Table 1. Baseline characteristics / logistic regression analysis

Variable	NOAR			ESPOIR		
	Low HAQ trajectory, mean (SD)	High HAQ trajectory, mean (SD)	OR (95% CI)	Low HAQ trajectory, mean (SD)	High HAQ trajectory, mean (SD)	OR (95% CI)
N (%)	343 (59%)	239 (41%)	-	131 (55%)	108 (45%)	-
Age, years	54.9 (14.2)	62.1 (13.8)	1.07 (1.05, 1.08)	47.8 (13.3)	51.8 (11.2)	1.04 (1.01, 1.06)
Women, N (%)	224 (65.3%)	176 (73.6%)	1.82 (1.12, 2.78)	100 (76.3%)	95 (88.0%)	2.73 (1.20, 6.23)
Symptom duration, months	7.8 (5.1)	8 (5.4)	1.10 (0.98, 1.05)	3.4 (1.8)	3.6 (1.8)	1.16 (0.98, 1.37)
Current smoker, N (%)	77 (22.4%)	50 (20.9%)	1.19 (0.71, 2.00)	61 (46.6%)	52 (48.1%)	1.52 (0.82, 2.83)
DAS28-2C	3.14 (1.46)	3.21 (1.56)	-	4.65 (1.31)	4.41 (1.35)	-
HAQ	0.8 (0.6)	1.4 (0.5)	-	1.1 (0.6)	1.6 (0.6)	-
Pain (0-10)	3.7 (2.4)	4.6 (2.5)	1.16 (1.07, 1.26)	4.1 (2.8)	5.1 (2.6)	1.07 (0.95, 1.20)
Fatigue (0-10)	4.3 (2.8)	5.3 (2.5)	1.16 (1.06, 1.28)	5.0 (2.6)	6.5 (2.5)	1.20 (1.05, 1.36)
AIMS anxiety	3.99 (1.96)	4.42 (1.99)	1.06 (0.88, 1.29)	4.9 (2.26)	5.98 (2.25)	1.10 (0.94, 1.29)
AIMS depression	2.85 (1.87)	3.38 (1.87)	1.10 (0.94, 1.29)	3.96 (1.99)	5.08 (2.32)	1.12 (0.94, 1.33)
RF+, N (%)	142 (41.4%)	106 (44.4%)	0.94 (0.60, 1.46)	79 (60.3%)	50 (46.3%)	0.77 (0.34, 1.75)
Anti-CCP+, N (%)	113 (32.9%)	86 (36.0%)	1.35 (0.84, 2.17)	76 (58.0%)	45 (41.7%)	0.89 (0.39, 2.05)

calculated from swollen joint counts and C-reactive protein level. Inclusion criteria for this analysis: <2 years baseline symptom duration; HAQ and DAS28-2C at baseline and one other follow-up; recruited after 1/1/2000. HAQ and DAS28-2C were modelled simultaneously using a multivariate group-based trajectory model, to identify groups of participants with similar trajectories of HAQ and DAS28-2C over 10 years. Baseline demographics and PROs were compared between the trajectory groups using logistic regression. Analyses performed separately in NOAR and ESPOIR.

Results: 1001 NOAR and 767 ESPOIR participants were included. In both cohorts, a four group trajectory model had the best fit (Figure). Two subgroups were identified in each cohort that demonstrated the hypothesised relationship: similar DAS28-2C but differing HAQ scores (red trajectories in Figure), titled "High HAQ" and "Low HAQ" (mean difference in HAQ over follow-up [95% confidence interval (CI)]: NOAR 0.76 [0.73, 0.80]; ESPOIR 0.89 [0.82, 0.96]). At baseline, the High HAQ groups in both NOAR and ESPOIR were older, had a higher proportion of women, and had higher levels of fatigue (NOAR: odds ratio [OR] 1.16 [95% CI 1.06, 1.28]; ESPOIR: OR 1.20 [95% CI 1.05, 1.36] [Table]) and pain (NOAR only).

Conclusion: There is a group of people with RA with high levels of disability, despite low inflammation. These results underline the potential need for pain and fatigue management in people with RA, even when inflammation is low.

REFERENCES:

[1] Hensor et al (2019). *Rheumatology (Oxford)* 58(8)

Acknowledgements: Thanks to the participants of NOAR and ESPOIR and those working in the recruiting centres

INSERM supported part of the biological database. The French Society of Rheumatology, Abbvie, Pfizer, Lilly and more recently Fresenius and Biogen supported the ESPOIR cohort study.

Disclosure of Interests: James Gwinnett Grant/research support from: Research grant from Bristol Myers Squibb unrelated to this project, Sam Norton Consultant of: Pfizer and AstraZeneca, Kimme Hyrich Consultant of: Abbvie, Grant/research support from: Pfizer and BMS, Mark Lunt: None declared, Bernard Combe: None declared, Nathalie Rincheval: None declared, Adeline Ruyssen-Witrand: None declared, Bruno Fautrel: None declared, Jacqueline Chipping: None declared, Alex MacGregor: None declared, Suzanne Verstappen: None declared

DOI: 10.1136/annrheumdis-2021-eular.1770

OP0184 PHENOTYPING OF MOLECULAR SIGNATURES IN THE SYNOVIAL TISSUE OF RHEUMATOID ARTHRITIS BY INTEGRATIVE SYSTEMS ANALYSIS

J. Qiao^{1,2,3}, S. X. Zhang^{1,2,3}, H. Wang^{1,2,3}, J. Q. Zhang^{1,2,3}, M. T. Qiu^{1,2,3}, M. J. Chang^{1,2,3}, R. Zhao^{1,2,3}, S. Song^{1,2,3}, G. Y. Liu¹, P. F. He⁴, X. Li^{1,2,3}. ¹The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China; ²Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China; ³Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China; ⁴Shanxi Medical University, Medical Data Sciences, Taiyuan, China

Background: Rheumatoid arthritis (RA) is an aggressive immune-mediated joint disease characterized by synovial proliferation and inflammation, cartilage destruction, and joint destruction¹. Despite efforts to characterize the disease subsets and to predict the differential prognosis in RA patients, disease heterogeneity is not adequately translated into the current clinical subclassification².

Objectives: To develop and validate an integrative system approach for stratifying patients with RA according to disease status and whole-genome gene expression data.

Methods: An RNA sequencing dataset of synovial tissues from 124 RA patients (including 57 patients with early RA, 95 with established RA) and 15 healthy controls (HC) was imported from the Gene Expression Omnibus (GEO) database (GSE89408) by software package R (version 4.0.3). After filtering of differentially expressed genes (DEGs) between RA and HC, non-negative matrix factorization, functional enrichment, and immune cell infiltration were applied to illustrate the landscapes of these patients for classification. Clinical features (age, gender, and auto-antibodies) were also compared to discover the signatures of these classifications.

Results: A matrix of 576 DEGs from RA samples was classified into 5 subtypes (early/C1–C3, established/C4–C5) with distinct molecular and cellular signatures and two sub-groups (S1 and S2) (Figure 1A–1D). New-onset patients (early C2) and established C4 patients were named as S1, they shared similar gene signatures mainly characterized by prominent immune cells and proinflammatory signatures, and enriched in the chemokine-mediated signaling pathway, lymphocyte activation, response to bacterium and Primary immunodeficiency. S2(C1, C3 and C5) were more occupied by synovial fibroblasts of destructive phenotype. They were mainly enriched in the response to external factors and PPAR signaling pathway (Figure 1E–1H). Interestingly, combined with clinical information, S1 and S2 had no significance in age and gender ($P > 0.05$). But patients in S1 had a stronger association with the presence of anti-citrullinated protein antibodies (ACPA) ($P < 0.05$) (Figure 1I–1J).

Conclusion: We successfully deconvoluted RA synovial tissues into pathobiological discrete subsets using an unsupervised machine learning method and described their distinct molecular and cellular characteristics. These results

Figure 1 - Trajectory analysis in NOAR (upper) and ESPOIR (lower) - dotted red = "high HAQ", solid red = "low HAQ", grey lines indicate other trajectory groups identified by the Group-Based Trajectory Analysis.

ESPOIR Funding: An unrestricted grant from Merck Sharp and Dohme (MSD) was allocated for the first 5 years of the cohort study. Two additional grants from

provide important insights into divergent and shared mechanistic features of RA and serve as a template for future studies to guide drug target discovery by synovial molecular signatures and de-sign stratified approaches for patients with RA.

REFERENCES:

- [1] Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet* 2016;388(10055):2023-38. doi: 10.1016/S0140-6736(16)30173-8 [published Online First: 2016/10/30]
- [2] Jung SM, Park KS, Kim KJ. Deep phenotyping of synovial molecular signatures by integrative systems analysis in rheumatoid arthritis. *Rheumatology (Oxford)* 2020 doi: 10.1093/rheumatology/keaa751 [published Online First: 2020/11/25]

Figure 1 Identification of RA patients using non-negative matrix factorization, functional enrichment, and immune cell infiltration in the differentially expressed genes set. (A-D) The consensus map of NMF clustering results in the total RNA sequencing dataset. Patients were divided into cluster 1-5 according to the expression profiles of 576 DEGs. Heatmap of five clusters defined by the cluster-based genes expression. (E-F) Gene Ontology (GO) terms and KEGG pathway related to common cluster-based gene signatures. (G-H) Cell subset enrichment score according to RA subgroup. (I-J) Distribution of the five RA subgroups by clinical phenotypes (the positivity of ACPA). (ns, not significant; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$)

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1970

OP0185

RADIOGRAPHIC PROGRESSION DESPITE PERSISTENT LDA OR REMISSION IS INFLUENCED BY CURRENT SMOKING RATHER THAN THE RESPECTIVE DAS 28 LEVEL, RESULTS OF THE SWISS RHEUMATOID ARTHRITIS REGISTER (SCQM)

L. Brandt^{1,2}, H. Schulze-Koops³, T. Hügler⁴, M. J. Nissen⁵, H. Paul⁶, B. Müller⁶.

¹Division of Rheumatology, Medical University Department, Kantonsspital Aarau, Aarau, Switzerland; ²Ludwig-Maximilians-University Munich, Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, Munich, Germany; ³Ludwig-Maximilians-University Munich, Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, Munich, Germany; ⁴University Lausanne, Division of Rheumatology, University Hospital Lausanne (CHUV), Lausanne, Switzerland; ⁵Geneva university hospital, Rheumatology, Geneva, Switzerland; ⁶Kantonsspital Aarau, Division of Rheumatology, Medical University Department, Aarau, Switzerland

Background: The therapeutic aim for rheumatoid arthritis (RA) is to control disease activity and prevent radiographic progression. Various clinical scores are utilized to describe disease activity in RA patients. The DAS28 score can define states of low disease activity (LDA) and remission. Despite achieving LDA or remission, radiographic progression may nevertheless occur. However, the rates and frequency of this occurrence have not been analyzed in detail.

Objectives: To describe the frequency and rate of radiographic progression in patients with persistent LDA or remission.

Methods: Analysis of RA patients from the SCQM cohort. Persistent LDA or remission were defined as DAS 28 ≤ 3.2 or < 2.6 respectively, at two subsequent follow up time points in the database. We included patients with at least two sets of radiographs within these intervals of LDA and/or remission. Radiographic progression was measured with the Raitingen-score (range 0-190), which describes joint erosions numerically. Repair was defined as an improvement in the Raitingen score > 5 points/year and progression as > 2 or > 5 points change in the Raitingen score within one year.

Results: Among 10'141 RA patients, 4'342 episodes of remission occurred in 3'927 patients with 1'776 sets of X rays available within these episodes. Similarly, 8'136 episodes of LDA in 6'765 patients and 2'358 sets of X rays were present within these intervals. For patients in LDA or remission, rates of repair were 5.5% and 4.8%, respectively, while for radiographic progression > 5 points in the Raitingen score/year were 10.3% in both groups and for > 2 points change of Raitingen score/year were 27.7 and 25.4%, respectively.

No differences for demographic factors or measures of disease activity, rheumatoid factor or ACPA were found comparing patients with radiographic progression or non-progression despite LDA or remission at the beginning of the episode of LDA and/or remission.

Interestingly, 42.9% of patients in LDA with progression of > 5 points in the Raitingen score/year were current smokers vs 29.4% among the non-progressors ($X^2 = 6.55$, $p = 0.01$). This significant difference vanished when the cut-off for radiographic progression was set at > 2 points yearly change in Raitingen score or in patients in remission.

Conclusion: Radiographic progression despite LDA or remission are more frequent than expected. No differences in radiographic progression were found comparing LDA and remission suggesting that the goal of LDA is appropriate. Smoking seems to be an independent risk factor for radiographic progression despite LDA. Why the effect of smoking could was not demonstrated in patients in remission, remains unclear.

Disclosure of Interests: Lena Brandt: None declared, Hendrik Schulze-Koops: None declared, Thomas Hügler Consultant of: GSK, Abbvie, Pfizer, Jansen, Novartis, Eli Lilly, Michael J. Nissen Consultant of: Abbvie, Celgene, Eli-Lilly, Janssen, Novartis and Pfizer, Hasler paul Consultant of: Abbvie, Lilly, Rudiger Muller Consultant of: Abbvie, Novartis, Grant/research support from: Gebro
DOI: 10.1136/annrheumdis-2021-eular.2557

Oncorheumatology: the crossroads of cancer and musculoskeletal diseases

OP0186

CHANGES IN CIRCULATING B CELL LEVELS AND IMMUNOPHENOTYPE ARE ASSOCIATED WITH DEVELOPMENT OF ARTHRITIS FOLLOWING TREATMENT WITH CHECKPOINT INHIBITORS

M. Gatto^{1,2,3}, S. Björsten^{3,4}, C. Jonell¹, C. Jonsson¹, S. McGrath¹, A. Rudin¹, M. Levin^{3,4,5}, I. Gertsson¹. ¹University of Gothenburg, Rheumatology and Inflammation Research, GOTHENBURG, Sweden; ²University of Padova, Unit of Rheumatology, Padova, Italy; ³University of Gothenburg, Oncology, Sahlgrenska University Hospital, GOTHENBURG, Sweden; ⁴University of Gothenburg, Oncology, Institute of Clinical Sciences, Sahlgrenska Academy, GOTHENBURG,