were more than 10 percentile was 81.46% at 6-9 months and 80.34% at 54-71 months.

Conclusion: The offspring of SLE patients were more likely to have low birthweight compared to general population, but majority of them showed the catch up growth at 4-6 month of age. The risk of low birthweight was especially high in the offspring from mothers who diagnosed SLE during pregnancy.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.4002

New technologies in basic research

OP0099 FUNCTIONAL MAPPING OF SYNOVIAL FIBROBLAST POPULATIONS IN HEALTH AND ARTHRITIC DISEASE: INSIGHTS INTO THE PATHOGENIC REMODELING OF SYNOVIAL MICROENVIRONMENT

D. Konstantopoulos3, C. Tzalferis2, M. Sakkou2, A. Liakos3, M. Lavigne3, D. Karamitos2, M. Fousteni1, M. Armaka1, G. Kollia2,3, 1B.S.R.C. ‘Alexander Fleming’; Institute of Fundamental Biomedical Research, Vari, Greece; 2B.S.R.C.’Alexander Fleming’; Institute of Bioinnovation, Vari, Greece; 3B.S.R.C.’Alexander Fleming’; Institute of Fundamental Biomedical Research, Vari, Greece; 4Medical School of Athens, Department of Physiology, Athens, Greece

Background: Our previous studies highlighted the fundamental in vivo role of synovial fibroblasts (SFs) in TNF-mediated murine chronic arthritis1,2 and recent findings identified different SF identities based on their transcriptomic profiles with distinct contributions in acute, autoimmunity-based, murine arthritis3. Objectives: In this study, we focus on delineating the map of SF subpopulations in healthy joint and in the course of arthritic disease and the underlying regulatory networks functioning towards pathogenicity.

Methods: Sorted single cell suspensions (CD45-, Pdpl+) and their fragmented nuclei from synovial joints of WT, early and late arthritic hTNFtg mice were processed for scRNAseq and scATAC employing a droplet-based technology (10x Genomics). To define the transcriptional and epigenetic signatures originating from the two different assays, we developed an integrative analysis pipeline based on the Seurat software package (v3.1). Meta-analysis of previously reported data of K/BxN serum transfer of arthritis was employed to define commonalities and differences in SF subsets among murine models.

Results: The transition from healthy to chronically affected synovial microenvironment (SME) due to overexpression of hTNF is characterized by a significant increase. The Lining arthritic Thy1low synovial environment (SME) due to overexpression of hTNF is characterized by a significant increase. The Lining arthritic Thy1low synovial environment (SME) due to overexpression of hTNF is characterized by a significant increase.

Conclusion: The offspring of SLE patients were more likely to have low birthweight compared to general population, but majority of them showed the catch up growth at 4-6 month of age. The risk of low birthweight was especially high in the offspring from mothers who diagnosed SLE during pregnancy.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.4002

OP0100 MOLECULAR PROFILING OF PERIPHERAL IMMUNE CELL SUBSETS IN PATIENTS WITH RHEUMATOID ARTHRITIS


Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that affects 1% of the world's population. Several key biological functions are dysregulated in RA, manifesting clinically as pain, fatigue, and synovitis, with articular destruction, organ-based comorbidities, and functional decline. Defining immune dysregulation in the peripheral blood of patients (pts) with RA will help inform future work to assess the extent to which immune homeostasis can be therapeutically achieved for these pts.

Objectives: To identify baseline molecular characteristics of the peripheral immune system, at the level of individual immune cell subsets, in pts with RA recruited to clinical trials of the oral, selective Janus kinase 1 (JAK1) inhibitor, filgotinib.

Methods: Peripheral blood mononuclear cells (PBMC) were collected from 324 pts with moderate to severe RA activity, who had an inadequate response to methotrexate (MTX), FINCH-1: NCT02889796; n=109) or who were MTX naive (FINCH-3: NCT02889728; n=215). PBMC were also collected from 50 demographically matched healthy volunteers (HV). The Immune Profiler platform was used to sort PBMC into 24 immune cell subsets, then quantify their gene expression and chromatin accessibility using RNA-seq and the assay for transposase-accessible chromatin with high-throughput sequencing (ATAC-seq), respectively. Differentially expressed genes (DEGs) and differentially accessible regions (DARs) were identified among immune cell subsets from pts with RA versus HV. Gene set signature scores of Molecular Signatures Database hallmark pathways were calculated using single sample gene set enrichment analysis (ssGSEA) to examine differences in pathway activity between groups.

Results: A total of 14,500 sequencing datasets were generated from the pt and HV immune cell subsets. Among these, over 26,000 DEGs and 220,000 DARs were identified in RA versus HV (false discovery rate <0.05) across the 24 immune cell subsets. DEGs were identified in all immune cell subsets tested and were most pronounced in natural killer (NK) subsets; most DARs were detected in myeloid and NK subsets. ssGSEA revealed differential pathway signaling in RA versus HV across multiple functions at the immune cell subset level. Myeloid subsets from pts with RA often showed elevated pathway activities versus HV whereas B, T and NK subsets showed a general decrease. In particular, monocytic populations from pts with RA versus HV had elevated pathway activities involved in inflammatory response and interleukin-6/Janus kinase/signal transducer and activator of transcription 3 signaling. The B, T and NK subsets showed a general decrease in tumor necrosis factor-a signaling; conversely, monocytic subsets showed an increase. Prior MTX exposure did not have a notable impact on the detected molecular profile.

Conclusion: Differences in gene expression, hallmark pathway activity, and chromatin accessibility were identified in RA versus HV at the immune cell subset level. Significant contributions to differences in chromatin accessibility identified in the myeloid and NK cell populations suggest that there are more active regulatory sequences in these cell types that are associated with RA. Further investigations based on these findings may increase understanding of the immune regulatory paradigm in the context of RA.

Acknowledgments: This study was funded by Gilead Sciences, Inc. Editorial support was provided by Fishawack Communications Inc and funded by Gilead Sciences, Inc.


DOI: 10.1136/annrheumdis-2020-eular.3967

65