

Table S1. The canonical markers for the 8 cell types identified within the FD tissue

Cell Type	Canonical Marker Genes	References
Myofibroblast	<i>ACTA2, TAGLN, TPM2</i>	[1]
Osteoblast	<i>SFRP4, SP7, RUNX2, ALPL</i>	[2,3]
Fibroblast type 1	<i>KCNMA1, ABI3BP, SMURF2, ADAMTSL1</i>	[4–7]
Fibroblast type 2	<i>COL4A1, COL4A2, IGFBP7</i>	[8]
Proliferating cell	<i>MKI67, PCNA, TOP2A, CENPF</i>	[9]
Myogenic cell	<i>SMYD3, NEAT1, MALAT1, BNC2</i>	[10–13]
Macrophage	<i>CD68</i>	[14]
Dendritic cell	<i>HLA-DRA, CD74</i>	[15]

Table S2. Target genes and their primer sequences

Gene Name	Forward primer (5'-3')	Reverse primer (5'-3')
<i>ACTA2</i>	CTATGCCTCTGGACGCACAACT	CAGATCCAGACGCATGATGGCA
<i>TAGLN</i>	TCCAGGTCTGGCTGAAGAATGG	CTGCTCCATCTGCTTGAAGACC
<i>TPM2</i>	GAGAGGTCTGTGGCAAAGTTGG	GGAGGTGATGTCATTGAGTGCG
<i>SFRP4</i>	CTATGACCGTGGCGTGTGCATT	GCTTAGGCGTTTACAGTCAACATC
<i>RUNX2</i>	TGGTTACTGTCATGGCGGGTA	TCTCAGATCGTTGAACCTTGCTA
<i>BICC1</i>	GATGTGTCCCTCCAAGTTTCC	GGCTTTCGGTAGCACTCAGTTC
<i>DCN</i>	GCTCTCCTACATCCGCATTGCT	GTCCTTTCAGGCTAGCTGCATC
<i>FBLN</i>	GGATACACAGGTGATGGCTTCAC	GTCGCATTACACAGCGGTATCCT
<i>ADAMTSL1</i>	TGACATCGGCTGAGTGCTACGA	GGCATGATCTGCTTGTATCCGTC
<i>KCNMA1</i>	TATCTCTCCAGTGCCTTCGTGG	CTCTCTCGGTTGGCAGACTTGT
<i>SMURF2</i>	TCCTCGGCTGTCTGCTAACTTG	CAGGCATTCTGTGTCATCAGGAC
<i>AB13BP</i>	CCTTCTACACCTAAACGACGCC	GGTGTGTCCATGTAGGTTTCAGG
<i>COL4A1</i>	TGTTGACGGCTTACCTGGAGAC	GGTAGACCAACTCCAGGCTCTC
<i>COL4A2</i>	GGATAACAGGCGTGACTGGAGT	CTTTGCCACCAGGCAGTCCAAT
<i>IGFBP7</i>	GCCATCACCCAGGTCAGCAAG	GGATTCCGATGACCTCACAGCT
<i>MKI67</i>	GAAAGAGTGGCAACCTGCCTTC	GCACCAAGTTTACTACATCTGCC
<i>PCNA</i>	CAAGTAATGTCGATAAAGAGGAGG	GTGTCACCGTTGAAGAGAGTGG
<i>TOP2</i>	GTGGCAAGGATTCTGCTAGTCC	ACCATTTCAGGCTCAACACGCTG
<i>CENPF</i>	AGCACGACTCCAGCTACAAGGT	CATCATGCTTTGGTGTCTTTCTG
<i>SMYD3</i>	TACTGCGAGCAGTCCGAGACA	TTGTCCTGGGTTTGGCAACGGA
<i>NEAT1</i>	GCTGGACCTTTCATGTAACGGG	TGAACTCTGCCGGTACAGGGAA
<i>BNC2</i>	ACTCTGCGGGACTATGTCCGAG	ACCGCAGAACTGCTGAAGGGT
<i>HLA-DRA</i>	AGCTGTGGACAAAGCCAACTG	CTCTCAGTTCCACAGGGCTGTT
<i>CD74</i>	AAGCCTGTGAGCAAGATGCGCA	AGCAGGTGCATCACATGGTCCT
<i>CD68</i>	CGAGCATCATTCTTTCACCAGCT	ATGAGAGGCAGCAAGATGGACC
<i>MMP9</i>	GCCACTACTGTGCCTTTGAGTC	CCCTCAGAGAATCGCCAGTACT
<i>OSX/SP7</i>	CTGCGGGACTCAACAACCTCT	GAGCCATAGGGGTGTGTCAT
<i>DLX5</i>	GAGTAGGTGTCCCGCCTCAGAACCC	CCAACCAGCCAGAGAAAGAA
<i>ALPL</i>	ACCACCACGAGAGTGAACCA	CGTTGTCTGAGTACCAGTCCC
<i>OCN/BGLAP</i>	CACTCCTCGCCCTATTGGC	CCCTCCTGCTTGGACACAAAG
<i>OPN/SPP1</i>	GCCGAGGTGATAGTGTGGTT	GCTTTCCATGTGTGAGGTGAT
<i>DMP1</i>	GATCAGCATCCTGCTCATGTT	AGCCAAATGACCCTTCCATTC
<i>SOST</i>	CCCTTTGAGACCAAAGACGTG	GGCCCATCGGTCACGTAG
<i>RANKL</i>	CCAAGATCTCCAACATGACTTAC	ACCATTAGTTGAAGATACT
<i>CAPG</i>	CTCCATTCCCAGGCTCAGT	GAAACCTCTTCTGGGCCATT
<i>TRAP/ACP5</i>	TTCTACCGCCTGCACTCCAA	AGCTGATCTCCACATAGGCA
<i>IL1β</i>	AAACAGATGAAGTGCTCCTTCCAGG	TGGAGAACACCACTTGTGCTCCA
<i>TNFα</i>	CTTCTTCTCCTTCTGATCGTGG	GCTGGTTATCTCTCAGCTCCA
<i>COL1A1</i>	GTGCGATGACGTGATCTGTGA	CGGTGGTTTCTTGGTCCGT
<i>TGFβ1</i>	TCGCCAGAGTGGTTATCTT	TAGTGAACCCGTTGATGTCC
<i>PLOD2</i>	GACAGCGTTCTCTTCGTCTCTCA	CTCCAGCCTTTTCGTGGTGACT
<i>GAPDH</i>	ACAGTTGCCATGTAGACC	TTTTTGGTTGAGCACAGG

Table S3. Cell counts and proportion per sample per cluster. The percentage of samples' cells in the cluster as indicated in brackets.

Cluster	FD3	FD4	FD5
Myofibroblast	3,154 (38.1)	3,676 (37.6)	2,055 (17.2)
Osteoblast	2,358 (28.5)	1,969 (20.1)	3,744 (31.3)
Fibroblast type 1	1,358 (16.4)	2,229 (22.8)	3,004 (25.1)
Fibroblast type 2	567 (6.8)	845 (8.6)	1,168 (9.8)
Proliferating S	345 (4.2)	359 (3.7)	831 (6.9)
Proliferating G2M	389 (4.7)	389 (4.0)	602 (5.0)
Myogenic	66 (0.8)	132 (1.4)	362 (3.0)
MPS	51 (0.6)	175 (1.8)	202 (1.7)

Supplementary references

1. Peyser, R.; MacDonnell, S.; Gao, Y.; Cheng, L.; Kim, Y.; Kaplan, T.; Ruan, Q.; Wei, Y.; Ni, M.; Adler, C.; et al. Defining the Activated Fibroblast Population in Lung Fibrosis Using Single-Cell Sequencing. *Am. J. Respir. Cell Mol. Biol.* **2019**, *61*, 74–85.
2. Komori, T. Regulation of Proliferation, Differentiation and Functions of Osteoblasts by Runx2. *Int. J. Mol. Sci.* **2019**, *20*, 1694.
3. Silvent, J.; Nassif, N.; Helary, C.; Azaïs, T.; Sire, J.-Y.; Guille, M.M.G. Collagen Osteoid-Like Model Allows Kinetic Gene Expression Studies of Non-Collagenous Proteins in Relation with Mineral Development to Understand Bone Biomineralization. *PLoS ONE* **2013**, *8*, e57344.
4. Wang, Y.; Guo, Q.; Hei, H.; Tao, J.; Zhou, Y.; Dong, J.; Xin, H.; Cai, H.; Gao, J.; Yu, K.; et al. BK Ablation Attenuates Osteoblast Bone Formation via Integrin Pathway. *Cell Death Dis.* **2019**, *10*, 738.
5. Hodgkinson, C.P.; Naidoo, V.; Patti, K.G.; Gomez, J.A.; Schmeckpeper, J.; Zhang, Z.; Davis, B.; Pratt, R.E.; Mirotso, M.; Dzau, V.J. Abi3bp Is a Multifunctional Autocrine/Paracrine Factor That Regulates Mesenchymal Stem Cell Biology. *Stem Cells* **2013**, *31*, 1669–1682.
6. Manikoth Ayyathan, D.; Koganti, P.; Marcu-Malina, V.; Litmanovitch, T.; Trakhtenbrot, L.; Emanuelli, A.; Apel-Sarid, L.; Blank, M. SMURF2 Prevents Detrimental Changes to Chromatin, Protecting Human Dermal Fibroblasts from Chromosomal Instability and Tumorigenesis. *Oncogene* **2020**, *39*, 3396–3410.
7. Rypdal, K.B.; Erusappan, P.M.; Melleby, A.O.; Seifert, D.E.; Palmero, S.; Strand, M.E.; Tønnessen, T.; Dahl, C.P.; Almaas, V.; Hubmacher, D.; et al. The Extracellular Matrix Glycoprotein ADAMTSL2 Is Increased in Heart Failure and Inhibits TGFβ Signalling in Cardiac Fibroblasts. *Sci. Rep.* **2021**, *11*, 19757.
8. Kreus, M.; Lehtonen, S.; Skarp, S.; Kaarteenaho, R. Extracellular Matrix Proteins Produced by Stromal Cells in Idiopathic Pulmonary Fibrosis and Lung Adenocarcinoma. *PloS One* **2021**, *16*, e0250109.
9. Li, R.; Wang, T.; Shelp-Peck, E.; Wu, S.-P.; DeMayo, F.J. The Single-Cell Atlas of Cultured Human Endometrial Stromal Cells. *FS Sci.* **2022**, *3*, 349–366.
10. Bobowski-Gerard, M.; Boulet, C.; Zummo, F.P.; Dubois-Chevalier, J.; Gheeraert, C.; Bou Saleh, M.; Strub, J.-M.; Farce, A.; Ploton, M.; Guille, L.; et al. Functional Genomics Uncovers the Transcription Factor BNC2 as Required for Myofibroblastic Activation in Fibrosis. *Nat. Commun.* **2022**, *13*, 5324.
11. Codato, R.; Perichon, M.; Divol, A.; Fung, E.; Sotiropoulos, A.; Bigot, A.; Weitzman, J.B.; Medjkane, S. The SMYD3 Methyltransferase Promotes Myogenesis by Activating the Myogenin Regulatory Network. *Sci. Rep.* **2019**, *9*, 17298.
12. Liu, C.; Gao, X.; Li, Y.; Sun, W.; Xu, Y.; Tan, Y.; Du, R.; Zhong, G.; Zhao, D.; Liu, Z.; et al. The Mechanosensitive lncRNA Neat1 Promotes Osteoblast Function through Paraspeckle-Dependent Smurf1 mRNA Retention. *Bone Res.* **2022**, *10*, 18.
13. Chen, X.; He, L.; Zhao, Y.; Li, Y.; Zhang, S.; Sun, K.; So, K.; Chen, F.; Zhou, L.; Lu, L.; et al. Malat1 Regulates Myogenic Differentiation and Muscle Regeneration through Modulating MyoD Transcriptional Activity. *Cell Discov.* **2017**, *3*, 17002.
14. Bisgaard, L.S.; Mogensen, C.K.; Rosendahl, A.; Cucak, H.; Nielsen, L.B.; Rasmussen, S.E.; Pedersen, T.X. Bone Marrow-Derived and Peritoneal Macrophages Have Different Inflammatory Response to oxLDL and M1/M2 Marker Expression - Implications for Atherosclerosis Research. *Sci. Rep.* **2016**, *6*, 35234.
15. Li, Y.; Jeong, J.; Song, W. Molecular Characteristics and Distribution of Adult Human Corneal Immune Cell Types. *Front. Immunol.* **2022**, *13*, 798346.