

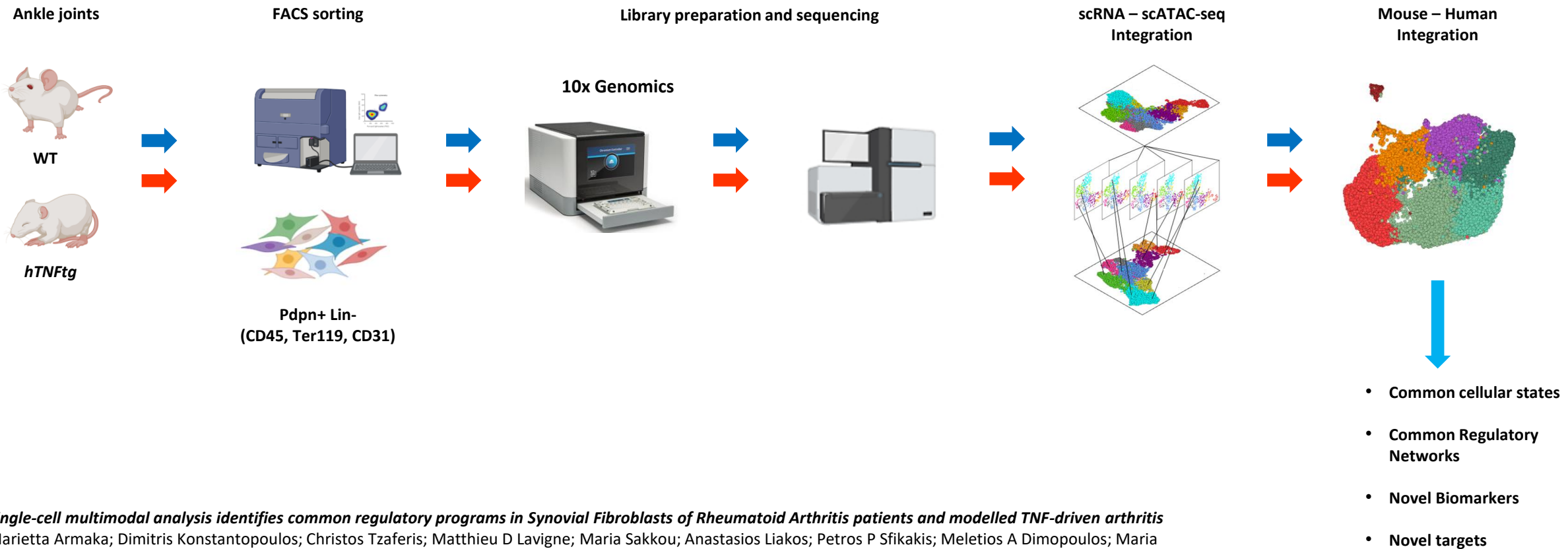
Single-cell Chromatin and Transcriptome dynamics of Synovial Fibroblasts (SFs) transitioning from homeostasis to pathology TNF-driven arthritis

Christos Tzaferis, MSc.
PhD student
Pr. George Kollias Lab
28/06/2022



“ALEXANDER FLEMING”
Biomedical Science Research Centre

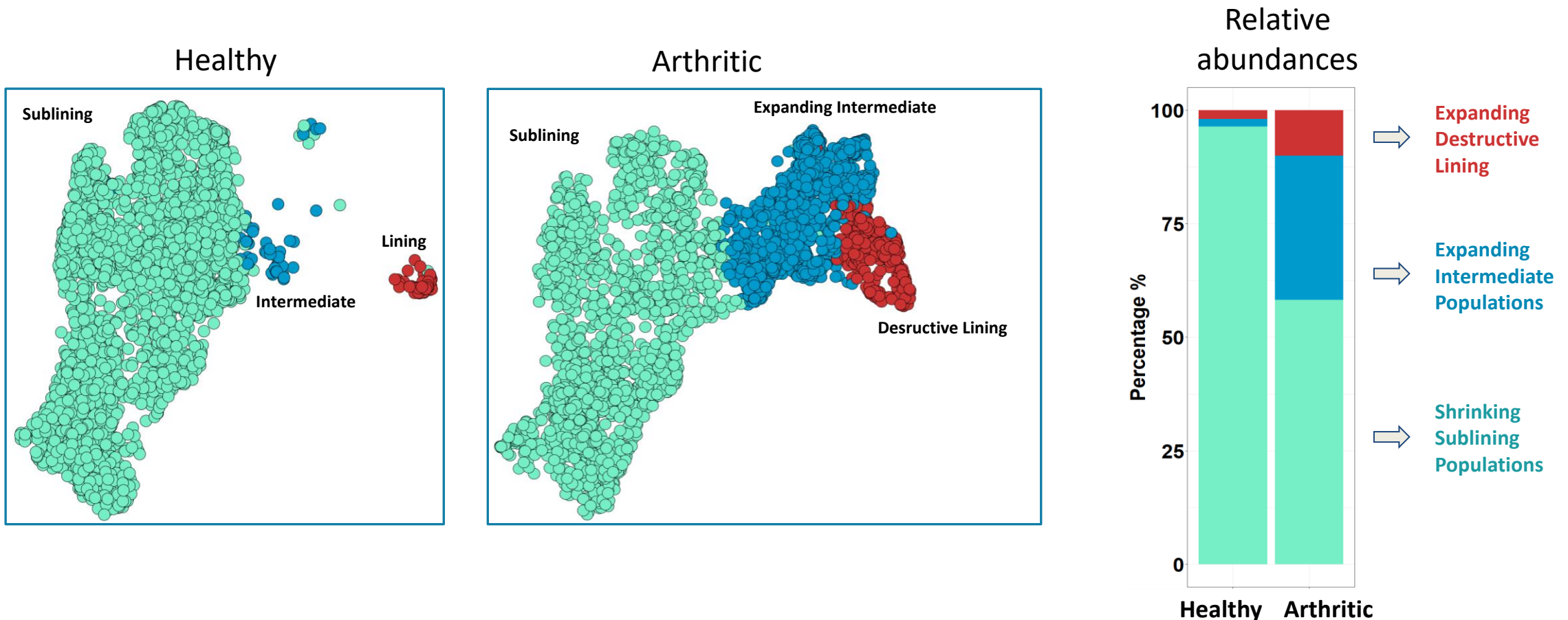
Overview of experimental design and bioinformatics analysis



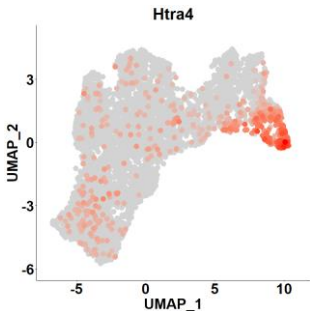
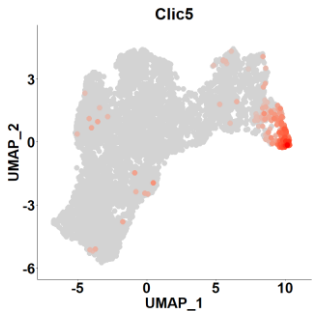
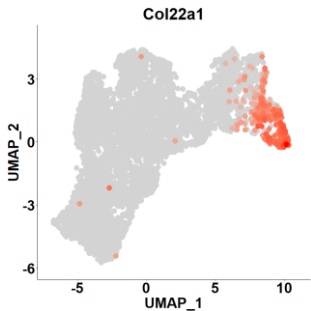
Single-cell multimodal analysis identifies common regulatory programs in Synovial Fibroblasts of Rheumatoid Arthritis patients and modelled TNF-driven arthritis

Marietta Armaka; Dimitris Konstantopoulos; Christos Tzaferis; Matthieu D Lavigne; Maria Sakkou; Anastasios Liakos; Petros P Sfikakis; Meletios A Dimopoulos; Maria Fousteri; George Kollias
Genome Medicine

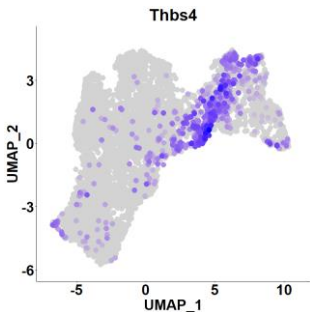
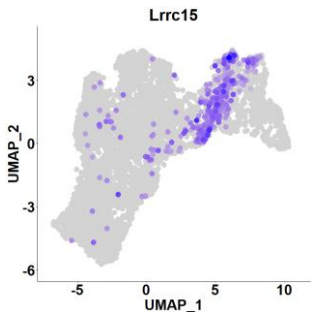
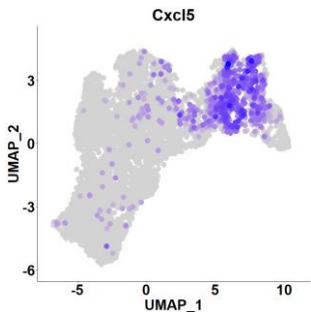
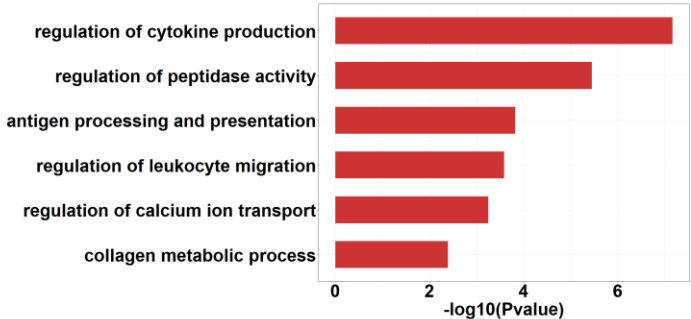
Pathogenic transition via dynamic transcriptional remodeling of homeostatic populations to proliferative, inflammatory and destructive SF populations



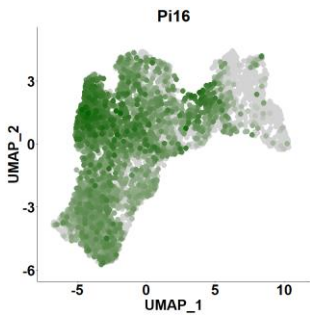
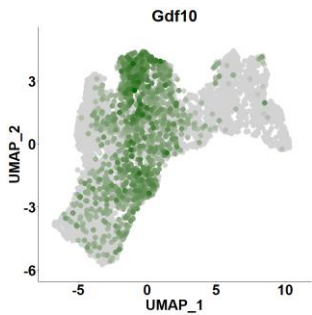
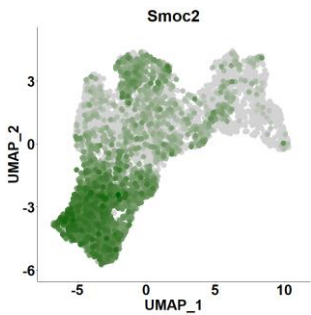
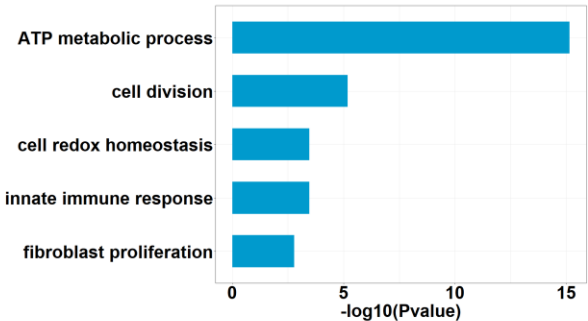
Subcluster-specific marker gene expression and functional enrichment analysis



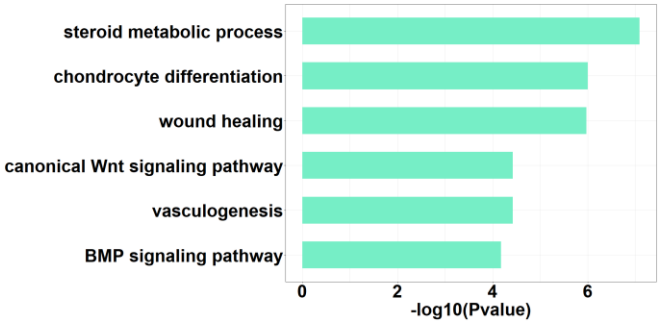
Lining



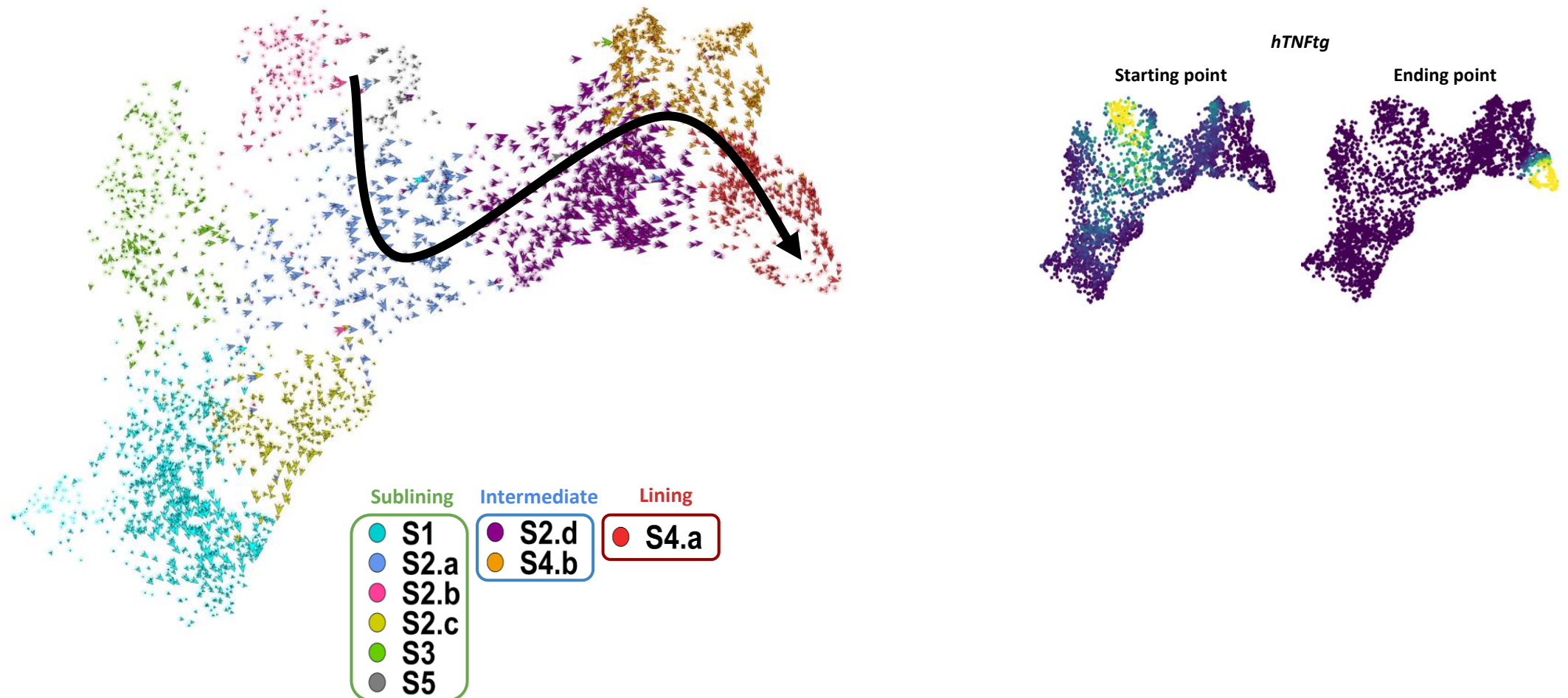
Intermediate



Sublining

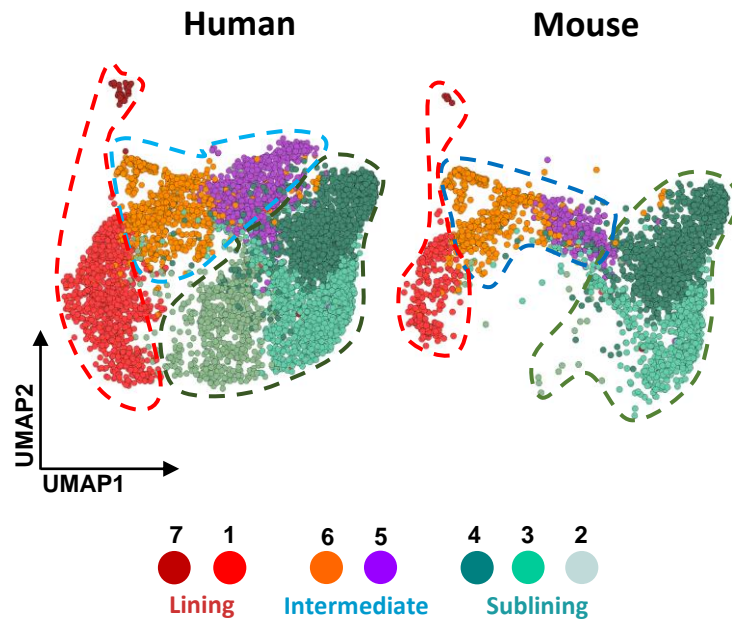


Trajectory analysis predicts dynamic cell-lineage transitions

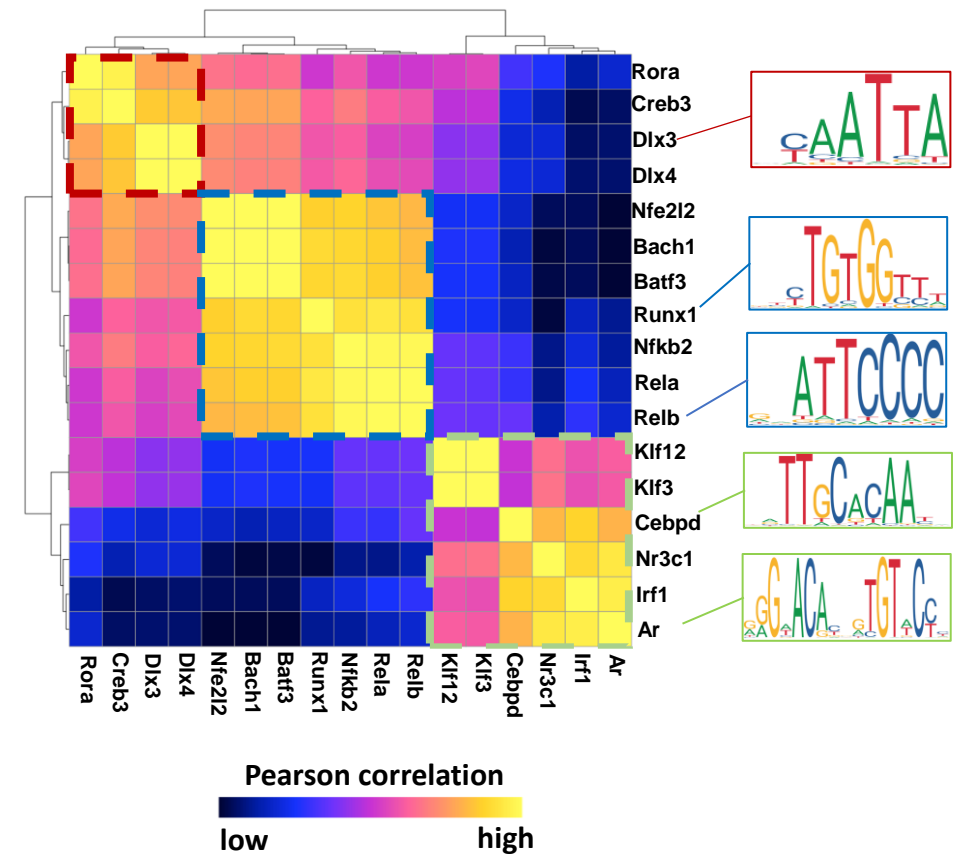


Integrative analysis of Human RA and Tg197 scRNA seq-profiles reveals shared cellular states & conserved regulatory networks

Shared cellular states



Common Regulatory Networks



Conclusions

- ❑ Single cell RNA and chromatin accessibility analyses of healthy and arthritogenic SFs from the huTNFtg model establishes the pathogenic transitions of specific homeostatic sublining populations to proinflammatory intermediate and tissue destructive lining SF populations
- ❑ Specific transcription factors and their target genes, predicted from integrated RNA, chromatin and mouse/human analyses, should provide new biomarkers and therapeutic targets
- ❑ Functional validations of novel effector molecules in specific subpopulations should inform the design of novel targeted therapies

Acknowledgements

Biomedical Sciences Research Center (BSRC) "Alexander Fleming"

Pr. George Kollias

Dr. Maria Fousteri

Dr. Marietta Armaka

Dr. Maria Sakkou

Dr. Dimitris Konstantopoulos

Dr. Matthieu Lavigne

Dr. Anastassios Liakos



Center of New Biotechnologies and Precision Medicine (CNBPM), Athens Medical School & pMEDGR

Pr. Petros Sfikakis

Pr. Thanos Dimopoulos

Kleio-Maria Verrou

