

Appendix B

Heterogeneity in primary human fibroblasts

Table B.1 Marker genes of *ex vivo* skin clusters

Gene name	P-value	Cluster
Fibroblast Type 1		
TNFAIP6	2.99E-269	0
SERPINE2	1.58E-177	0
MEDAG	1.15E-169	0
CTSL	9.59E-162	0
THBS2	9.21E-158	0
PTGES	2.56E-135	0
PDPN	3.43E-132	0
AKR1C1	9.68E-122	0
BNIP3	5.09E-110	0
NAMPT	1.55E-107	0
GLUL	2.18E-100	0
IL6	1.85E-87	0
FST	6.85E-85	0
PTX3	2.59E-74	0
MGST1	3.74E-72	0
MT1X	1.21E-68	0
ACKR3	2.83E-52	0
CXCL1	4.75E-52	0
G0S2	5.90E-21	0
COMP	2.20E-16	0
Vascular Endothelium		
TM4SF1	1.21E-207	1
DSTN	2.73E-205	1
ACTB	1.44E-165	1
HLA-DRB1	1.94E-160	1
ACTG1	6.35E-158	1
UPP1	3.84E-143	1
NCOA7	1.15E-133	1
HLA-DRA	6.80E-131	1
TSC22D1	4.41E-123	1
PLS3	5.67E-121	1
GBP2	9.47E-116	1
PRSS23	2.72E-115	1
HLA-DQB1	6.10E-112	1
SAT1	1.46E-110	1

Gene name	P-value	Cluster
SERPINE1	9.65E-110	1
YWHAH	4.29E-109	1
NEDD9	1.46E-102	1
CYR61	4.72E-101	1
SOX17	1.04E-99	1
EDN1	1.10E-60	1

Fibroblast Type 2

PLAC9	4.67E-104	2
SFRP2	2.72E-103	2
CXCL12	4.64E-87	2
PPIC	4.18E-79	2
S100A4	6.55E-78	2
SEPP1	1.86E-76	2
TPPP3	5.44E-76	2
OLFML3	6.50E-76	2
TSC22D3	7.26E-75	2
ARL6IP5	1.28E-74	2
CRIP1	3.10E-70	2
CTSK	6.79E-70	2
ADH1B	1.00E-68	2
PTGDS	6.25E-65	2
CRABP2	6.33E-63	2
COL1A1	8.38E-43	2
COL3A1	9.42E-42	2
SOSTDC1	2.89E-35	2
GADD45B	5.53E-34	2
APOE	1.51E-21	2

Pericytes

RGS5	2.38E-93	3
NDUFA4L2	1.40E-75	3
CALD1	1.57E-64	3
C11orf96	6.90E-53	3
LURAP1L	6.87E-52	3
MTHFD2	2.06E-49	3
CPM	4.33E-48	3
CHN1	1.19E-45	3
ID4	6.04E-43	3
EDNRB	6.38E-43	3

Gene name	P-value	Cluster
TFPI	1.40E-42	3
RRAD	2.79E-42	3
KCNE4	9.81E-37	3
VEGFA	1.86E-36	3
TPM2	1.89E-34	3
CPE	5.59E-33	3
HES4	1.32E-32	3
SRGN	6.27E-30	3
ACTA2	4.86E-29	3
MT1A	1.26E-27	3

Lymphatic Endothelium

CCL21	6.47E-114	4
TFF3	3.94E-87	4
MMRN1	4.83E-84	4
CLDN5	2.03E-51	4
FABP5	9.07E-50	4
PPFIBP1	7.79E-46	4
LYVE1	4.55E-45	4
GNAS	1.78E-37	4
LAPTM5	2.06E-37	4
GNG11	1.58E-26	4
SDPR	1.90E-25	4
RAMP2	2.95E-25	4
EGLN3	9.43E-24	4
HYAL2	2.94E-22	4
SNCG	4.56E-20	4
IRF8	1.00E-18	4
ANGPT2	3.56E-18	4
FABP4	3.63E-16	4
CXCL8	2.38E-10	4
CXCL2	2.55E-08	4

Vascular Endothelium

CCL14	4.38E-45	5
GNG11	1.94E-41	5
ACKR1	1.62E-39	5
CD74	2.00E-39	5
HLA-DRA	5.77E-36	5
CYTL1	2.13E-34	5

Gene name	P-value	Cluster
AQP1	1.11E-32	5
ITM2A	1.09E-30	5
HLA-DPA1	3.09E-30	5
CD34	3.43E-30	5
TXNIP	5.15E-30	5
PECAM1	9.57E-30	5
TSPAN7	6.29E-29	5
CTGF	5.58E-28	5
RND1	2.09E-25	5
SELE	1.52E-22	5
FOS	9.76E-19	5
DNAJB1	9.94E-16	5
HSPA1B	1.53E-15	5
HSPA1A	3.74E-14	5

Table B.2 GO term enrichment in unstimulated fibroblast clusters

GO term ID	GO term name	Enrichment p-value
Non-cycling 1		
GO:0071705	nitrogen compound transport	0.0363
GO:0007044	cell-substrate junction assembly	0.0194
GO:0050765	negative regulation of phagocytosis	0.0405
GO:2000808	negative regulation of synaptic vesicle clustering	0.0132
GO:2001202	negative regulation of transforming growth factor-beta secretion	0.0132
GO:0030198	extracellular matrix organization	0.00337
GO:0018149	peptide cross-linking	0.00442
GO:2000761	positive regulation of N-terminal peptidyl-lysine acetylation	0.0132
GO:0006543	glutamine catabolic process	0.0186
GO:0001666	response to hypoxia	0.0477
GO:0002902	regulation of B cell apoptotic process	0.0436
GO:0061002	negative regulation of dendritic spine morphogenesis	0.0301
GO:0060179	male mating behavior	0.0268
GO:0007166	cell surface receptor signaling pathway	0.00639
GO:0071257	cellular response to electrical stimulus	0.0381
GO:0048681	negative regulation of axon regeneration	0.0375
GO:0009612	response to mechanical stimulus	0.0375
GO:0098698	postsynaptic specialization assembly	0.0301
GO:0052047	interaction with other organism via secreted substance involved in symbiotic interaction	0.0186
GO:0060070	canonical Wnt signaling pathway	0.0424
GO:1990138	neuron projection extension	0.0301
GO:0007160	cell-matrix adhesion	0.00306
GO:2000134	negative regulation of G1/S transition of mitotic cell cycle	0.0203
GO:0071310	cellular response to organic substance	0.00306
GO:0001667	ameboidal-type cell migration	0.00337
GO:0048468	cell development	0.00852
GO:0071603	endothelial cell-cell adhesion	0.0268

GO term ID	GO term name	Enrichment p-value
GO:1904209	positive regulation of chemokine (C-C motif) ligand 2 secretion	0.0186
GO:0032286	central nervous system myelin maintenance	0.0186
GO:0051674	localization of cell	0.00337
GO:1903984	positive regulation of TRAIL-activated apoptotic signaling pathway	0.0241
GO:0090071	negative regulation of ribosome biogenesis	0.0268
GO:0046466	membrane lipid catabolic process	0.0489
GO:0033622	integrin activation	0.0436
GO:0051090	regulation of DNA-binding transcription factor activity	0.0186
GO:0097105	presynaptic membrane assembly	0.0351
GO:1990523	bone regeneration	0.0186
GO:0002328	pro-B cell differentiation	0.0371
GO:0010663	positive regulation of striated muscle cell apoptotic process	0.0371
GO:0003174	mitral valve development	0.0371
GO:1903690	negative regulation of wound healing, spreading of epidermal cells	0.0268
GO:0046855	inositol phosphate dephosphorylation	0.0371
GO:0060024	rhythmic synaptic transmission	0.0268
GO:0051705	multi-organism behavior	0.0124
GO:0003215	cardiac right ventricle morphogenesis	0.0405
GO:0060134	prepulse inhibition	0.0363
GO:0097267	omega-hydroxylase P450 pathway	0.0335
GO:0009888	tissue development	0.00306
GO:1904706	negative regulation of vascular smooth muscle cell proliferation	0.047
GO:0048514	blood vessel morphogenesis	0.00306
GO:0009404	toxin metabolic process	0.0449
GO:0071702	organic substance transport	0.0427
GO:0060414	aorta smooth muscle tissue morphogenesis	0.0241
GO:0097107	postsynaptic density assembly	0.0301
GO:1990314	cellular response to insulin-like growth factor stimulus	0.0363

GO term ID	GO term name	Enrichment p-value
GO:0035025	positive regulation of Rho protein signal transduction	0.0489
GO:0071307	cellular response to vitamin K	0.0186
GO:0045475	locomotor rhythm	0.0375
GO:0032228	regulation of synaptic transmission, GABAergic	0.0489
GO:0048589	developmental growth	0.00852
GO:0007270	neuron-neuron synaptic transmission	0.0351
GO:0048870	cell motility	0.00337
GO:1904668	positive regulation of ubiquitin protein ligase activity	0.0405
GO:0008361	regulation of cell size	0.0335
GO:1901564	organonitrogen compound metabolic process	0.0407
GO:0006469	negative regulation of protein kinase activity	0.0415
GO:0042574	retinal metabolic process	0.0375
GO:0008285	negative regulation of cell proliferation	0.0363
GO:2000272	negative regulation of signaling receptor activity	0.00639
GO:0006537	glutamate biosynthetic process	0.0268
GO:0003284	septum primum development	0.0268
GO:0060044	negative regulation of cardiac muscle cell proliferation	0.0392
GO:0070372	regulation of ERK1 and ERK2 cascade	0.0392
GO:0060613	fat pad development	0.0335
GO:0060736	prostate gland growth	0.0375
GO:0019373	epoxygenase P450 pathway	0.0392
GO:0014067	negative regulation of phosphatidylinositol 3-kinase signaling	0.0381
GO:0051895	negative regulation of focal adhesion assembly	0.0424
GO:0030334	regulation of cell migration	0.00337

Cycling 1

GO:0046826	negative regulation of protein export from nucleus	0.0282
GO:0007049	cell cycle	3.01e-06
GO:0051301	cell division	2.81e-06
GO:0051382	kinetochore assembly	0.00174
GO:0031441	negative regulation of mRNA 3'-end processing	0.0344
GO:0002052	positive regulation of neuroblast proliferation	0.0466

GO term ID	GO term name	Enrichment p-value
GO:0051253	negative regulation of RNA metabolic process	0.00887
GO:0000280	nuclear division	0.000116
	positive regulation of single stranded viral RNA	
GO:0045870	replication via double stranded DNA interme- diate	0.0106
GO:0045769	negative regulation of asymmetric cell division	0.0106
GO:0000712	resolution of meiotic recombination intermedi- ates	0.0449
GO:0085020	protein K6-linked ubiquitination	0.0327
GO:0045786	negative regulation of cell cycle	0.00651
GO:0030263	apoptotic chromosome condensation	0.0263
GO:0031508	pericentric heterochromatin assembly	0.0152
GO:0099606	microtubule plus-end directed mitotic chromo- some migration	0.0106
GO:0021873	forebrain neuroblast division	0.0263
GO:0042981	regulation of apoptotic process	0.0114
GO:0034508	centromere complex assembly	0.000175
GO:0007292	female gamete generation	0.0206
GO:0032501	multicellular organismal process	0.0344
GO:0045892	negative regulation of transcription, DNA- templated	0.0241
GO:0006259	DNA metabolic process	0.0199
GO:0007051	spindle organization	0.0039
GO:0051304	chromosome separation	0.000643
GO:0061469	regulation of type B pancreatic cell proliferation	0.0366
GO:1990001	inhibition of cysteine-type endopeptidase activ- ity involved in apoptotic process	0.0327

Non-cycling 2

No significant gene sets

Transitional

GO:0051651	maintenance of location in cell	0.0479
GO:0048145	regulation of fibroblast proliferation	0.0479
GO:0034118	regulation of erythrocyte aggregation	0.0371
GO:0002317	plasma cell differentiation	0.0479
GO:0030239	myofibril assembly	0.0371

GO term ID	GO term name	Enrichment p-value
GO:1905273	positive regulation of proton-transporting ATP synthase activity, rotational mechanism	0.0371
GO:0035606	peptidyl-cysteine S-trans-nitrosylation	0.0371
GO:0007249	I-kappaB kinase/NF-kappaB signaling	0.0371

Cycling 2

GO:0000226	microtubule cytoskeleton organization	0.0163
GO:0051494	negative regulation of cytoskeleton organization	0.0495
GO:0007049	cell cycle	0.00457
GO:0000281	mitotic cytokinesis	0.0315
GO:0051301	cell division	0.00457
GO:1903901	negative regulation of viral life cycle	0.0358