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

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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. Konstantopoulos¹, C. Tzaferis², M. Sakkou², A. Liakos³, M. Lavigne³, D. Karamitros², M. Fousteri¹, M. Armaka¹, G. Kollias^{2,4}. 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 arthritis^{1,2} 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⁻, Pdp1⁺) 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 modelled disease.

Results: The transition from healthy to chronically affected synovial microenvironment (SME) due to overexpression of hTNF is characterized by a dynamic transformation of SF clusters. The Lining arthritic Thy1^{low} synovial layer (L-SFs) is hyper-populated while Sub-Lining Thy1^{high} SF clusters (SL-SFs) are remodeled towards catabolic and inflammatory phenotypes compared to naïve SF organization pattern. Interestingly, trajectory analysis revealed that the SL clusters, which normally exhibit a gradual developmental-like process towards different profiles, differentially change during disease. We identified that the previously reported proliferating SL cluster is absent in healthy synovium, dominates mainly in early stages of chronic arthritis and it is closely related to the L-SFs. Mapping of the gene regulatory networks by RNAseq was supported by scATAC analysis. Similarly, meta-analysis of SF profiles derived from naïve and the K/BxN-serum-treated mice showed significant differences, possibly reflecting the phenotypes of the two established models of arthritis.

Conclusion: Our approach unravels for the first time the regulatory heterogeneity and gene expression profiling of SF subpopulations in normal synovium, and reveals deep biological insights of the functional re-organization of SME during development of disease. It further identifies the common and divergent features of the different subtypes of murine arthritis that may well reflect the diversity of RA subtypes and the response to therapies.

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OP0100

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

P.C. Taylor¹, J. Liu², L. Zhuo², Y. Tian², T. Snyder³, C. Kim³, P. Kheradpour³, K. Drake³, S. Kim², R. E. Hawtin². ¹University of Oxford, Botnar Research Centre, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom; ²Gilead Sciences Inc., Foster City, United States of America; ³Verily Life Sciences, South San Francisco, United States of America

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 severely active RA, who had an inadequate response to methotrexate ([MTX], FINCH-1; NCT02889796; n=109) or who were MTX naïve (FINCH-3; NCT02886728; 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, monocyte 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-α signaling; conversely, monocyte 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.

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