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**


**Background:** Our previous studies highlighted the fundamental in vivo role of synovial fibroblasts (SFs) in TNF-mediated murine chronic arthritis and recent findings identified different SF identities based on their transcriptomic profiles with distinct contributions in acute, autoimmunity-based, murine arthritis.

**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 throughout the pipeline.

**Results:** 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 naive and the K/BxN-serum–treated mice showed significant differences, possibly reflecting the phenotypes of the two established mouse 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.

**References:**
[2] Armaka et al; Nat Commun (2018); 9(1);618.
[3] Croft et al; Nature (2019); 570(7760);246-251.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2020-eular.1839