



## Supplementary Text, Tables and Figures

### The Role of Synovial Fibroblast Subsets across Synovial Pathotypes in Rheumatoid Arthritis: A Deconvolution Analysis.

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## 1 Supplementary Text 1: Overview and integration of individual scRNA-seq datasets

In addition to the in house dataset, the following scRNA-seq datasets were used:

1. Stephenson, W. et al. Single-cell RNA-seq of rheumatoid arthritis synovial tissue using low-cost microfluidic instrumentation. *Nat. Commun.* 9, 791 (2018): synovial tissue from knees of five seropositive RA patients. A 3D printed droplet microfluidic control instrument was used to separate single cells. Libraries were sequenced on the Illumina HiSeq 2500 platform. Datasets were acquired directly from the publisher.
2. Mizoguchi, F. et al. Functionally distinct disease-associated fibroblast subsets in rheumatoid arthritis. *Nat. Commun.* 9, 789 (2018): synovial tissue from two RA patients. Single fibroblasts were isolated by flow cytometry (PTPRC (CD45)<sup>-</sup>, GYPA<sup>-</sup>, PECAM1 (CD31)<sup>-</sup>, and PDPN<sup>+</sup>) followed by single-cell library generation with the Smart-Seq2 protocol. The Illumina HiSeq 2500 platform was used for sequencing. The dataset with the primary accession code GSE109450 was downloaded from GEO.
3. Zhang, F. et al. Defining inflammatory cell states in rheumatoid arthritis joint synovial tissues by integrating single-cell transcriptomics and mass cytometry. *Nat Immunol.* 20 (7), 928-942 (2019): synovial tissues of 18 RA patients. Single SF were sorted (CD45–CD31–PDPN<sup>+</sup>), libraries produced with CEL-Seq2 protocol and sequenced on the Illumina HiSeq 2500 platform. The datasets were downloaded from Immport (study accession code SDY998).
4. Alivernini, S., MacDonald, L., Elmesmari, A. et al. Distinct synovial tissue macrophage subsets regulate inflammation and remission in rheumatoid arthritis. *Nat Med* (2020): synovial tissues of 4 RA patients. SF were sorted (CD45–PDPN<sup>+</sup>). The 10x Genomics controller was used for single cell sorting and cells were sequenced on the Illumina HiSeq 4000 platform. The datasets were directly provided from the authors upon request.

Processed (as described in the individual method sections) and aligned data were used. GeneID were matched using BioMart package for R. As part of the standardized Seurat workflow, we performed a quality control for each individual dataset. We filtered cells with high expression of mitochondrial ( $\sim>25\%$ ) and ribosomal genes ( $\sim>20\%$ ), low or aberrantly high gene count. We defined individual thresholds for each dataset and parameter. Next, we followed the standardized Seurat protocol to cluster genes. The expression of COL1A2 and lack of expression of PTPRC (CD45) and von Willebrand factor (VWF) were used to select SF in the individual datasets.

The integration of SF of individual datasets was again performed following the standardized Seurat protocol. Seurat Wrappers package was used for the alternative integration by Harmony and Liger. Harmony and Liger were applied after normalization, variable feature finding and scaling of the data.

## 2 Supplementary Table 1: Top 20 Markers per Cluster using Harmony

**cluster:** number corresponding to cluster

**gene:** gene id

**avg\_logFC:** average log<sub>2</sub> fold change. Positive values indicate that the gene is more highly expressed in the cluster.

**pct.1:** The percentage of cells where the gene is detected in the cluster

**pct.2:** The percentage of cells where the gene is detected on average in the other clusters

**p\_val:** p-value not adjusted for multiple test correction

**p\_val\_adj:** Adjusted p-value, based on bonferroni correction using all genes in the dataset, used to determine significance

Supplementary Table 1: Top 20 Markers per Clusters using Harmony

cluster	gene	avg_logFC	pct.1	pct.2	p_val	p_val_adj
PRG4+ SF	MMP3	1.6689195	0.972	0.922	0	0
PRG4+ SF	PRG4	1.4420054	1.000	0.996	0	0
PRG4+ SF	HBEGF	1.2381446	0.811	0.680	0	0
PRG4+ SF	TWISTNB	1.2117909	0.808	0.663	0	0
PRG4+ SF	DEFB1	1.1991416	0.811	0.679	0	0
PRG4+ SF	MT1G	1.1300576	0.731	0.647	0	0
PRG4+ SF	ERRFI1	1.1168152	0.902	0.769	0	0
PRG4+ SF	ITGB8	1.0080298	0.944	0.832	0	0
PRG4+ SF	TIMP3	0.9436856	0.985	0.925	0	0
PRG4+ SF	CLIC5	0.9230258	0.722	0.644	0	0
PRG4+ SF	HTRA1	0.8993930	0.989	0.967	0	0
PRG4+ SF	TPR	0.8804717	0.929	0.865	0	0
PRG4+ SF	SEMA3C	0.8721120	0.960	0.860	0	0
PRG4+ SF	SPARCL1	0.8719018	0.986	0.937	0	0
PRG4+ SF	CRTAC1	0.8511226	0.998	0.975	0	0
PRG4+ SF	SEMA5A	0.8335538	0.852	0.751	0	0
PRG4+ SF	FN1	0.8177386	1.000	1.000	0	0
PRG4+ SF	TMEM196	0.7862366	0.870	0.757	0	0
PRG4+ SF	NTN4	0.7840508	0.810	0.696	0	0
PRG4+ SF	GPR1	0.9430909	0.652	0.583	0	0
CXCL12+ SF	CXCL12	1.1435460	0.981	0.881	0	0
CXCL12+ SF	CHI3L2	1.0329602	0.926	0.888	0	0
CXCL12+ SF	APOE	1.0071812	0.887	0.778	0	0
CXCL12+ SF	COL14A1	0.7937245	0.929	0.775	0	0
CXCL12+ SF	IGFBP4	0.6852576	0.947	0.896	0	0
CXCL12+ SF	MMP2	0.4651900	0.981	0.929	0	0
CXCL12+ SF	EFEMP1	0.4680502	0.961	0.911	0	0
CXCL12+ SF	CP	0.8193885	0.764	0.709	0	0
CXCL12+ SF	PTGDS	0.7593949	0.795	0.712	0	0
CXCL12+ SF	JUN	0.6383443	0.901	0.870	0	0
CXCL12+ SF	EGR1	0.5487874	0.939	0.931	0	0

Supplementary Table 1: Top 20 Markers per Clusters using Harmony (*continued*)

cluster	gene	avg_logFC	pct.1	pct.2	p_val	p_val_adj
CXCL12+ SF	ZFP36	0.5329108	0.911	0.900	0	0
CXCL12+ SF	ID3	0.4947533	0.676	0.562	0	0
CXCL12+ SF	SOCS3	0.5110791	0.734	0.677	0	0
CXCL12+ SF	GAS1	0.5411549	0.694	0.619	0	0
CXCL12+ SF	CCL2	0.7069788	0.609	0.501	0	0
CXCL12+ SF	CHI3L1	0.6680245	0.752	0.748	0	0
CXCL12+ SF	SFRP1	0.6955069	0.646	0.620	0	0
CXCL12+ SF	NR4A1	0.5504829	0.793	0.798	0	0
CXCL12+ SF	ADAMTS1	0.6206479	0.637	0.615	0	0
POSTN+ SF	POSTN	2.0035254	0.837	0.645	0	0
POSTN+ SF	ASPN	1.6194365	0.877	0.607	0	0
POSTN+ SF	COL1A1	1.4817755	0.997	0.925	0	0
POSTN+ SF	AEBP1	1.0805850	0.967	0.784	0	0
POSTN+ SF	COL3A1	1.0560598	0.998	0.971	0	0
POSTN+ SF	SPARC	1.0453331	0.994	0.957	0	0
POSTN+ SF	FNDC1	1.0420500	0.801	0.526	0	0
POSTN+ SF	THBS2	0.9753493	0.844	0.630	0	0
POSTN+ SF	DPT	0.9055038	0.949	0.791	0	0
POSTN+ SF	COL5A1	0.9475570	0.908	0.741	0	0
POSTN+ SF	OGN	0.9997344	0.851	0.630	0	0
POSTN+ SF	IGFBP6	1.0404002	0.863	0.689	0	0
POSTN+ SF	FBLN2	1.0077096	0.706	0.450	0	0
POSTN+ SF	FBN1	0.9250509	0.885	0.820	0	0
POSTN+ SF	COMP	0.9596725	0.681	0.488	0	0
POSTN+ SF	SFRP4	0.9501918	0.590	0.342	0	0
POSTN+ SF	HTRA3	0.9894649	0.757	0.634	0	0
POSTN+ SF	MFAP5	1.7247568	0.601	0.427	0	0
POSTN+ SF	TGFBI	0.8809938	0.770	0.671	0	0
POSTN+ SF	PI16	1.4221365	0.544	0.514	0	0
CXCL14+ SF	CXCL14	3.1378174	0.932	0.563	0	0
CXCL14+ SF	IGF1	1.9636672	0.988	0.568	0	0
CXCL14+ SF	SFRP2	2.3343852	0.898	0.442	0	0
CXCL14+ SF	FBLN1	1.6184022	0.960	0.628	0	0
CXCL14+ SF	SPON1	0.9377024	0.898	0.525	0	0
CXCL14+ SF	VCAN	1.1414542	0.997	0.788	0	0
CXCL14+ SF	C3	1.3076994	0.984	0.788	0	0
CXCL14+ SF	FBLN2	1.0280592	0.915	0.477	0	0
CXCL14+ SF	COMP	1.1353777	0.913	0.505	0	0
CXCL14+ SF	IGFBP4	1.0224563	0.997	0.912	0	0
CXCL14+ SF	ABCA8	1.1033658	0.837	0.477	0	0
CXCL14+ SF	RARRES1	1.0847465	0.917	0.585	0	0
CXCL14+ SF	KCTD12	0.9120418	0.941	0.680	0	0
CXCL14+ SF	CHI3L1	1.1995322	0.960	0.739	0	0
CXCL14+ SF	SRPX	0.9806312	0.807	0.409	0	0
CXCL14+ SF	THY1	0.9958183	0.924	0.666	0	0
CXCL14+ SF	SFRP1	0.9980582	0.898	0.617	0	0

Supplementary Table 1: Top 20 Markers per Clusters using Harmony (*continued*)

cluster	gene	avg_logFC	pct.1	pct.2	p_val	p_val_adj
CXCL14+ SF	IGFBP7	1.1596791	0.905	0.656	0	0
CXCL14+ SF	SFRP4	1.1178745	0.745	0.370	0	0
CXCL14+ SF	APOD	1.4297955	0.682	0.448	0	0

### 3 Supplementary Table 2: Top 20 Markers per Cluster using Liger

**cluster:** number corresponding to cluster

**gene:** gene id

**avg\_logFC:** average log<sub>2</sub> fold change. Positive values indicate that the gene is more highly expressed in the cluster.

**pct.1:** The percentage of cells where the gene is detected in the cluster

**pct.2:** The percentage of cells where the gene is detected on average in the other clusters

**p\_val:** p-value not adjusted for multiple test correction

**p\_val\_adj:** Adjusted p-value, based on bonferroni correction using all genes in the dataset, used to determine significance

Supplementary Table 2: Top 20 Markers per Cluster using Liger

cluster	gene	avg_logFC	pct.1	pct.2	p_val	p_val_adj
PRG4+ SF	MMP3	1.9005077	0.980	0.913	0.0000000	0.0000000
PRG4+ SF	PRG4	1.3766373	1.000	0.996	0.0000000	0.0000000
PRG4+ SF	HBEGF	1.1835346	0.829	0.658	0.0000000	0.0000000
PRG4+ SF	TWISTNB	1.1726858	0.826	0.640	0.0000000	0.0000000
PRG4+ SF	ERRFI1	1.1407273	0.923	0.745	0.0000000	0.0000000
PRG4+ SF	ITGB8	1.0955050	0.960	0.813	0.0000000	0.0000000
PRG4+ SF	DEFB1	1.0376007	0.812	0.668	0.0000000	0.0000000
PRG4+ SF	MT1G	1.0204360	0.756	0.624	0.0000000	0.0000000
PRG4+ SF	HTRA1	0.9408190	0.995	0.961	0.0000000	0.0000000
PRG4+ SF	CRTAC1	0.9114027	0.999	0.973	0.0000000	0.0000000
PRG4+ SF	FN1	0.8770788	1.000	1.000	0.0000000	0.0000000
PRG4+ SF	CLIC5	0.8665568	0.742	0.625	0.0000000	0.0000000
PRG4+ SF	TIMP3	0.8427655	0.986	0.919	0.0000000	0.0000000
PRG4+ SF	TMEM196	0.8332307	0.892	0.734	0.0000000	0.0000000
PRG4+ SF	ITGBL1	0.8303512	0.955	0.816	0.0000000	0.0000000
PRG4+ SF	SEMA3C	0.8292631	0.969	0.846	0.0000000	0.0000000
PRG4+ SF	SEMA5A	0.8084560	0.869	0.732	0.0000000	0.0000000
PRG4+ SF	TPR	0.7778672	0.935	0.855	0.0000000	0.0000000
PRG4+ SF	CXCL1	0.8909513	0.729	0.629	0.0000000	0.0000000
PRG4+ SF	GPR1	0.8670175	0.655	0.576	0.0000000	0.0000000
CXCL12+ SF	CXCL12	1.1136772	0.976	0.900	0.0000000	0.0000000
CXCL12+ SF	COL14A1	0.8394538	0.938	0.797	0.0000000	0.0000000
CXCL12+ SF	IGFBP4	0.8062527	0.956	0.900	0.0000000	0.0000000
CXCL12+ SF	VCAN	0.6274536	0.903	0.754	0.0000000	0.0000000
CXCL12+ SF	MMP2	0.4611524	0.982	0.937	0.0000000	0.0000000
CXCL12+ SF	CP	0.8528093	0.788	0.708	0.0000000	0.0000000
CXCL12+ SF	APOE	0.6883078	0.870	0.803	0.0000000	0.0000000
CXCL12+ SF	CHI3L2	0.7213706	0.918	0.898	0.0000000	0.0000000
CXCL12+ SF	JUN	0.6139665	0.906	0.873	0.0000000	0.0000000
CXCL12+ SF	PTGDS	0.7042929	0.801	0.723	0.0000000	0.0000000
CXCL12+ SF	EGR1	0.4652603	0.947	0.929	0.0000000	0.0000000
CXCL12+ SF	SFRP1	0.8242785	0.671	0.614	0.0000000	0.0000000

Supplementary Table 2: Top 20 Markers per Cluster using Liger  
(continued)

cluster	gene	avg_logFC	pct.1	pct.2	p_val	p_val_adj
CXCL12+ SF	ZFP36	0.4941613	0.916	0.900	0.0000000	0.0000000
CXCL12+ SF	CCL2	0.7434335	0.631	0.509	0.0000000	0.0000000
CXCL12+ SF	RARRES2	0.5024883	0.672	0.618	0.0000000	0.0000000
CXCL12+ SF	GAS1	0.5282676	0.706	0.626	0.0000000	0.0000000
CXCL12+ SF	CHI3L1	0.6761219	0.765	0.744	0.0000000	0.0000000
CXCL12+ SF	TGM2	0.4586252	0.542	0.534	0.0000000	0.0000000
CXCL12+ SF	ADAMTS1	0.6241184	0.649	0.614	0.0000000	0.0000000
CXCL12+ SF	NR4A1	0.5064209	0.792	0.797	0.0000000	0.0000000
POSTN+ SF	COL1A1	1.4626799	0.983	0.932	0.0000000	0.0000000
POSTN+ SF	COL3A1	1.1486743	0.994	0.973	0.0000000	0.0000000
POSTN+ SF	SPARC	1.0767274	0.985	0.960	0.0000000	0.0000000
POSTN+ SF	COL1A2	0.7695611	0.999	0.998	0.0000000	0.0000000
POSTN+ SF	POSTN	2.2583517	0.783	0.664	0.0000000	0.0000000
POSTN+ SF	LGALS1	0.8074278	0.937	0.880	0.0000000	0.0000000
POSTN+ SF	AEBP1	1.0535251	0.943	0.798	0.0000000	0.0000000
POSTN+ SF	OGN	1.1147183	0.834	0.645	0.0000000	0.0000000
POSTN+ SF	COL5A2	0.9989658	0.933	0.847	0.0000000	0.0000000
POSTN+ SF	BGN	0.7689010	0.968	0.879	0.0000000	0.0000000
POSTN+ SF	DPT	0.8977423	0.931	0.803	0.0000000	0.0000000
POSTN+ SF	ASPN	1.1924601	0.795	0.635	0.0000000	0.0000000
POSTN+ SF	COL5A1	0.9090995	0.864	0.757	0.0000000	0.0000000
POSTN+ SF	THBS2	0.8665934	0.784	0.652	0.0000000	0.0000000
POSTN+ SF	TGFBI	1.2474761	0.766	0.677	0.0000000	0.0000000
POSTN+ SF	CTHRC1	0.8091164	0.603	0.458	0.0000000	0.0000000
POSTN+ SF	THBS1	0.7757673	0.562	0.425	0.0000000	0.0000000
POSTN+ SF	TNC	0.8396933	0.919	0.917	0.0000000	0.0000000
POSTN+ SF	SERPINE1	0.9181357	0.538	0.475	0.0000000	0.0000000
POSTN+ SF	COMP	0.8123489	0.565	0.518	0.0000000	0.0000000
CXCL14+ SF	CXCL14	2.7716879	0.902	0.532	0.0000000	0.0000000
CXCL14+ SF	MFAP5	2.2453973	0.928	0.388	0.0000000	0.0000000
CXCL14+ SF	SFRP2	1.6479126	0.792	0.414	0.0000000	0.0000000
CXCL14+ SF	IGF1	1.5936196	0.940	0.534	0.0000000	0.0000000
CXCL14+ SF	FBLN2	1.5623647	0.930	0.432	0.0000000	0.0000000
CXCL14+ SF	C3	1.3753513	0.982	0.769	0.0000000	0.0000000
CXCL14+ SF	FBLN1	1.3347839	0.940	0.599	0.0000000	0.0000000
CXCL14+ SF	AKAP12	1.1394606	0.914	0.469	0.0000000	0.0000000
CXCL14+ SF	DCN	1.1113345	0.999	0.961	0.0000000	0.0000000
CXCL14+ SF	VCAN	1.1077632	0.994	0.768	0.0000000	0.0000000
CXCL14+ SF	ASPN	1.0158434	0.934	0.615	0.0000000	0.0000000
CXCL14+ SF	THY1	1.0044410	0.945	0.638	0.0000000	0.0000000
CXCL14+ SF	GSN	0.9850361	0.996	0.929	0.0000000	0.0000000
CXCL14+ SF	CPE	0.9192026	0.869	0.511	0.0000000	0.0000000
CXCL14+ SF	SFRP4	1.4028819	0.792	0.327	0.0000000	0.0000000
CXCL14+ SF	FBN1	1.0725564	0.978	0.810	0.0000000	0.0000000
CXCL14+ SF	PI16	1.8125847	0.754	0.484	0.0000000	0.0000000
CXCL14+ SF	IGFBP6	1.0132739	0.905	0.694	0.0000000	0.0000000

Supplementary Table 2: Top 20 Markers per Cluster using Liger  
*(continued)*

cluster	gene	avg_logFC	pct.1	pct.2	p_val	p_val_adj
CXCL14+ SF	HTRA3	1.1240940	0.835	0.630	0.0000000	0.0000000
CXCL14+ SF	APOD	0.9956194	0.657	0.429	0.0000000	0.0000000
HLA-DRAhigh SF	CD52	0.3000363	0.235	0.724	0.0000000	0.0000000
HLA-DRAhigh SF	SMARCD2	0.3008243	0.256	0.737	0.0000000	0.0000000
HLA-DRAhigh SF	VIT	0.3182642	0.240	0.684	0.0000000	0.0000000
HLA-DRAhigh SF	PTPRD	0.3245123	0.190	0.629	0.0000000	0.0000000
HLA-DRAhigh SF	GSN	0.5685173	0.836	0.941	0.0000000	0.0000000
HLA-DRAhigh SF	CCL5	0.4839060	0.266	0.696	0.0000000	0.0000000
HLA-DRAhigh SF	PDGFD	0.3349510	0.306	0.702	0.0000000	0.0000000
HLA-DRAhigh SF	LRRC17	0.3578868	0.195	0.577	0.0000000	0.0000000
HLA-DRAhigh SF	UACA	0.3012307	0.367	0.782	0.0000000	0.0000000
HLA-DRAhigh SF	TPD52L1	0.3260495	0.245	0.633	0.0000000	0.0000001
HLA-DRAhigh SF	CXCL12	0.3318812	0.847	0.925	0.0000000	0.0000001
HLA-DRAhigh SF	PLAC9	0.3912306	0.741	0.918	0.0000000	0.0000003
HLA-DRAhigh SF	APOE	0.7087620	0.691	0.827	0.0000000	0.0000003
HLA-DRAhigh SF	SNAI2	0.4693505	0.261	0.613	0.0000000	0.0000615
HLA-DRAhigh SF	FGL2	0.3636680	0.219	0.562	0.0000067	0.0133576
HLA-DRAhigh SF	DPT	0.3586153	0.683	0.825	0.0000101	0.0201307
HLA-DRAhigh SF	ECM2	0.3306732	0.414	0.771	0.0000337	0.0674906
HLA-DRAhigh SF	DDIT4	0.5054716	0.327	0.650	0.0000638	0.1276192
HLA-DRAhigh SF	MAMDC2	0.5591747	0.277	0.603	0.0000659	0.1318233
HLA-DRAhigh SF	FHL1	0.5319592	0.530	0.748	0.0036782	1.0000000

#### 4 Supplementary Table 3: Top 20 Markers per Cluster using Seurat

**cluster:** number corresponding to cluster

**gene:** gene id

**avg\_logFC:** average log<sub>2</sub> fold change. Positive values indicate that the gene is more highly expressed in the cluster.

**pct.1:** The percentage of cells where the gene is detected in the cluster

**pct.2:** The percentage of cells where the gene is detected on average in the other clusters

**p\_val:** p-value not adjusted for multiple test correction

**p\_val\_adj:** Adjusted p-value, based on bonferroni correction using all genes in the dataset, used to determine significance

Supplementary Table 3: Top 20 Markers per Cluster using Seurat

cluster	gene	avg_log2FC	pct.1	pct.2	p_val	p_val_adj
PRG4+ SF	MMP3	2.3766583	0.972	0.923	0	0
PRG4+ SF	PRG4	2.1155221	0.999	0.997	0	0
PRG4+ SF	HBEGF	1.8317452	0.822	0.676	0	0
PRG4+ SF	DEFB1	1.7715059	0.816	0.677	0	0
PRG4+ SF	TWISTNB	1.7158783	0.805	0.666	0	0
PRG4+ SF	ERRFI1	1.5903250	0.903	0.770	0	0
PRG4+ SF	ITGB8	1.4380856	0.947	0.832	0	0
PRG4+ SF	TIMP3	1.3975999	0.988	0.924	0	0
PRG4+ SF	CLIC5	1.3525268	0.727	0.642	0	0
PRG4+ SF	HTRA1	1.3179831	0.989	0.967	0	0
PRG4+ SF	TPR	1.2907349	0.931	0.864	0	0
PRG4+ SF	SPARCL1	1.2802342	0.988	0.936	0	0
PRG4+ SF	CRTAC1	1.2565476	0.998	0.976	0	0
PRG4+ SF	SEMA3C	1.2473876	0.962	0.860	0	0
PRG4+ SF	SEMA5A	1.2138182	0.858	0.749	0	0
PRG4+ SF	NTN4	1.1596111	0.818	0.694	0	0
PRG4+ SF	FN1	1.1536931	1.000	1.000	0	0
PRG4+ SF	ITGBL1	1.1172159	0.943	0.834	0	0
PRG4+ SF	MT1G	1.4917388	0.727	0.650	0	0
PRG4+ SF	GPR1	1.3898948	0.657	0.581	0	0
CXCL12+ SF	CXCL12	1.8284605	0.976	0.879	0	0
CXCL12+ SF	CHI3L2	1.4950540	0.913	0.896	0	0
CXCL12+ SF	APOE	1.4624243	0.867	0.788	0	0
CXCL12+ SF	COL14A1	1.3302467	0.930	0.765	0	0
CXCL12+ SF	IGFBP4	1.0306055	0.939	0.898	0	0
CXCL12+ SF	EFEMP1	0.7181541	0.955	0.913	0	0
CXCL12+ SF	LAMB1	0.7614818	0.846	0.821	0	0
CXCL12+ SF	CP	1.2556109	0.744	0.721	0	0
CXCL12+ SF	PTGDS	1.0816397	0.772	0.725	0	0
CXCL12+ SF	JUN	0.8819251	0.886	0.880	0	0
CXCL12+ SF	EGR1	0.7248503	0.928	0.939	0	0

Supplementary Table 3: Top 20 Markers per Cluster using Seurat (*continued*)

cluster	gene	avg_log2FC	pct.1	pct.2	p_val	p_val_adj
CXCL12+ SF	ZFP36	0.7573155	0.896	0.911	0	0
CXCL12+ SF	CCL2	1.0688430	0.598	0.503	0	0
CXCL12+ SF	ID3	0.7210793	0.657	0.570	0	0
CXCL12+ SF	GAS1	0.8488028	0.674	0.630	0	0
CXCL12+ SF	SOCS3	0.7232791	0.713	0.690	0	0
CXCL12+ SF	CHI3L1	0.9407506	0.736	0.762	0	0
CXCL12+ SF	SFRP1	1.1087085	0.631	0.630	0	0
CXCL12+ SF	AHR	0.7142492	0.617	0.614	0	0
CXCL12+ SF	ADAMTS1	0.8737535	0.615	0.631	0	0
POSTN+ SF	POSTN	3.6411872	0.881	0.660	0	0
POSTN+ SF	COL1A1	2.5289003	1.000	0.932	0	0
POSTN+ SF	COL3A1	1.9495208	1.000	0.974	0	0
POSTN+ SF	SPARC	1.8844938	0.999	0.960	0	0
POSTN+ SF	COL1A2	1.3966806	1.000	0.998	0	0
POSTN+ SF	LGALS1	1.3801775	0.960	0.881	0	0
POSTN+ SF	COL5A2	1.6870175	0.982	0.846	0	0
POSTN+ SF	AEBP1	1.7974480	0.982	0.801	0	0
POSTN+ SF	ADAM12	1.3854510	0.776	0.458	0	0
POSTN+ SF	OGN	1.6938078	0.904	0.648	0	0
POSTN+ SF	COL5A1	1.6280052	0.944	0.755	0	0
POSTN+ SF	ASPN	1.8538019	0.850	0.638	0	0
POSTN+ SF	DPT	1.4138406	0.954	0.807	0	0
POSTN+ SF	THBS2	1.5324346	0.872	0.649	0	0
POSTN+ SF	TGFBI	2.1159826	0.856	0.672	0	0
POSTN+ SF	IGFBP3	1.3847477	0.724	0.489	0	0
POSTN+ SF	CTHRC1	1.4347093	0.712	0.454	0	0
POSTN+ SF	THBS1	1.3881507	0.674	0.421	0	0
POSTN+ SF	TNC	1.5309977	0.959	0.913	0	0
POSTN+ SF	SERPINE1	1.6676636	0.644	0.467	0	0
CXCL14+ SF	CXCL14	4.0649690	0.927	0.536	0	0
CXCL14+ SF	MFAP5	3.3430585	0.952	0.396	0	0
CXCL14+ SF	FBLN2	2.3137222	0.950	0.439	0	0
CXCL14+ SF	IGF1	2.3092488	0.951	0.541	0	0
CXCL14+ SF	SFRP4	2.1161868	0.838	0.330	0	0
CXCL14+ SF	FBLN1	1.9793883	0.952	0.604	0	0
CXCL14+ SF	C3	1.9601399	0.987	0.773	0	0
CXCL14+ SF	AKAP12	1.7092664	0.935	0.475	0	0
CXCL14+ SF	DCN	1.6526851	0.999	0.962	0	0
CXCL14+ SF	VCAN	1.5412463	0.995	0.773	0	0
CXCL14+ SF	ASPN	1.5216365	0.950	0.619	0	0
CXCL14+ SF	GSN	1.4603612	0.999	0.930	0	0
CXCL14+ SF	THY1	1.4346248	0.952	0.643	0	0
CXCL14+ SF	CPE	1.4276914	0.887	0.516	0	0
CXCL14+ SF	SFRP2	2.4624075	0.814	0.418	0	0
CXCL14+ SF	FBN1	1.6191282	0.984	0.813	0	0
CXCL14+ SF	IGFBP6	1.5892252	0.923	0.695	0	0

Supplementary Table 3: Top 20 Markers per Cluster using Seurat (*continued*)

cluster	gene	avg_log2FC	pct.1	pct.2	p_val	p_val_adj
CXCL14+ SF	PI16	2.8064814	0.758	0.489	0	0
CXCL14+ SF	HTRA3	1.7392298	0.842	0.633	0	0
CXCL14+ SF	APOD	1.4422161	0.685	0.430	0	0

## 5 Supplementary Table 4: KEGG Pathway Analysis of Synovial Fibroblast Marker Genes

Supplementary Table 4: KEGG Pathway Analysis of Synovial Fibroblast Marker Genes

Cluster	Description	p.adjust	qvalue	geneID
PRG4+ SF	Complement and coagulation cascades	0.0001214	0.0001116	1191/1604/2153/10544/1675/3426/7035/624/5265
PRG4+ SF	Focal adhesion	0.0001214	0.0001116	3696/2335/857/7060/3914/7424/56034/4233/2317/3685/5228/3655/
PRG4+ SF	PI3K-Akt signaling pathway	0.0021362	0.0019637	3696/2335/7060/9586/3914/2255/7424/56034/4233/7533/3685/6446
PRG4+ SF	Mineral absorption	0.0046666	0.0042898	4495/4502/4501/4494/4499/4493
PRG4+ SF	ECM-receptor interaction	0.0046666	0.0042898	3696/2335/7060/3914/3685/3655/1282
PRG4+ SF	Proteoglycans in cancer	0.0082382	0.0075731	1839/7078/2335/857/288/4233/2317/7042/3685/3710
PRG4+ SF	Malaria	0.0116926	0.0107486	7060/4233/7042/7412/6403
PRG4+ SF	Biosynthesis of nucleotide sugars	0.0302808	0.0278362	6675/7360/9945/7358
PRG4+ SF	AGE-RAGE signaling pathway in diabetic complications	0.0366708	0.0337103	2335/7424/2308/7042/7412/1282
PRG4+ SF	Amoebiasis	0.0366708	0.0337103	2335/3914/3315/7042/2919/1282
CXCL12+ SF	TNF signaling pathway	0.0005136	0.0003950	3725/2353/6347/9021/4323/4792/3659/3569/3383
CXCL12+ SF	PI3K-Akt signaling pathway	0.0005136	0.0003950	3912/3910/1291/1293/1292/5156/5159/54541/2252/3164/80310/918
CXCL12+ SF	Rheumatoid arthritis	0.0005136	0.0003950	6387/3725/2353/6347/284/3569/3383/10673
CXCL12+ SF	Pertussis	0.0009347	0.0007188	3725/718/715/2353/710/3659/3569
13	CXCL12+ SF AGE-RAGE signaling pathway in diabetic complications	0.0044135	0.0033941	4313/3725/1958/6347/2152/3569/3383
CXCL12+ SF	Protein digestion and absorption	0.0044315	0.0034079	7373/1307/1291/1293/1292/80781/1295
CXCL12+ SF	Focal adhesion	0.0093042	0.0071551	3912/3725/3910/1291/1293/1292/5156/5159/80310
CXCL12+ SF	MAPK signaling pathway	0.0093042	0.0071551	3725/2353/1843/5156/5159/2252/4616/3164/80310/284/4254
CXCL12+ SF	Chagas disease	0.0195349	0.0150227	3725/718/2353/6347/4792/3569
CXCL12+ SF	Melanoma	0.0227534	0.0174978	5156/5159/2252/4616/80310
CXCL12+ SF	JAK-STAT signaling pathway	0.0326178	0.0250837	9021/5156/5159/316/9180/2273/3569
CXCL12+ SF	Cholesterol metabolism	0.0326178	0.0250837	348/51129/5360/341
CXCL12+ SF	Rap1 signaling pathway	0.0326178	0.0250837	55740/5156/5159/2252/80310/284/3397/4254
CXCL12+ SF	Complement and coagulation cascades	0.0326178	0.0250837	718/715/710/2152/730
CXCL12+ SF	Lipid and atherosclerosis	0.0326178	0.0250837	3725/2353/6347/4792/6648/8743/3569/3383
CXCL12+ SF	Influenza A	0.0326178	0.0250837	6347/9021/4792/8743/3337/3569/3383
CXCL12+ SF	ECM-receptor interaction	0.0326178	0.0250837	3912/3910/1291/1293/1292
CXCL12+ SF	IL-17 signaling pathway	0.0409782	0.0315131	3725/2353/6347/4792/3569
CXCL12+ SF	Coronavirus disease - COVID-19	0.0418936	0.0322171	3725/718/715/2353/6347/4792/730/3569
CXCL12+ SF	Fluid shear stress and atherosclerosis	0.0419777	0.0322818	4313/3725/2353/6347/1843/3383
CXCL12+ SF	Choline metabolism in cancer	0.0419777	0.0322818	3725/2353/5156/5159/80310
CXCL12+ SF	Viral protein interaction with cytokine and cytokine receptor	0.0436608	0.0335761	6387/6347/6355/8743/3569

Supplementary Table 4: KEGG Pathway Analysis of Synovial Fibroblast Marker Genes (*continued*)

Cluster	Description	p.adjust	qvalue	geneID	
CXCL12+ SF	Kaposi sarcoma-associated herpesvirus infection	0.0453373	0.0348653	3725/718/2353/7538/4792/3569/3383	
CXCL12+ SF	NF-kappa B signaling pathway	0.0453373	0.0348653	6387/4616/4792/3383/10673	
CXCL12+ SF	C-type lectin receptor signaling pathway	0.0453373	0.0348653	3725/4792/3659/1960/3569	
CXCL12+ SF	Nicotinate and nicotinamide metabolism	0.0491566	0.0378024	4837/316/10135	
CXCL12+ SF	Th17 cell differentiation	0.0491566	0.0378024	3725/2353/196/4792/3569	
POSTN+ SF	Protein digestion and absorption	0.0000000	0.0000000	1277/1281/1278/1290/1301/1293/1289/1291/1292/1295/1307/50509	
POSTN+ SF	ECM-receptor interaction	0.0000000	0.0000000	1277/1278/1293/6696/1291/7058/1292/8515/7057/3371/1311/7059/	
POSTN+ SF	Focal adhesion	0.0000000	0.0000000	1277/1278/1293/6696/1291/7058/1292/8515/7057/4638/3371/87/13	
POSTN+ SF	Human papillomavirus infection	0.0000112	0.0000098	1277/1278/1293/6696/1291/7058/1292/8515/7057/3371/4854/1311/	
POSTN+ SF	PI3K-Akt signaling pathway	0.0000241	0.0000212	1277/1278/1293/6696/1291/7058/1292/8515/7057/3371/1311/5159/	
POSTN+ SF	Proteoglycans in cancer	0.0000716	0.0000629	1277/1278/7291/7057/4313/1634/4060/3339/287/6383/7422/3693/5	
POSTN+ SF	AGE-RAGE signaling pathway in diabetic complications	0.0073777	0.0064806	1277/1281/1278/2152/5054/4313/7422	
POSTN+ SF	Malaria	0.0091456	0.0080336	7058/7057/1311/7059/6383	
I4	POSTN+ SF	Regulation of actin cytoskeleton	0.0393501	0.0345653	8515/4638/87/4628/5159/10398/55740/22801/3693
	CXCL14+ SF	Complement and coagulation cascades	0.0000282	0.0000256	718/5104/716/1675/5328/10544/3075/710/7056/730
	CXCL14+ SF	ECM-receptor interaction	0.0000282	0.0000256	3908/1311/6382/7058/1277/22801/1278/7057/3339/7060
	CXCL14+ SF	Phagosome	0.0004382	0.0003981	718/1311/7058/7280/7846/7057/203068/84790/1514/347733/7060
	CXCL14+ SF	Protein digestion and absorption	0.0005187	0.0004712	1803/1296/1277/1289/2006/1278/7373/1303/1306
	CXCL14+ SF	Focal adhesion	0.0035594	0.0032332	3479/3908/1311/7058/1277/22801/5159/1278/7057/3725/7060
	CXCL14+ SF	Gap junction	0.0062713	0.0056967	2977/7280/5159/7846/203068/84790/347733
	CXCL14+ SF	Proteoglycans in cancer	0.0135625	0.0123197	3479/1634/6382/1277/5328/1278/7057/1514/3339/3481
	CXCL14+ SF	Malaria	0.0140897	0.0127985	1311/6382/7058/7057/7060
	CXCL14+ SF	PI3K-Akt signaling pathway	0.0230576	0.0209447	3479/3908/1311/7058/1277/22801/4915/2252/5159/1278/7057/3481
	CXCL14+ SF	Arachidonic acid metabolism	0.0280907	0.0255165	5740/2687/5320/2878/8644
	CXCL14+ SF	TGF-beta signaling pathway	0.0316998	0.0287949	1634/2200/7048/2331/7057/653

## 6 Supplementary Table 5: Top 100 differential expressed genes along Pseudotime

Supplementary Table 5: Top 100 differential expressed genes along Pseudotime

	Gene	P-Value	Q-Value
CXCL14	CXCL14	0e+00	0e+00
MMP3	MMP3	0e+00	0e+00
MFAP5	MFAP5	0e+00	0e+00
COMP	COMP	0e+00	0e+00
SFRP4	SFRP4	0e+00	0e+00
POSTN	POSTN	0e+00	0e+00
ASPN	ASPN	0e+00	0e+00
IGF1	IGF1	0e+00	0e+00
GPR1	GPR1	0e+00	0e+00
SCG2	SCG2	0e+00	0e+00
COL1A1	COL1A1	0e+00	0e+00
MT1G	MT1G	0e+00	0e+00
GJB2	GJB2	0e+00	0e+00
TWISTNB	TWISTNB	0e+00	0e+00
COL3A1	COL3A1	0e+00	0e+00
FBLN1	FBLN1	0e+00	0e+00
HTRA1	HTRA1	0e+00	0e+00
TNFAIP6	TNFAIP6	0e+00	0e+00
C3	C3	0e+00	0e+00
LOX	LOX	0e+00	0e+00
FBLN2	FBLN2	0e+00	0e+00
MT1X	MT1X	0e+00	0e+00
HBEGF	HBEGF	0e+00	0e+00
CLU	CLU	0e+00	0e+00
FBN1	FBN1	0e+00	0e+00
SPARC	SPARC	0e+00	0e+00
CPE	CPE	0e+00	0e+00
STEAP4	STEAP4	0e+00	0e+00
FN1	FN1	0e+00	0e+00
THBS4	THBS4	0e+00	0e+00
CLIC5	CLIC5	0e+00	0e+00
ERRFI1	ERRFI1	0e+00	0e+00
HAS1	HAS1	0e+00	0e+00
HTRA4	HTRA4	0e+00	0e+00
CXCL12	CXCL12	0e+00	0e+00
FNDC1	FNDC1	0e+00	0e+00
CRTAC1	CRTAC1	0e+00	0e+00
DEFB1	DEFB1	0e+00	0e+00
PRG4	PRG4	0e+00	0e+00
THY1	THY1	0e+00	0e+00
TIMP3	TIMP3	0e+00	0e+00
PPP1R1A	PPP1R1A	0e+00	0e+00

Supplementary Table 5: Top 100 differential expressed genes along Pseudotime (*continued*)

	Gene	P-Value	Q-Value
	OGN	0e+00	0e+00
	DCN	0e+00	0e+00
	AKAP12	0e+00	0e+00
	IGFBP7	0e+00	0e+00
	MT2A	0e+00	0e+00
	ITGB8	0e+00	0e+00
	VCAN	0e+00	0e+00
	SEMA5A	0e+00	0e+00
	MAP1B	0e+00	0e+00
	VCAM1	0e+00	0e+00
	AEBP1	0e+00	0e+00
	ITGBL1	0e+00	0e+00
	SEMA3C	0e+00	0e+00
	SPON2	0e+00	0e+00
	SEMA3A	0e+00	0e+00
	CD34	0e+00	0e+00
	COL6A3	0e+00	0e+00
	IGFBP4	0e+00	0e+00
	SPON1	0e+00	0e+00
	DPT	0e+00	0e+00
	SPARCL1	0e+00	0e+00
	THBS2	0e+00	0e+00
	COL8A1	0e+00	0e+00
	BGN	0e+00	0e+00
	EDIL3	0e+00	0e+00
	GABRA4	0e+00	0e+00
	COL1A2	0e+00	0e+00
	COL14A1	0e+00	0e+00
	MT1F	0e+00	0e+00
	PODN	0e+00	0e+00
	MDK	0e+00	0e+00
	TMEM196	0e+00	0e+00
	OLFML3	0e+00	0e+00
	COL5A1	0e+00	0e+00
	FGF10	0e+00	0e+00
	NTN4	0e+00	0e+00
	TPM1	0e+00	0e+00
	MFAP4	0e+00	0e+00
	FBLN5	0e+00	0e+00
	CAV1	0e+00	0e+00
	COL22A1	0e+00	0e+00
	SMOC2	0e+00	0e+00
	SERPINF1	0e+00	0e+00
	UAP1	0e+00	0e+00
	MXRA5	0e+00	0e+00
	PCSK5	0e+00	0e+00

Supplementary Table 5: Top 100 differential expressed genes along Pseudotime (*continued*)

	Gene	P-Value	Q-Value
	COL6A1	COL6A1	0e+00
	EFNB2	EFNB2	0e+00
	RARRES2	RARRES2	0e+00
	ZNF385B	ZNF385B	0e+00
	SCARA5	SCARA5	0e+00
	COL6A2	COL6A2	0e+00
	SMIM14	SMIM14	0e+00
	SEMA3E	SEMA3E	0e+00
	SORBS2	SORBS2	0e+00
	ECM2	ECM2	0e+00
	SOX5	SOX5	0e+00
	CIT	CIT	0e+00

## 7 Supplementary Table 6: Top 20 Markers per Synovial Cluster using Seurat

**cluster:** number corresponding to cluster

**gene:** gene id

**avg\_logFC:** average log<sub>2</sub> fold change. Positive values indicate that the gene is more highly expressed in the cluster.

**pct.1:** The percentage of cells where the gene is detected in the cluster

**pct.2:** The percentage of cells where the gene is detected on average in the other clusters

**p\_val:** p-value not adjusted for multiple test correction

**p\_val\_adj:** Adjusted p-value, based on bonferroni correction using all genes in the dataset, used to determine significance

Supplementary Table 6: Top 20 Markers per Synovial Cluster

cluster	gene	avg_log2FC	pct.1	pct.2	p_val	p_val_adj
Macrophages	C1QA	3.270703	0.901	0.269	0.0000000	0.0000000
Macrophages	C1QB	3.214003	0.882	0.248	0.0000000	0.0000000
Macrophages	C1QC	3.010247	0.833	0.144	0.0000000	0.0000000
Macrophages	FTL	2.782173	0.998	0.919	0.0000000	0.0000000
Macrophages	MARCO	2.670485	0.782	0.182	0.0000000	0.0000000
Macrophages	LGMN	2.491979	0.769	0.189	0.0000000	0.0000000
Macrophages	PLTP	2.480665	0.756	0.158	0.0000000	0.0000000
Macrophages	FOLR2	2.411251	0.684	0.100	0.0000000	0.0000000
Macrophages	CFD	2.282148	0.864	0.366	0.0000000	0.0000000
Macrophages	CTSB	2.218864	0.958	0.500	0.0000000	0.0000000
Macrophages	CD163	2.184028	0.732	0.158	0.0000000	0.0000000
Macrophages	CTSL	2.177246	0.846	0.264	0.0000000	0.0000000
Macrophages	GPNMB	2.172317	0.761	0.157	0.0000000	0.0000000
Macrophages	CTSZ	2.077923	0.872	0.353	0.0000000	0.0000000
Macrophages	CD68	1.973195	0.859	0.266	0.0000000	0.0000000
Macrophages	APOC1	2.495792	0.469	0.072	0.0000000	0.0000000
Macrophages	APOE	2.663634	0.552	0.202	0.0000000	0.0000000
Macrophages	CCL18	2.123385	0.329	0.072	0.0000000	0.0000000
Macrophages	SELENOP	2.256367	0.252	0.083	0.0000000	0.0000000
Macrophages	SPP1	2.649579	0.267	0.103	0.0000000	0.0000000
Dendritic Cells	FCN1	2.633882	0.715	0.115	0.0000000	0.0000000
Dendritic Cells	LGALS2	1.605338	0.503	0.058	0.0000000	0.0000000
Dendritic Cells	S100A12	2.617722	0.299	0.014	0.0000000	0.0000000
Dendritic Cells	LYZ	2.154120	0.970	0.588	0.0000000	0.0000000
Dendritic Cells	FCER1A	2.320922	0.292	0.026	0.0000000	0.0000000
Dendritic Cells	SERPINA1	1.312990	0.703	0.238	0.0000000	0.0000000
Dendritic Cells	CSTA	1.429357	0.641	0.209	0.0000000	0.0000000
Dendritic Cells	EREG	1.576328	0.432	0.086	0.0000000	0.0000000
Dendritic Cells	MNDA	1.547418	0.729	0.300	0.0000000	0.0000000
Dendritic Cells	VCAN	1.923529	0.644	0.251	0.0000000	0.0000000
Dendritic Cells	CLEC10A	1.614396	0.441	0.112	0.0000000	0.0000000

Supplementary Table 6: Top 20 Markers per Synovial Cluster  
(continued)

cluster	gene	avg_log2FC	pct.1	pct.2	p_val	p_val_adj
Dendritic Cells	LST1	1.333471	0.848	0.453	0.0000000	0.0000000
Dendritic Cells	THBS1	1.657484	0.359	0.074	0.0000000	0.0000000
Dendritic Cells	G0S2	1.854443	0.356	0.080	0.0000000	0.0000000
Dendritic Cells	PPIF	1.336503	0.520	0.176	0.0000000	0.0000000
Dendritic Cells	NAMPT	1.299452	0.871	0.585	0.0000000	0.0000000
Dendritic Cells	IL1B	1.462670	0.356	0.106	0.0000000	0.0000000
Dendritic Cells	C15orf48	1.313572	0.492	0.203	0.0000000	0.0000000
Dendritic Cells	S100A8	2.562396	0.559	0.337	0.0000000	0.0000000
Dendritic Cells	S100A9	2.866128	0.657	0.445	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	KRT5	2.896356	0.389	0.000	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	GZMB	4.600128	0.944	0.060	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	PLD4	2.641535	0.667	0.029	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	SPIB	2.501050	0.611	0.025	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	JCHAIN	3.559169	0.833	0.057	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	TSPAN13	2.491728	0.667	0.036	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	PTPRS	2.411002	0.500	0.022	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	IRF4	2.532822	0.611	0.047	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	PLAC8	2.738324	0.778	0.085	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	ITM2C	2.286710	0.667	0.077	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	IL3RA	2.329804	0.667	0.088	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	C12orf75	2.587694	0.611	0.081	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	PTGDS	3.852393	0.444	0.056	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	AL807752.7	3.852393	0.444	0.056	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	TCF4	2.744307	0.889	0.285	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	SOX4	2.539614	0.611	0.111	0.0000000	0.0000000
Plasmacytoid Dendritic Cells	CCDC50	2.340237	0.722	0.189	0.0000000	0.0000001
Plasmacytoid Dendritic Cells	PPP1R14B	2.727477	0.722	0.200	0.0000000	0.0000002
Plasmacytoid Dendritic Cells	IRF8	2.543887	0.778	0.241	0.0000000	0.0000008
Plasmacytoid Dendritic Cells	IRF7	2.569980	0.667	0.185	0.0000000	0.0000284
T-Cells	TRAC	2.308472	0.718	0.109	0.0000000	0.0000000
T-Cells	LTB	2.540834	0.740	0.130	0.0000000	0.0000000
T-Cells	CD2	2.303958	0.740	0.134	0.0000000	0.0000000
T-Cells	SPOCK2	2.141784	0.642	0.091	0.0000000	0.0000000
T-Cells	TRBC2	2.299287	0.724	0.137	0.0000000	0.0000000
T-Cells	IL7R	2.788816	0.763	0.190	0.0000000	0.0000000
T-Cells	CD3D	1.864072	0.679	0.124	0.0000000	0.0000000
T-Cells	IL32	2.134170	0.796	0.208	0.0000000	0.0000000
T-Cells	ETS1	1.952110	0.661	0.154	0.0000000	0.0000000
T-Cells	CD3G	1.604033	0.546	0.087	0.0000000	0.0000000
T-Cells	KLRB1	2.200842	0.448	0.061	0.0000000	0.0000000
T-Cells	CD3E	1.563749	0.499	0.079	0.0000000	0.0000000
T-Cells	BCL11B	1.621941	0.421	0.054	0.0000000	0.0000000
T-Cells	SYNE2	1.842676	0.620	0.172	0.0000000	0.0000000
T-Cells	CD52	1.587951	0.822	0.360	0.0000000	0.0000000
T-Cells	RORA	1.776030	0.503	0.120	0.0000000	0.0000000
T-Cells	CTLA4	1.591630	0.256	0.026	0.0000000	0.0000000

Supplementary Table 6: Top 20 Markers per Synovial Cluster  
*(continued)*

cluster	gene	avg_log2FC	pct.1	pct.2	p_val	p_val_adj
T-Cells	TNFAIP3	1.820825	0.699	0.339	0.0000000	0.0000000
T-Cells	TCF7	1.478455	0.366	0.093	0.0000000	0.0000000
T-Cells	CXCL13	1.648631	0.106	0.020	0.0000000	0.0000000
NK-Cells	CCL5	4.120856	0.916	0.116	0.0000000	0.0000000
NK-Cells	NKG7	3.917145	0.813	0.050	0.0000000	0.0000000
NK-Cells	GZMA	3.101365	0.839	0.069	0.0000000	0.0000000
NK-Cells	CST7	2.879376	0.799	0.092	0.0000000	0.0000000
NK-Cells	CTSW	2.460584	0.619	0.040	0.0000000	0.0000000
NK-Cells	GZMK	2.987679	0.628	0.048	0.0000000	0.0000000
NK-Cells	GZMH	2.515564	0.451	0.012	0.0000000	0.0000000
NK-Cells	CD8A	2.193468	0.487	0.023	0.0000000	0.0000000
NK-Cells	GZMM	1.809187	0.537	0.052	0.0000000	0.0000000
NK-Cells	GZMB	2.728472	0.415	0.023	0.0000000	0.0000000
NK-Cells	PRF1	1.823520	0.345	0.016	0.0000000	0.0000000
NK-Cells	KLRD1	1.812116	0.312	0.011	0.0000000	0.0000000
NK-Cells	IL32	2.170977	0.815	0.217	0.0000000	0.0000000
NK-Cells	CD3D	1.899073	0.655	0.138	0.0000000	0.0000000
NK-Cells	DUSP2	2.214014	0.758	0.277	0.0000000	0.0000000
NK-Cells	RUNX3	1.880237	0.633	0.169	0.0000000	0.0000000
NK-Cells	GNLY	4.123200	0.326	0.036	0.0000000	0.0000000
NK-Cells	TUBA4A	1.968858	0.530	0.147	0.0000000	0.0000000
NK-Cells	PIK3R1	1.965656	0.619	0.271	0.0000000	0.0000000
NK-Cells	CCL4	2.194415	0.595	0.221	0.0000000	0.0000000
B-Cells	MS4A1	4.039114	0.899	0.015	0.0000000	0.0000000
B-Cells	CD79A	3.570239	0.882	0.028	0.0000000	0.0000000
B-Cells	CD19	2.102564	0.437	0.006	0.0000000	0.0000000
B-Cells	BANK1	2.722387	0.731	0.039	0.0000000	0.0000000
B-Cells	IGHD	2.033999	0.294	0.001	0.0000000	0.0000000
B-Cells	LINC00926	1.875828	0.429	0.009	0.0000000	0.0000000
B-Cells	CD22	2.034731	0.387	0.014	0.0000000	0.0000000
B-Cells	RALGPS2	2.149965	0.496	0.044	0.0000000	0.0000000
B-Cells	CD79B	2.015057	0.462	0.044	0.0000000	0.0000000
B-Cells	LY9	2.469157	0.471	0.054	0.0000000	0.0000000
B-Cells	CCR7	2.342653	0.513	0.077	0.0000000	0.0000000
B-Cells	ADAM28	2.126509	0.571	0.126	0.0000000	0.0000000
B-Cells	CD37	2.322980	0.874	0.482	0.0000000	0.0000000
B-Cells	HVCN1	1.840175	0.471	0.090	0.0000000	0.0000000
B-Cells	LTB	1.824453	0.689	0.190	0.0000000	0.0000000
B-Cells	SELL	1.903521	0.479	0.094	0.0000000	0.0000000
B-Cells	POU2F2	2.278333	0.639	0.193	0.0000000	0.0000000
B-Cells	BIRC3	2.152789	0.739	0.285	0.0000000	0.0000000
B-Cells	SMIM14	2.183403	0.496	0.216	0.0000000	0.0000000
B-Cells	CD69	1.996912	0.555	0.258	0.0000000	0.0000000
Plasmacells	MZB1	4.234966	0.922	0.031	0.0000000	0.0000000
Plasmacells	DERL3	3.214092	0.811	0.014	0.0000000	0.0000000
Plasmacells	IGLL5	4.733066	0.344	0.005	0.0000000	0.0000000

Supplementary Table 6: Top 20 Markers per Synovial Cluster  
(continued)

cluster	gene	avg_log2FC	pct.1	pct.2	p_val	p_val_adj
Plasmacells	FKBP11	2.987502	0.867	0.102	0.0000000	0.0000000
Plasmacells	IGHG2	6.273913	0.744	0.072	0.0000000	0.0000000
Plasmacells	IGKJ4	3.197374	0.133	0.001	0.0000000	0.0000000
Plasmacells	JCHAIN	5.185341	0.533	0.049	0.0000000	0.0000000
Plasmacells	IGHG4	6.720259	0.800	0.139	0.0000000	0.0000000
Plasmacells	IGHG1	7.566796	0.956	0.276	0.0000000	0.0000000
Plasmacells	IGHG3	6.880335	0.944	0.271	0.0000000	0.0000000
Plasmacells	IGHGP	5.446226	0.322	0.021	0.0000000	0.0000000
Plasmacells	IGKV4-1	2.741264	0.178	0.005	0.0000000	0.0000000
Plasmacells	XBP1	3.158973	0.956	0.363	0.0000000	0.0000000
Plasmacells	SSR4	2.904618	0.933	0.642	0.0000000	0.0000000
Plasmacells	WT1-AS	2.743880	0.111	0.006	0.0000000	0.0000000
Plasmacells	IGLC3	7.342620	0.500	0.160	0.0000000	0.0000000
Plasmacells	IGHM	6.625196	0.544	0.197	0.0000000	0.0000000
Plasmacells	IGLC2	8.470061	0.600	0.266	0.0000000	0.0000000
Plasmacells	IGKC	7.105117	0.789	0.475	0.0000000	0.0000000
Plasmacells	IGHA1	5.000537	0.422	0.134	0.0000000	0.0000000
Mastcells	CPA3	4.660256	0.526	0.002	0.0000000	0.0000000
Mastcells	TPSAB1	5.866691	0.561	0.005	0.0000000	0.0000000
Mastcells	MS4A2	2.837601	0.439	0.002	0.0000000	0.0000000
Mastcells	TPSB2	6.168258	0.456	0.003	0.0000000	0.0000000
Mastcells	HDC	2.810267	0.404	0.002	0.0000000	0.0000000
Mastcells	KIT	2.627171	0.404	0.003	0.0000000	0.0000000
Mastcells	CTSG	4.872125	0.368	0.002	0.0000000	0.0000000
Mastcells	SLC18A2	2.535432	0.316	0.002	0.0000000	0.0000000
Mastcells	ADCYAP1	2.366685	0.211	0.000	0.0000000	0.0000000
Mastcells	GATA2	2.591010	0.404	0.014	0.0000000	0.0000000
Mastcells	HPGD	4.554725	0.544	0.045	0.0000000	0.0000000
Mastcells	HPGDS	2.952823	0.509	0.099	0.0000000	0.0000000
Mastcells	COL6A3	2.390881	0.316	0.072	0.0000000	0.0000000
Mastcells	MTRNR2L2	4.483101	0.105	0.011	0.0000000	0.0000012
Mastcells	TUBA1A	2.355365	0.667	0.480	0.0000000	0.0000374
Mastcells	COL1A1	3.840824	0.333	0.102	0.0000000	0.0000834
Mastcells	COL1A2	2.658687	0.386	0.169	0.0000007	0.0182000
Mastcells	CD69	2.409889	0.474	0.264	0.0000010	0.0259156
Mastcells	COL3A1	2.975013	0.368	0.156	0.0000024	0.0634800
Mastcells	BGN	2.199685	0.175	0.075	0.0019884	1.0000000
Endothelial Cells	TM4SF1	4.503155	0.767	0.034	0.0000000	0.0000000
Endothelial Cells	AQP1	3.082235	0.610	0.022	0.0000000	0.0000000
Endothelial Cells	RAMP2	2.688395	0.680	0.016	0.0000000	0.0000000
Endothelial Cells	VWF	2.658656	0.620	0.014	0.0000000	0.0000000
Endothelial Cells	PLVAP	2.597516	0.587	0.012	0.0000000	0.0000000
Endothelial Cells	CLEC14A	2.269672	0.590	0.006	0.0000000	0.0000000
Endothelial Cells	ACKR1	3.619720	0.510	0.015	0.0000000	0.0000000
Endothelial Cells	CLDN5	2.515011	0.443	0.010	0.0000000	0.0000000
Endothelial Cells	CAV1	3.072425	0.737	0.071	0.0000000	0.0000000

Supplementary Table 6: Top 20 Markers per Synovial Cluster  
*(continued)*

cluster	gene	avg_log2FC	pct.1	pct.2	p_val	p_val_adj
Endothelial Cells	SPARCL1	3.923887	0.760	0.088	0.0000000	0.0000000
Endothelial Cells	HSPG2	2.339203	0.553	0.034	0.0000000	0.0000000
Endothelial Cells	GNG11	3.139170	0.743	0.100	0.0000000	0.0000000
Endothelial Cells	ADIRF	3.000902	0.710	0.104	0.0000000	0.0000000
Endothelial Cells	IGFBP7	3.354316	0.793	0.165	0.0000000	0.0000000
Endothelial Cells	ID1	2.198087	0.443	0.038	0.0000000	0.0000000
Endothelial Cells	POSTN	2.311330	0.373	0.024	0.0000000	0.0000000
Endothelial Cells	MGP	2.552454	0.633	0.127	0.0000000	0.0000000
Endothelial Cells	IFITM3	2.249718	0.913	0.495	0.0000000	0.0000000
Endothelial Cells	FABP4	3.741082	0.327	0.045	0.0000000	0.0000000
Endothelial Cells	CXCL10	2.449981	0.153	0.034	0.0000000	0.0000000
Smooth Muscle Cells	RGS5	4.137281	0.585	0.005	0.0000000	0.0000000
Smooth Muscle Cells	ACTA2	5.499940	0.854	0.023	0.0000000	0.0000000
Smooth Muscle Cells	SOD3	2.928606	0.659	0.014	0.0000000	0.0000000
Smooth Muscle Cells	RERGL	3.192290	0.390	0.003	0.0000000	0.0000000
Smooth Muscle Cells	TPM2	4.186571	0.878	0.031	0.0000000	0.0000000
Smooth Muscle Cells	MYH11	3.102201	0.634	0.014	0.0000000	0.0000000
Smooth Muscle Cells	NDUFA4L2	3.278826	0.707	0.024	0.0000000	0.0000000
Smooth Muscle Cells	MYL9	4.751715	0.902	0.055	0.0000000	0.0000000
Smooth Muscle Cells	C11orf96	3.816176	0.756	0.044	0.0000000	0.0000000
Smooth Muscle Cells	COL18A1	2.715739	0.732	0.055	0.0000000	0.0000000
Smooth Muscle Cells	TAGLN	5.490175	0.927	0.104	0.0000000	0.0000000
Smooth Muscle Cells	CALD1	3.883760	0.878	0.092	0.0000000	0.0000000
Smooth Muscle Cells	ADIRF	4.128781	0.927	0.142	0.0000000	0.0000000
Smooth Muscle Cells	SPARCL1	2.920864	0.902	0.131	0.0000000	0.0000000
Smooth Muscle Cells	IGFBP7	4.341736	0.902	0.206	0.0000000	0.0000000
Smooth Muscle Cells	TPM1	3.093231	0.780	0.158	0.0000000	0.0000000
Smooth Muscle Cells	MGP	3.383159	0.805	0.159	0.0000000	0.0000000
Smooth Muscle Cells	TIMP3	2.759214	0.707	0.131	0.0000000	0.0000000
Smooth Muscle Cells	DSTN	2.839775	0.902	0.504	0.0000000	0.0000000
Smooth Muscle Cells	CCL2	3.168996	0.683	0.245	0.0000000	0.0000000

## 8 Supplementary Table 7: Pearson correlation of different clinical parameters with SF subtypes across pathotypes

**FDR:** False Detection Rate

**SF:** Synovial Fibroblast

**SJC:** Swollen Joint Count

**TCJ:** Tender Joint Count

**HAQ:** Health Assessment Questionnaire

**CRP:** C-reactive Protein

**ESR:** Erythrocyte Sedimentation Rate

**VAS:** Pain on Visual Analog Scale

**DAS:** Disease Activity Score (28 joints)

Supplementary Table 7: Pearson correlation of different clinical parameters with SF subtypes across pathotypes

SF Subtype	Pathotype	Clinical Parameter	Correlation (R)	p-value	FDR adjusted p-value
PRG4+ SF	All	SJC	-0.0390	0.75000	0.8624000
		TJC	0.0610	0.61000	0.8231325
		HAQ	-0.1400	0.24000	0.5719149
		CRP	0.0100	0.93000	0.9826415
		ESR	-0.1500	0.22000	0.5600000
		VAS	0.0006	0.96000	0.9900000
		DAS	-0.0610	0.61000	0.8231325
	fibroid	SJC	0.2500	0.44000	0.7700000
		TJC	0.4200	0.17000	0.5448649
		HAQ	0.6700	0.01700	0.1866667
		CRP	0.2000	0.53000	0.8172973
		ESR	0.5200	0.08400	0.4704000
		VAS	0.4300	0.16000	0.5448649
	lymphoid	DAS	0.6600	0.02000	0.1866667
		SJC	0.1500	0.40000	0.7644444
		TJC	0.2600	0.13000	0.5392593
		HAQ	0.0520	0.77000	0.8624000
		CRP	0.0260	0.88000	0.9476923
		ESR	-0.0740	0.67000	0.8521739
		VAS	-0.0013	0.99000	0.9900000
	myeloid	DAS	0.0570	0.75000	0.8624000
		SJC	-0.6300	0.00061	0.0227733
		TJC	-0.4800	0.01300	0.1820000
		HAQ	-0.0086	0.97000	0.9900000
		CRP	-0.1600	0.43000	0.7644444
		ESR	-0.4400	0.02400	0.2067692
		VAS	-0.1500	0.46000	0.7926154
		DAS	-0.5200	0.00670	0.1072000

Supplementary Table 7: Pearson correlation of different clinical parameters with SF subtypes across pathotypes (*continued*)

SF Subtype	Pathotype	Clinical Parameter	Correlation (R)	p-value	FDR adjusted p-value
CXCL12+ SF	All	SJC	0.0560	0.67000	0.8521739
		TJC	0.0880	0.49000	0.8070588
		HAQ	-0.1100	0.37000	0.7534545
		CRP	0.0550	0.67000	0.8521739
		ESR	0.1000	0.43000	0.7644444
		VAS	-0.1600	0.20000	0.5600000
		DAS	0.0650	0.61000	0.8231325
	fibroid	SJC	0.1800	0.70000	0.8521739
		TJC	-0.1000	0.58000	0.8222785
		HAQ	0.3700	0.42000	0.7644444
		CRP	0.1200	0.80000	0.8871287
		ESR	0.5600	0.10000	0.4869565
lymphoid	lymphoid	VAS	0.2300	0.61000	0.8231325
		DAS	0.3000	0.52000	0.8172973
		SJC	0.0630	0.70000	0.8521739
		TJC	-0.0660	0.54000	0.8172973
		HAQ	-0.1600	0.32000	0.6762264
	myeloid	CRP	0.0530	0.75000	0.8624000
		ESR	-0.0350	0.83600	0.9179608
		VAS	-0.2300	0.16000	0.5448649
		DAS	-0.0470	0.77000	0.8624000
		SJC	0.1300	0.64000	0.8432941
myeloid	myeloid	TJC	-0.0250	0.88000	0.9476923
		HAQ	-0.0990	0.71000	0.8550538
		CRP	-0.0110	0.97000	0.9900000
		ESR	0.3300	0.21000	0.5600000
		VAS	-0.1600	0.56000	0.8222785
		DAS	0.2900	0.28000	0.6400000

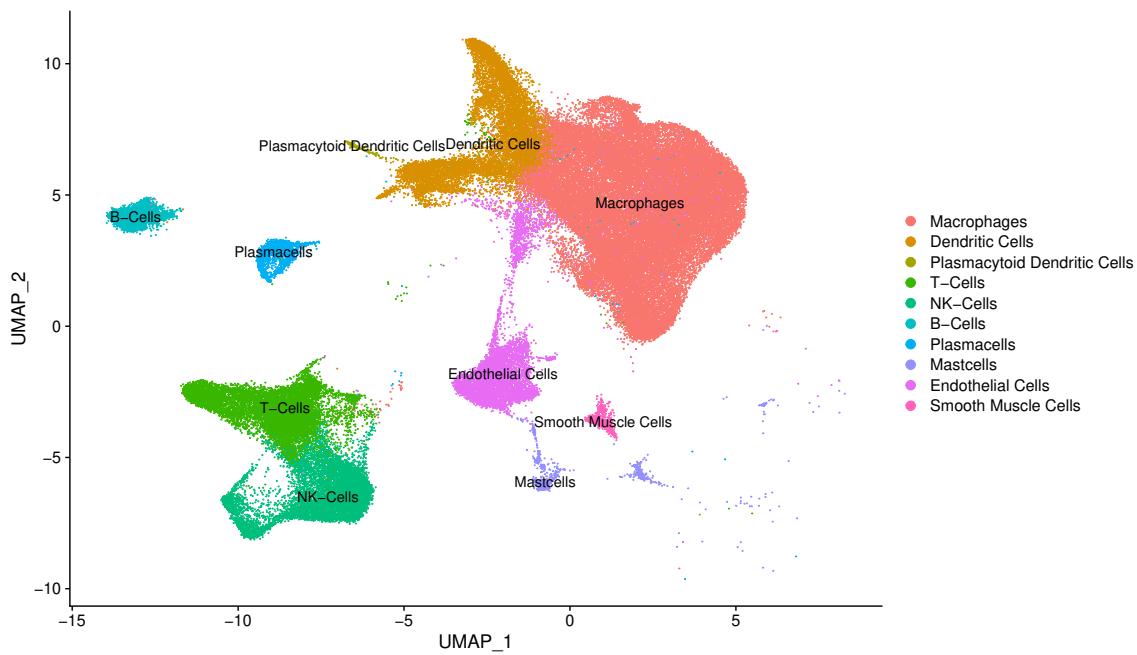
Supplementary Table 7: Pearson correlation of different clinical parameters with SF subtypes across pathotypes (*continued*)

SF Subtype	Pathotype	Clinical Parameter	Correlation (R)	p-value	FDR adjusted p-value
POSTN+ SF	All	SJC	0.0370	0.64000	0.8432941
		TJC	0.0560	0.48000	0.8070588
		HAQ	-0.0790	0.32000	0.6762264
		CRP	0.1600	0.04600	0.3030588
		ESR	-0.0640	0.42000	0.7644444
		VAS	-0.1900	0.01700	0.1866667
		DAS	-0.0540	0.50000	0.8115942
	fibroid	SJC	0.0590	0.76000	0.8624000
		TJC	-0.2500	0.17000	0.5448649
		HAQ	-0.4200	0.01900	0.1866667
		CRP	-0.0740	0.70000	0.8521739
		ESR	-0.1600	0.39000	0.7644444
lymphoid	lymphoid	VAS	-0.2800	0.14000	0.5448649
		DAS	-0.2400	0.21000	0.5600000
		SJC	0.2300	0.03200	0.2560000
		TJC	0.3300	0.00150	0.0420000
		HAQ	0.0840	0.43000	0.7644444
	myeloid	CRP	0.3800	0.00024	0.0134400
		ESR	0.1300	0.23000	0.5600000
		VAS	-0.0740	0.49000	0.8070588
		DAS	0.2000	0.05900	0.3671111
		SJC	-0.2400	0.13000	0.5392593
myeloid	myeloid	TJC	-0.2200	0.18000	0.5448649
		HAQ	-0.2000	0.23000	0.5600000
		CRP	0.1000	0.54000	0.8172973
		ESR	-0.0027	0.99000	0.9900000
		VAS	-0.2500	0.11000	0.5133333
		DAS	-0.1600	0.32000	0.6762264

Supplementary Table 7: Pearson correlation of different clinical parameters with SF subtypes across pathotypes (*continued*)

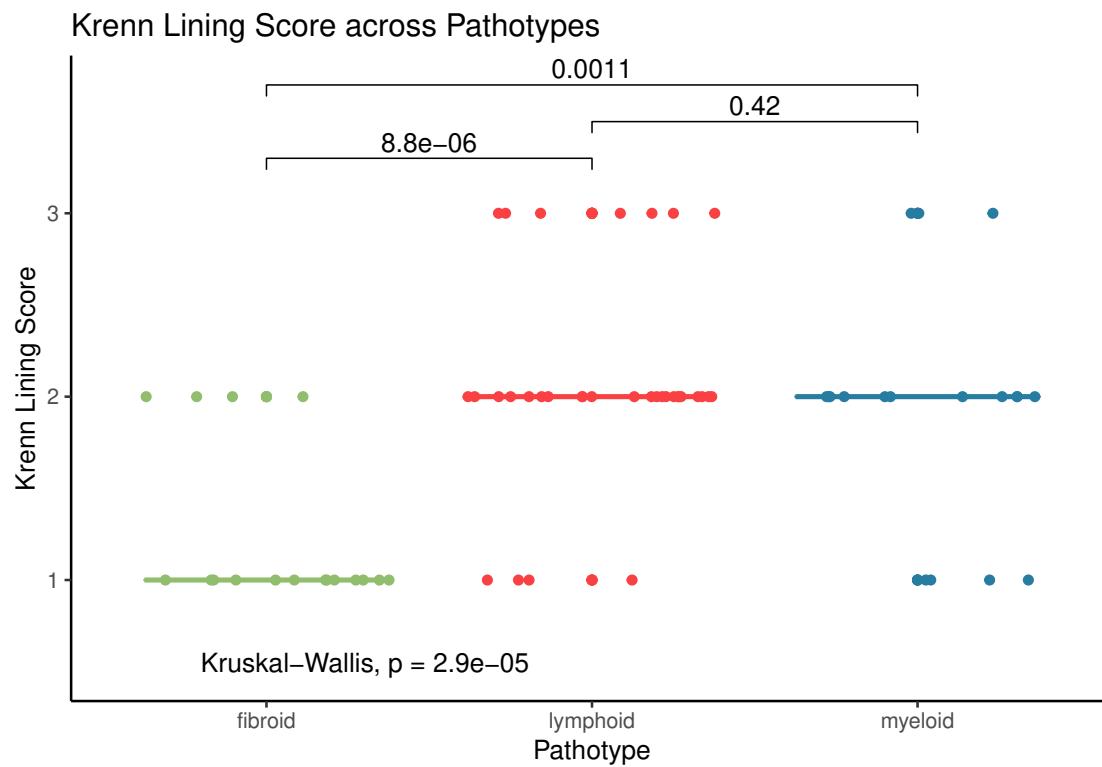
SF Subtype	Pathotype	Clinical Parameter	Correlation (R)	p-value	FDR adjusted p-value
CXCL14+ SF	All	SJC	-0.6100	0.00220	0.0466667
		TJC	-0.3300	0.13000	0.5392593
		HAQ	-0.1300	0.57000	0.8222785
		CRP	-0.3700	0.09100	0.4853333
		ESR	-0.3500	0.10000	0.4869565
		VAS	-0.2900	0.18000	0.5448649
		DAS	-0.6400	0.00000	0.0000000
	fibroid	SJC	-0.4800	0.16000	0.5448649
		TJC	-0.3300	0.06500	0.3831579
		HAQ	-0.4600	0.18000	0.5448649
		CRP	0.4300	0.21000	0.5600000
		ESR	0.2000	0.58000	0.8222785
lymphoid	lymphoid	VAS	-0.3600	0.32000	0.6762264
		DAS	-0.4200	0.23000	0.5600000
		SJC	-0.0120	0.98000	0.9900000
		TJC	-0.2100	0.04500	0.3030588
		HAQ	-0.0530	0.90000	0.9600000
	myeloid	CRP	0.5600	0.20000	0.5600000
		ESR	0.2600	0.54000	0.8172973
		VAS	0.2500	0.55000	0.8213333
		DAS	-0.1700	0.68000	0.8521739
		SJC	-0.8900	0.04400	0.3030588
myeloid	myeloid	TJC	-0.1500	0.37000	0.7534545
		HAQ	0.7500	0.15000	0.5448649
		CRP	-0.4800	0.41000	0.7644444
		ESR	-0.6100	0.27000	0.6300000
		VAS	-0.1900	0.76000	0.8624000
		DAS	-0.9800	0.00250	0.0466667

## 9 Supplementary Figure 1: Umap Plot of all integrated scRNA-seq of the synovium excluding synovial fibroblasts



## 11 Supplementary Figure 2: Krenn Lining Score across Pathotypes

P-values for Wilcoxon Rank Sum tests and Kruskal-Wallis are shown.



## 12 Supplementary Figure 3: Linear relationship between disease activity measurements and Celltypes across synovial pathotypes using linear regression analysis

p values are unadjusted

