higher or lower concentrations in the PsA group compared to the control or the RA group. We selected two of these significant metabolites to build a classification model based on the linear support vector machine (SVM) method, and the area-under-the-curve (AUC) value of the resulting receiver operating characteristic (ROC) curve was 0.929 (95% confidence interval: 0.899-0.956). Similarly, 37 metabolites could differentiate AS samples from RAs and controls. A proposed diagnostic panel containing four metabolites demonstrated an AUC value of 0.890 (0.843-0.934). For the last step, distinguishing between PsA and AS, there were 15 significantly increased metabolites and 9 lowered ones. The biomarker panel consisting of the top three metabolites also achieved good discriminatory power with AUC = 0.827 (0.717-0.919).

Conclusion: Isotope-labeling-LC-MS-based metabolomics has revealed biomarker candidates that can specifically differentiate PsA or AS patients from control populations.

Disclosure of Interests: Wei Han: None declared, Xiaohang Wang: None declared, Liang Li: None declared, Stephanie Wichuk: None declared, Edna Hutchings: None declared, Rana Dadashova: None declared, Joel Paschke: None declared, Walter P Maksymowych Grant/research support from: Received research and/or educational grants from Abbvie, Novartis, Pfizer, UCB, Consultant of: WPM is Chief Medical Officer of CARE Arthritis Limited, has received consultant/participated in advisory boards for Abbvie, Boehringer, Celgene, Eli-Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, UCB, Speakers bureau: Received speaker fees from Abbvie, Janssen, Novartis, Pfizer, UCB.

DOI: 10.1136/annrheumdis-2020-eular.5912

OP0305

RHO-GTPASE PATHWAYS MAY DIFFERENTIATE RESPONDER AND NON-RESPONDERS TO TUMOUR NECROSIS FACTOR INHIBITOR (TNFi) AND INTERLEUKIN-17A INHIBITOR (IL-17Ai) THERAPY IN PSORIATIC ARTHRITIS (PSA)

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Background: In PsA there is a pressing need to develop a coherent strategy for identifying initial and subsequent biologic responders. PsA patients present substantial heterogeneity in response to biologics, and molecular subtyping will help to identify the right patient for the right treatment.

Objectives: To identify transcript profiles (biomarkers) that will select TNFi and IL-17Ai responders in PsA using baseline CD4+ cells; and elucidate novel signaling pathways relevant to biologic disease modifying antirheumatic drug (bDMARD) response using a systems biology approach.

Methods: Consenting patients initiating TNFi agents (20 patients) or IL-17Ai agents (20 patients) with moderate-to-severe PsA were assessed with a comprehensive standardized protocol at baseline and at 3 months. Responder to bDMARDs was defined by Disease Activity Index for Psoriatic Arthritis (DAPSA) score of less than 14 (low disease activity). Global transcript profiling was performed on all patients prior to initiation of and 3 months post bDMARDs. We mapped RNA-seq reads to the hg19 reference genome using STAR and quantified transcripts with Cufflinks. The transcripts per million (TPM) values were log-transformed for statistical analyses

Results: The demographics of PsA patients for both treatment groups are presented (Table 1). Differentially expressed genes (DEGs) were identified using the limma tool for TNFi and IL-17Ai responders and non-responders (Figure 1) as well as DEGs that differentiated TNFi from IL-17Ai response and non-response. Integration of differential gene expression data with tissue-specific protein-protein interactions (IID version 2018-11) identified 117 and 132 DEGs between responders and non-responders to TNFi and IL-17Ai treatments, respectively. Comprehensive pathway enrichment analysis of these genes using pathDIP (v 4.1) revealed 576 (out of 5380) pathways enriched in 117 DEGs between responders and non-responders to TNFi, and 125 pathways enriched in 132 DEGs between responders and non-responders to IL-17Ai. Interestingly, while these two gene lists share only 17 genes, they have 79 enriched pathways in common suggesting potential effect of two different treatments on similar pathways but through different pathway members (Figure 2). Moreover, it suggests potential importance of the 17 shared genes in association with these pathways. Most of these pathways are related to innate and adaptive immune system, and to "osteoclast differentiation". Among 46 pathways specific to response to IL-17Ai, multiple Rho-GTPase-related pathways were identified. It has been shown that experimental inhibition of ROCK2, a target of Rho-GTPase family is effective in psoriatic disease through regulation of IL-17/23/10, but not IL-6 and TNFα.

Table 1. Demographics of psoriatic arthritis (PsA) patients.

	IL-17Ai	TNFi
Number of PsA patients	20	20
Gender (% female)	55%	75%
Mean Age (Years)	55.9 (9.5)	56.8 (7.9)
Mean Disease Duration (Years)	10.4 (6.9)	7.3 (7.9)
Mean DAPSA baseline	38.8 (17.5)	45.6 (28.9)
Responders (%) (DAPSA <14)	35%	65%
Biologic naïve (%)	40%	60%

Figure 1. PCA plots illustrating that DEGs of CD4+ cells can differentiate responders from non-responders when treated with: A. IL-17Ai; and B. TNFi.

Figure 2. Over-represented terms in significantly enriched pathways considering DEGs between: A. IL-17i responders and non-responders (125 pathways); B. TNFi responders and non-responders (576 pathways).

Conclusion: Integration of cell-specific transcriptomic data with protein networks represents a very promising strategy for identifying biologic responders and pathways involved in predicting response that may have identified the Rho-GTP pathway as a potential marker to guide the choice of biologic agents for individual patients.

Disclosure of Interests: Sara Rahmati: None declared, Darren O'Rielly: None declared, Quan Li: None declared, Dianne Codner: None declared, Amanda Dohey: None declared, Kari Jenkins: None declared, Igor Jurisica Grant/research support from: IBM, Dafna D Gladman Grant/research support from: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – grant/research support, Consultant of: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – consultant, Vinod Chandran Grant/research support from: AbbVie, Celgene, Consultant of: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Employee of: Spouse employed by Eli Lilly, Proton Rahman Grant/research support from: Janssen and Novartis, Consultant of: Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, and Pfizer., Speakers bureau: Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, Pfizer

DOI: 10.1136/annrheumdis-2020-eular.2317

Newly identified cell subsets driving disease pathogenesis

OP0306

CD11C-SPECIFIC ABLATION OF SHP1 INDUCES AUTOIMMUNE SIALADENITIS SIMILAR TO SJÖGREN'S SYNDROME

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