These results were also similar using SDAI or CDAI.

Evolution of renal function over time based on disease activity

Conclusions: Lower disease activity results in slower renal impairment. Because the effects of disease activity on renal function are mild, additional measures to protect renal function, such as avoiding nephrotoxic medications and treating cardiovascular risk factors are important.

Disclosure of Interest: None declared

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OP0153 RECURRENT INFECTIONS IN RHEUMATOID ARTHRITIS PATIENTS, RESULTS FROM THE BSRBR

S. Subesinghe¹, A.I. Rutherford¹, R. Byng-Maddick², J.B. Galloway¹.

¹Rheumatology, King's College London; ²Homerton Hospital, London, United Kingdom

Background: Rheumatoid arthritis (RA) patients have an increased susceptibility to infection.

Objectives: 1.To establish the rate of recurrent infection in RA patients recruited to the British Society of Rheumatology Biologics Registry Rheumatoid Arthritis (BSRBR-RA).2.To establish whether the organ class of index infection predicted future serious infection.

Methods: The BSRBR-RA is a prospective observational cohort, previously described. Patients with at least one episode of serious infection requiring hospitalisation were included if they occurred whilst on anti-rheumatic drug therapy or within 5 drug half-lives of stopping. Infections were coded by MedDRA classification in to 7 categories. Infections occurring over 14 days after the first index infection were considered as new events. Event rates were calculated and compared using a Cox proportional hazards model with adjustments made for age, gender, disease duration, baseline DAS28 score, smoking status and seropositivity.

Results: See Table 1.

In total, 21,943 subjects with 115,423 patient-years follow up were studied, 5365 subjects reported at least one serious infection. Comparing organ classes of prior infection at baseline, each group had comparable age, disease duration, baseline DAS28 and HAQ scores. The cohort characteristics are tabulated. The baseline annual rate of first serious infection was 4.6% (95% CI 4.5–4.7). Following an

Abstract OP0153 – Table 1

	Overall	Patients with infection	Respiratory	Gastrointestinal	Genitourinary	Musculoskeletal	Sepsis	Skin/Soft Tissue	Other
Age, years (SD)	57.3 (12.5)	61.5 (11.7)	60.0 (11.5)	61.7 (11.1)	59.8 (11.9)	58.7 (10.5)	63.5 (11.2)	57.9 (11.9)	55.3 (11.4)
Female (%)	75.7	72.6	74.8	77.4	89.2	70.2	76.6	79.5	83.3
Baseline DAS28 (SD)	6.2 (1.2)	6.4 (1.2)	6.3 (1.2)	6.3 (1.1)	6.3 (1.2)	6.5 (1.2)	6.4 (1.1)	6.4 (1.1)	6.3 (1.1)
Baseline HAQ (SD)	1.9 (0.7)	2.1 (0.6)	2.0 (0.6)	2.1 (0.6)	2.1 (0.6)	2.1 (0.6)	2.2 (0.5)	2.0 (0.6)	1.9 (0.6)
Steroid use, n (%)	8346 (38.2)	2632 (49.4)	2832 (43.8)	493 (51.5)	1226 (44.5)	390 (51.6)	316 (57.3)	1583 (45.2)	1267 (39.6)
Current smoker, n (%)	4682 (21.7)	1159 (21.9)	1422 (22.1)	165 (17.3)	452 (16.4)	186 (24.8)	122 (22.4)	692 (19.9)	573 (18.0)
RhFactor positive, n (%)	13,340 (63.2)	3533 (67.5)	4176 (66.1)	626 (66.2)	1737 (64.6)	527 (71.4)	361 (66.1)	2241 (65.6)	2003 (64.0)
Recurrent infection rate, % per annum (95% CI)	—	12.7 (12.1–13.2)	15.0 (13.9–16.2)	10.8 (9.2–12.8)	14.5 (12.7–16.5)	10.1 (8.7–11.8)	19.7 (15.1–25.7)	11.2 (10.1–12.5)	9.1 (7.3–11.4)
Adjusted Hazard Ratio for annual incidence of recurrent infection (95% CI)	—	—	REF	0.79 (0.65–0.95)	0.97 (0.83–1.14)	0.81 (0.67–0.96)	1.33 (1.01–1.76)	0.87 (0.77–1.0)	0.70 (0.54–0.91)

index infection, the annual rate of serious infection was 12.7% (95% CI 12.1–13.3). Respiratory infections were the most common (41.4% of all events). The system class of index infection was associated with the risk of a recurrent event; subjects who experienced sepsis had the highest risk of subsequent serious infection within 12 months:19.7%. Compared to an index respiratory tract infection, sepsis conferred a 33% increased hazard for recurrent serious infection within a year (HR 1.33, 95% CI 1.01–1.76). Increasing age was a significant predictor of infection recurrence.

Conclusions: There is a high risk of recurrent infection in RA patients with past serious infection. Work is ongoing to determine whether organ class of recurrent infection event mirrors index events and the impact of biologic treatment decisions following the index infection.

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THURSDAY, 15 JUNE 2017
Advances in RA and SpA pathophysiology

OP0154 **ALTERED LYMPH NODE STROMAL CELLS DURING THE EARLIEST PHASES OF RHEUMATOID ARTHRITIS**

C. Ospelt¹, E. Karouzakis¹, J. Hähnlein², J.F. Semmlink², R.E. Gay¹, P.P. Tak^{2,3}, D.M. Gerlag^{2,4}, S. Gay¹, L.G. van Baarsen². ¹Center of Experimental Rheumatology, University Hospital of Zurich, Zurich, Switzerland; ²Academic Medical Center, Amsterdam, Netherlands; ³Cambridge and GlaxoSmithKline, University of Cambridge, Stevenage; ⁴R&D Projects Clinical Platforms & Sciences, GSK Clinical Unit Cambridge, Cambridge, United Kingdom

Background: Lymph node stromal cells (LNSC) play a crucial role in shaping the immune response and maintaining peripheral tolerance. We developed an experimental model for studying the functional capacities of human LNSC during the earliest phases of RA and compared their cellular and molecular characteristics to LNSC from healthy volunteers.

Methods: ACPA+ RA patients (n=24), ACPA+ RA-risk individuals (n=23) and seronegative healthy controls (n=14;HC) underwent ultrasound-guided inguinal lymph node biopsy. Human LNSCs were isolated and expanded *in vitro* for cellular (flow cytometry), molecular (methylome, transcriptome and microRNA) and functional (contraction) analyses.

Results: RNA sequencing was performed on LNSC of HC (n=5), ACPA+ RA-risk individuals (n=6) and ACPA+ RA patients (n=4). Of interest, LNSC from ACPA+ RA-risk individuals and ACPA+ RA patients were more similar to each other compared with HC. Pathway analysis of commonly increased genes in RA (-risk) LNSC showed, among others, significant enrichment of pathways affecting actin cytoskeleton, focal adhesion and cell junction. DNA methylation (Illumina HumanMethylation450 array) analyses revealed 459 differentially methylated CpG sites (DMS) in LNSC from ACPA+ RA patients (n=5) versus HC (n=4), 504 DMS between ACPA+ RA-risk individuals (n=3) versus HC and 665 DMS when comparing RA patients with RA-risk individuals (delta β -value >0.1, p<0.05). 34 DMS were different in both RA and RA-risk LNSC compared to healthy LNSC. 80% of these DMS were significantly hypomethylated and associated with antigen processing and presentation (HLA-DRB1), immune response and regulation of actin cytoskeleton.

Accordingly, in a gel contraction assay LNSC from ACPA+ RA-risk individuals and RA patients showed impaired collagen contraction compared to healthy LNSC. Healthy LNSC (n=5) covered 26.5% $\pm$ 2.5 of the well, while RA-risk (n=4) and RA (n=5) LNSC only covered 33.9% $\pm$ 5.9 and 30.6% $\pm$ 6.5.

Conclusions: This data point towards alterations in the cytoskeleton and antigen-processing and presentation in LNSC from ACPA+ RA-risk individuals and RA patients. Further studies are required to investigate the influence of this LNSC abnormality on immune responses.

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OP0155 **MDM2-MEDIATED SUMOYLATION OF P53 CONTRIBUTES TO THE MIGRATION AND INVASION OF FIBROBLAST-LIKE SYNOVIOCYTES FROM PATIENTS WITH RHEUMATOID ARTHRITIS**

M. Shi^{1,2}, H. Xu¹, G. Chen². ¹Department of Rheumatology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou; ²Department of Rheumatology, The First People's Hospital of Foshan, Foshan, China

Background: Fibroblast-like synoviocytes (FLSs) in the synovial intimal lining are essential in the maintenance of synovial inflammation and progressive joint destruction in the development of Rheumatoid arthritis (RA). However, the precise molecular mechanisms by which this pathogenic process is regulated are not clearly defined.

Objectives: Increasing evidence indicates that p53 plays a critical role in the invasion and metastasis of cancer cells. This study aims to investigate the role of MDM2-mediated sumoylation of p53 in regulating the migration and invasion of fibroblast-like synoviocytes (FLSs) from patients with RA.

Methods: Synovial tissues were obtained from OA and RA patients, and then FLSs were separated from synovial tissues. Protein expression was measured by Western blotting or IHC staining. The sumoylation of p53 in cells was determined by immunoprecipitation. A specific inhibitor of MDM2-p53 interaction was used to inhibit the sumoylation of p53. Migration and invasion of FLSs *in vitro* were measured by the Boyden chamber assay.

Results: MDM2, SUMO1, and SUMO2 expression was significantly increased in the synovial tissue and FLSs of RA patients. Stimulation with TNF- α increased MDM2 expression and p53 sumoylation in RA FLSs. MDM2 shRNA inhibited p53 sumoylation, pro-inflammatory cytokines and MMPs expression, and capacity of *in vitro* migration and invasion in RA FLSs. Inhibition of p53 sumoylation by MDM2 shRNA promoted apoptosis and reduced proliferation of RA FLSs. p38 MAPK signal pathway was involved in the downstream signal transduction in RA FLSs. Administration of MDM2 shRNA expressing lentivirus attenuate the severity of rats with collagen-induced arthritis (CIA).

Conclusions: Increased MDM2-mediated p53 sumoylation contributes to aberrant aggressive behaviours of RA FLSs. Our findings suggests inhibition of MDM2 or p53 sumoylation might be a novel therapeutic strategy to prevent synovial invasiveness and joint destruction in RA.

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