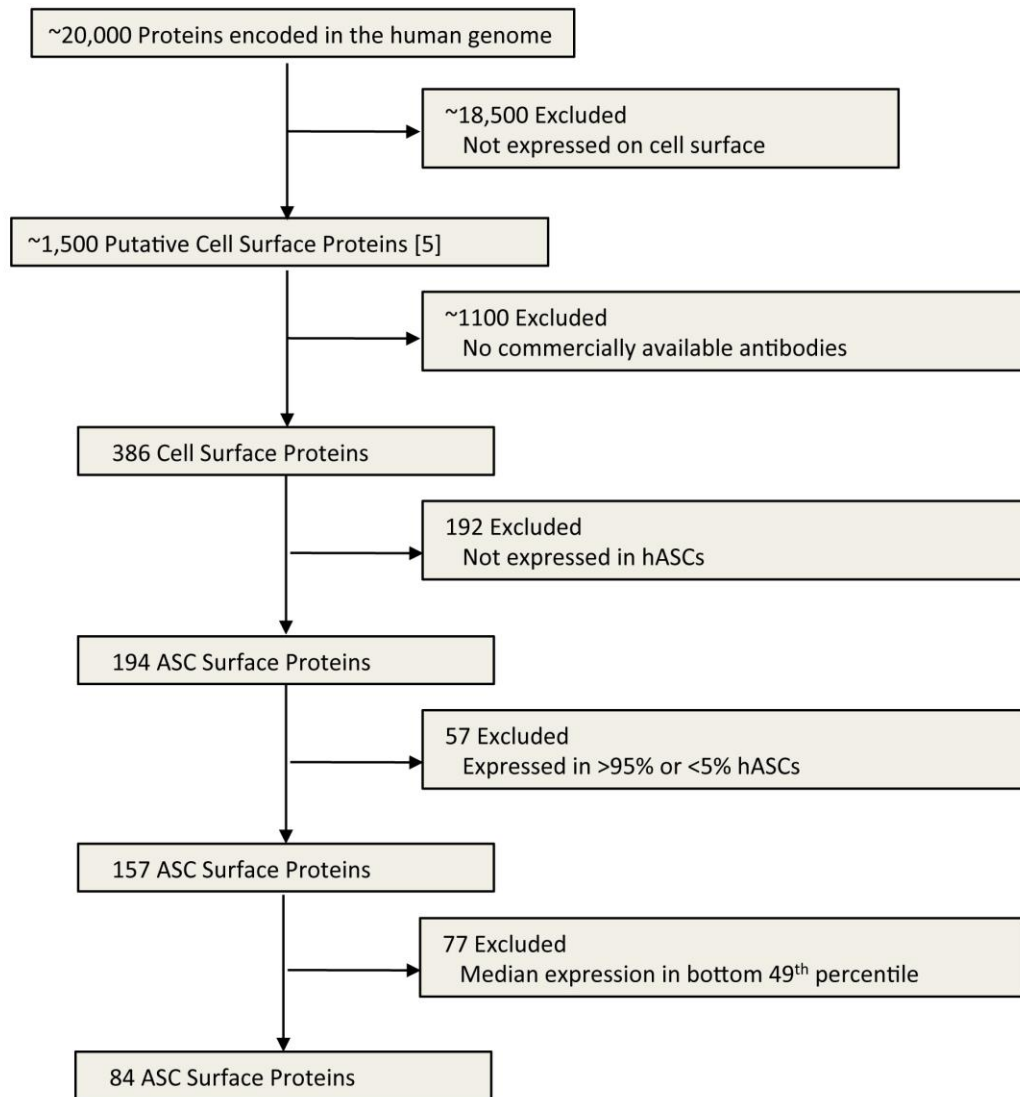
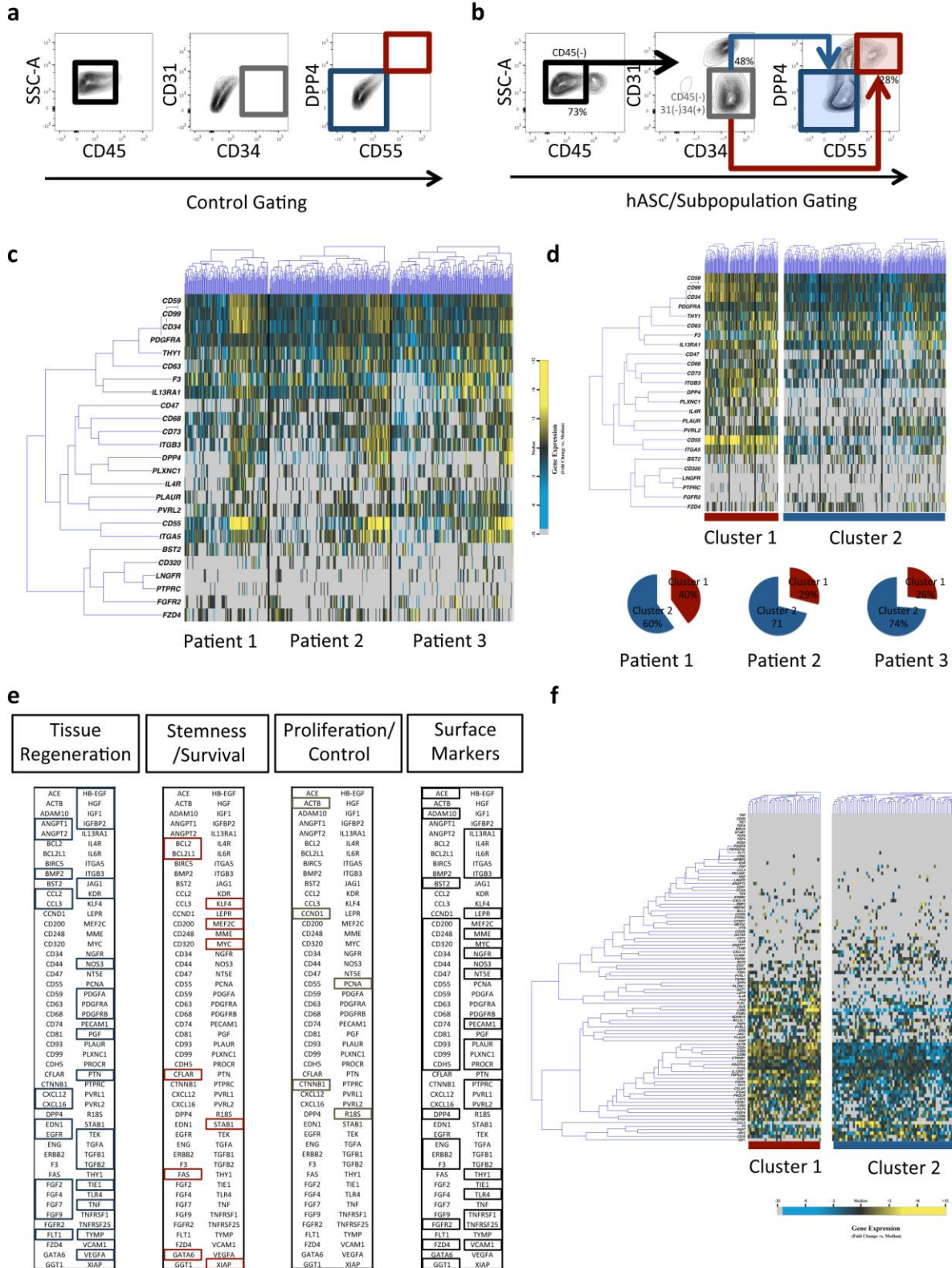


Supplementary Figure 1:



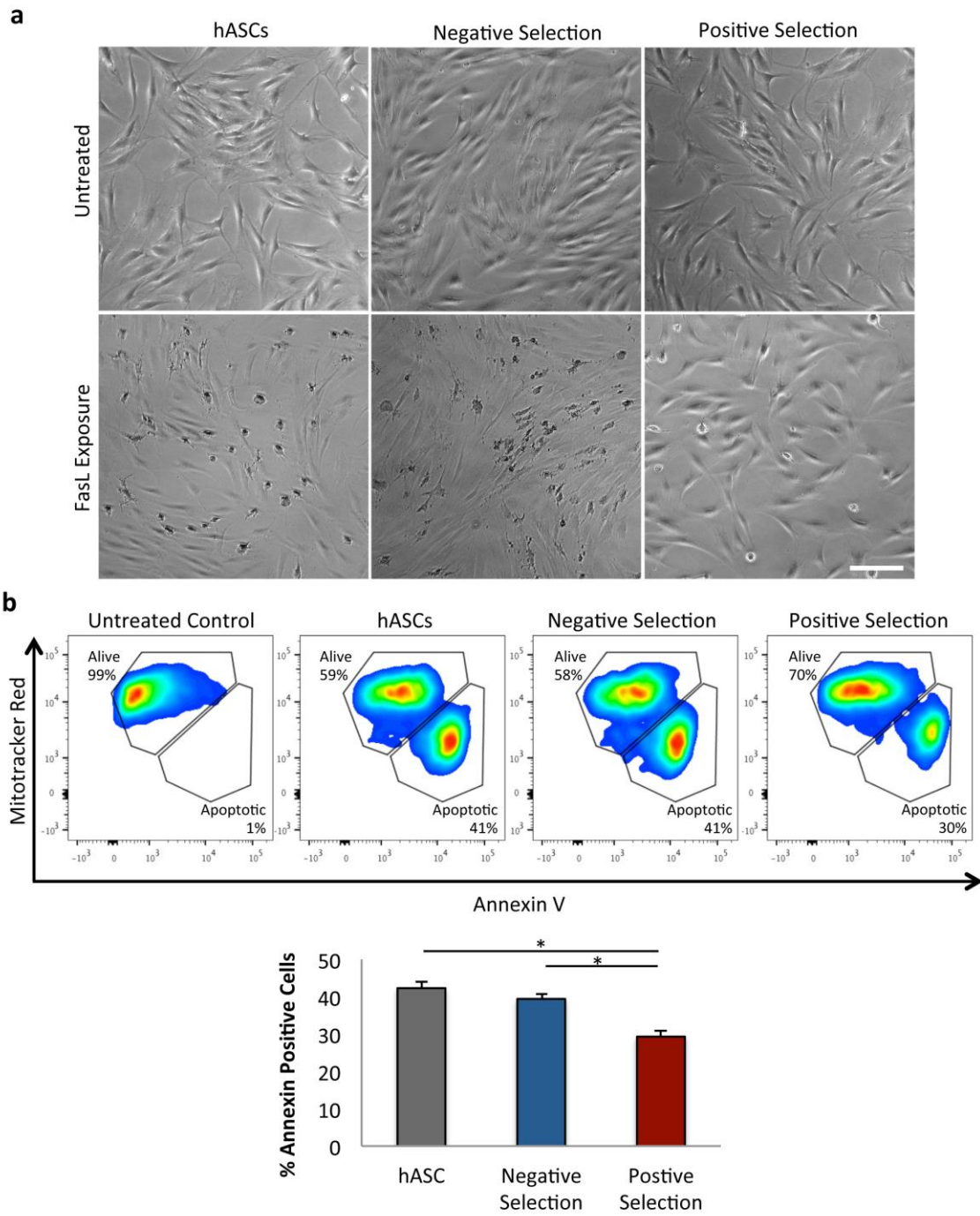
Supplementary Figure 1: Summary of the exclusionary approach to surface marker selection for initial single-cell analysis, with a pragmatic focus on surface markers with the highest potential for protein based sub-fractionation.

Supplementary Figure 2:



Supplementary Figure 2: hASC subpopulation identification across patient samples and functionalized gene lists. (a-b) Flow cytometry gating scheme for hASCs and subpopulation isolation from the stromal vascular fraction. hASCs were defined as CD45-/CD31-/CD34+ cells within the stromal vascular fraction to exclude contaminating hematopoietic and endothelial cells. DPP4 and CD55 were surface markers used to prospectively isolate the transcriptionally identified hASC subpopulation (%'s reported represent fraction of cells from the parent gate). (c-d) Single cell transcriptional screening of multiple patient samples consistently identifies the hASC subpopulation following k-means clustering (k=2). Gene expression presented as fold change from median (yellow - high expression, 32-fold above median to blue - low expression, 32-fold below median; gray - no expression). (e) Creation of an assay list screening for gene expression related to tissue regeneration, cell stemness, survival and proliferation, in addition to selected surface markers. (f) K-means clustering (k=2) of hASCs with the functionalized gene list re-identifies the cell subpopulation, which displays enhanced expression of multiple genes related to tissue regeneration.

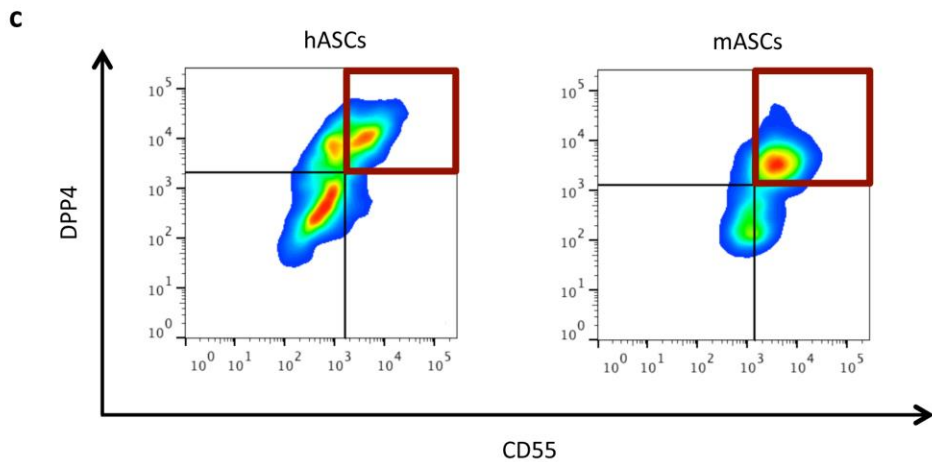
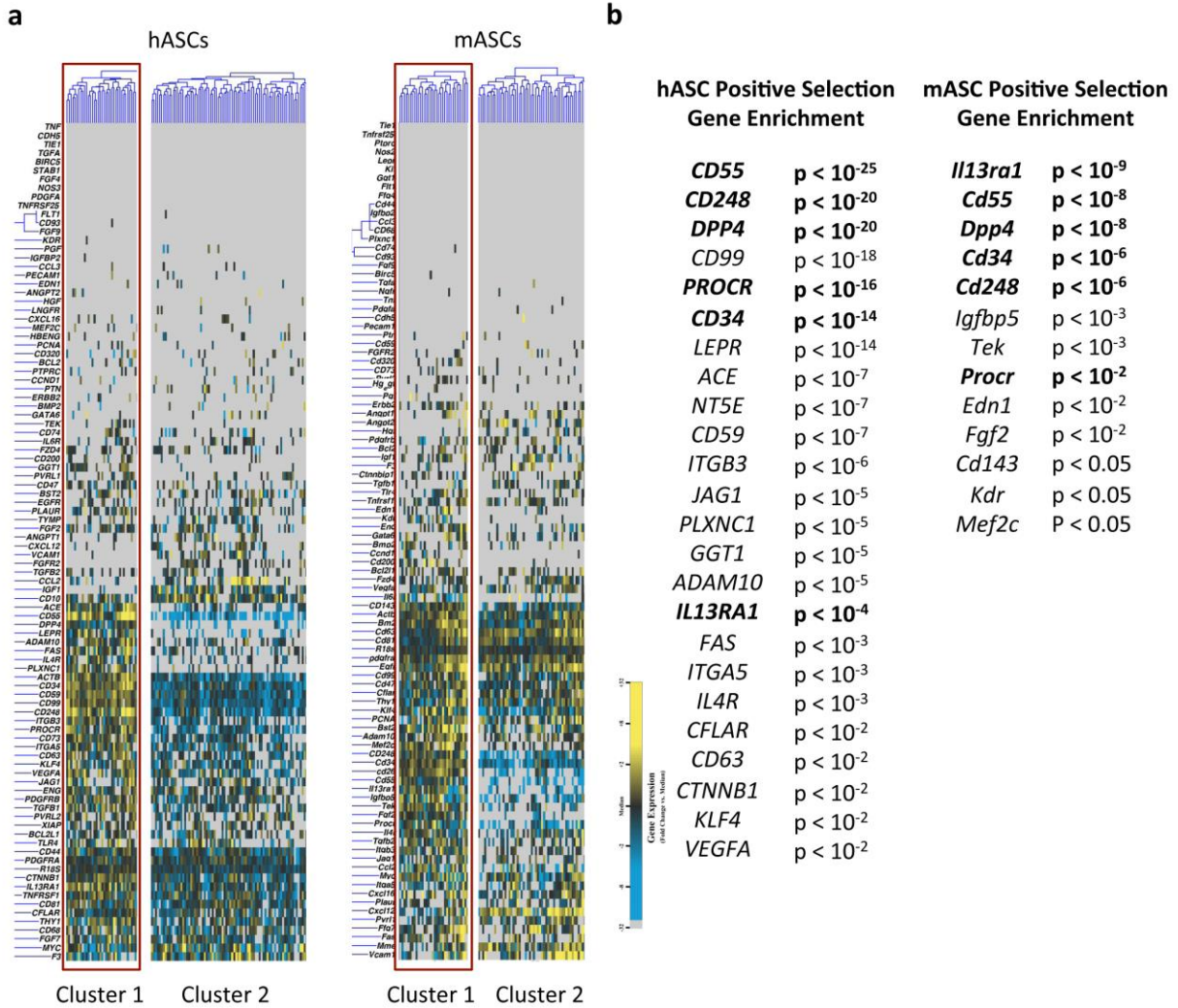
Supplementary Figure 3:



Supplementary Figure 3: Prospective hASC subpopulation enrichment enhances cell survival. (a)

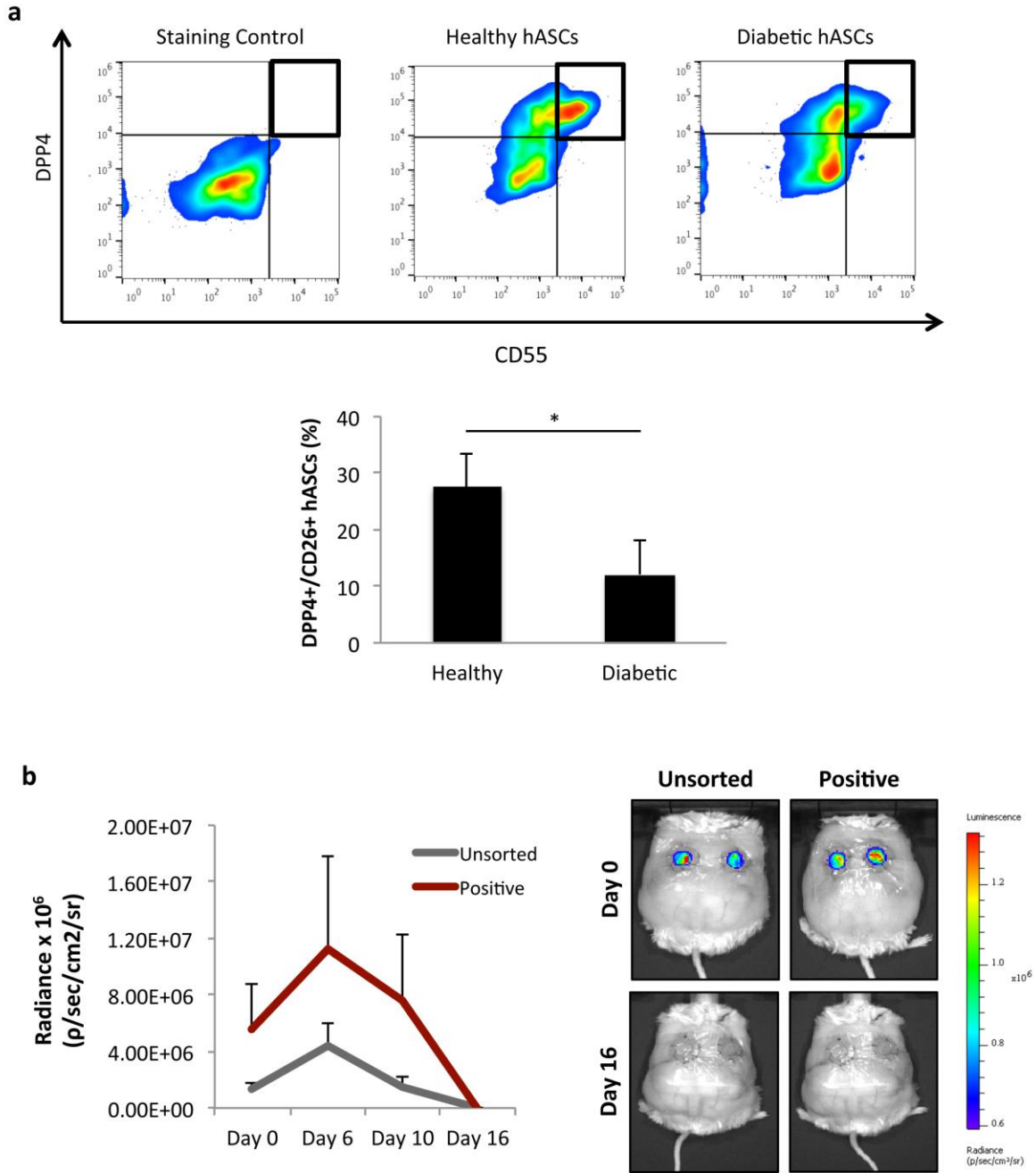
Light micrograph images of cells following exposure to an apoptotic stimulus (FasL; as seen in **Fig. 2a**) reveals enhanced survival in positively selected cells. (b) Analysis of downstream apoptotic signaling (Annexin V) following exposure to FasL confirms the survival benefit of hASC positive subpopulation selection. * indicates $p \leq 0.05$ via Student's t-test. Error bars represent SEM. Scale bar = 50 μ m.

Supplementary Figure 4:



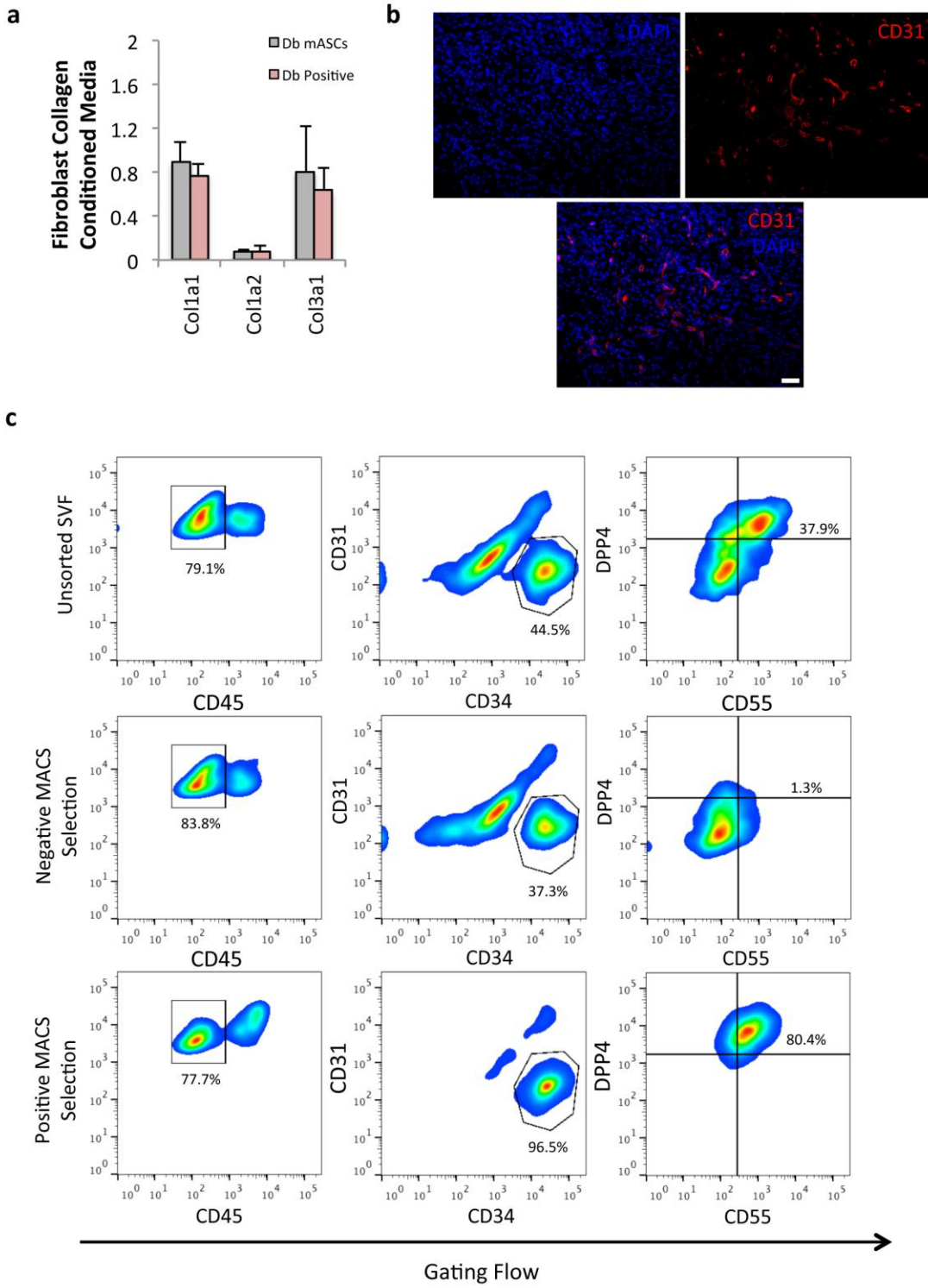
Supplementary Figure 4: The transcriptionally identified ASC subpopulation is present in both humans and mice. (a) Single cell transcriptional analysis for human and murine ASCs reveals the presence of a similar cell subpopulation. (b) Kolmogorov-Smirnov analysis of positively selected hASCs and mASCs reveals similar gene distribution profiles across species (list of non-control hASC and mASC genes positively regulated following subpopulation enrichment, with common genes bolded). (c) Flow cytometric confirmation of cross-species presence of the ASC subpopulation, as defined by the surface markers DPP4 and CD55.

Supplementary Figure 5:



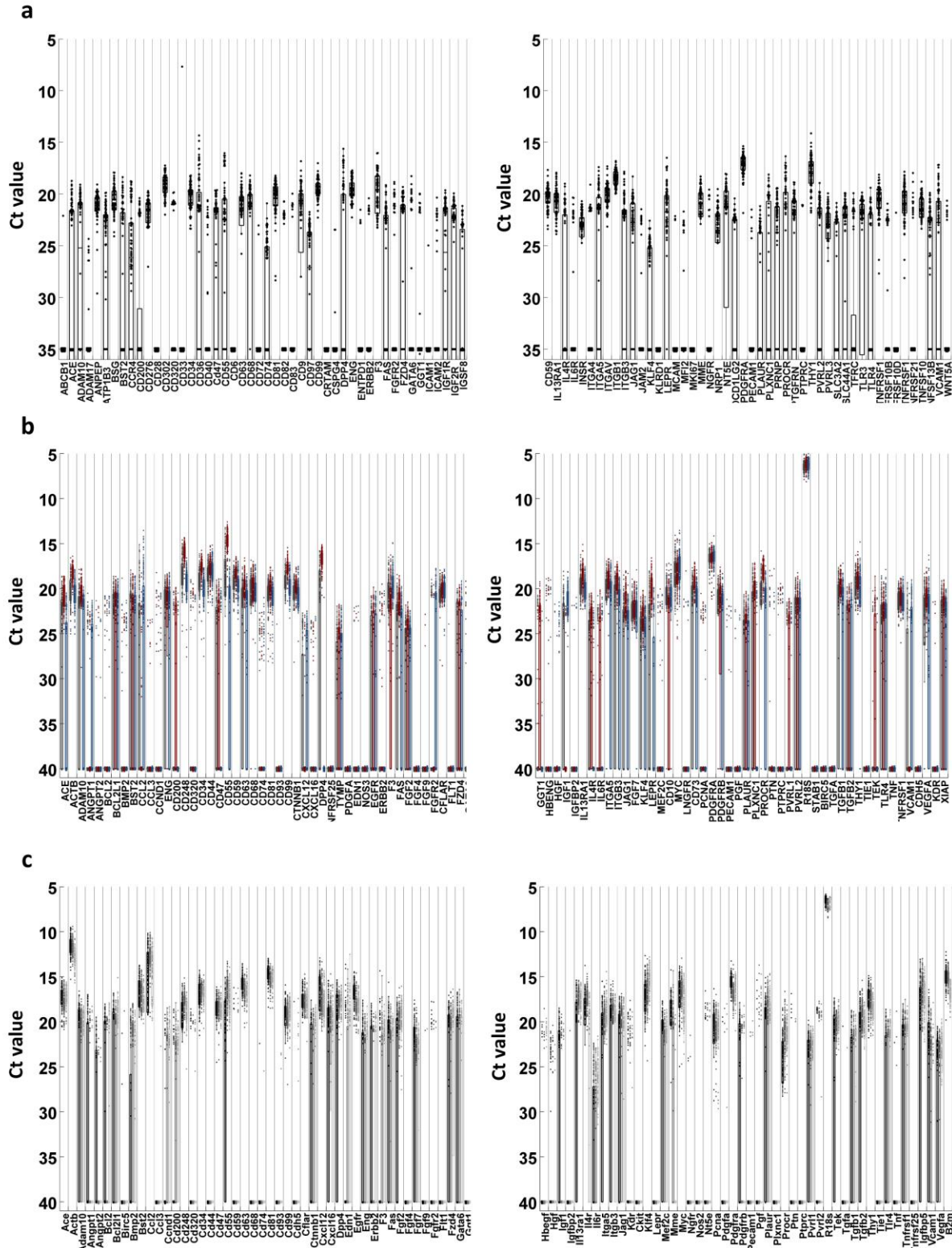
Supplementary Figure 5: Effect of diabetes on the transcriptionally identified hASC subpopulation and *in vivo* cell dynamics following application of enriched hASCs. (a) The transcriptionally identified hASC subpopulation is significantly depleted in patients with diabetes as compared to healthy, non-diabetic controls (bar graph represents total number of DPP4+/CD55+ ASCs as a fraction of total ASCs within the SVF). (b) hASCs persist for up to 16 days *in vivo* (assessed via IVIS tracking), with trends toward improved early engraftment/survival of enriched versus unsorted hASCs. * indicates $p \leq 0.05$ via Student's t-test. Error bars represent SEM.

Supplementary Figure 6:



Supplementary Figure 6: Need for allogenic cell sourcing, treated wound vascularity, and demonstration of rapid subpopulation enrichment of hASCs via magnetic assisted cell sorting (MACS). (a) Unlike healthy ASCs, enrichment of diabetic mASCs failed to improved secondary fibroblast collagen production. (b) Diabetic wounds treated with enriched mASCs demonstrate robust vascularity immediately after closure via immunohistochemical staining for the endothelial cell marker CD31. Representative images; scale bar = 100 μ m. (c) Flow cytometric analysis of unsorted and subpopulation enriched and depleted hASCs via dual-antibody MACS confirms the ability to efficiently and rapidly isolate the identified hASC subpopulation for potential clinical application (%'s reported represent fraction of cells from the parent gate). Error bars represent SEM.

Supplementary Figure 7:



Supplementary Figure 7: Whisker plots. (a) Whisker plots presenting raw qPCR cycle threshold values for each gene across all cells for the initial single-cell gene distribution subpopulation analysis of hASCs. Informed by the n= 386 surface marker screen, high copy number, differentially expressed surface markers (>5 and <95% cell expression, with a cycle threshold [Ct] < 21) were preferentially included to distinguish biologically important cell subsets, in addition to selected control and cell-cycle related probes (full gene list available in **Supplementary Table 2**). Individual dots represent single gene/cell qPCR reactions, with increased cycle threshold values corresponding to decreased mRNA content. Cycle threshold values of 40 represent failed amplifications. (b) Whisker plots for functionalized single-cell gene distribution analyses of unsorted and enriched hASCs (gray = hASCs, red = positively selected cells, and blue = negatively selected cells). Genes specifically relating to tissue regeneration, cell stemness, survival, and proliferation were chosen, in addition to selected control and surface marker related probes (full gene list available in **Supplementary Table 3**). (c) Whisker plots for single-cell gene distribution analyses of mASCs (black = healthy mASCs, dark gray = aged mASCs, and light gray = diabetic mASCs). Genes specifically relating to tissue regeneration, cell stemness, survival, and proliferation were chosen, in addition to selected control and surface marker related probes (full gene list available in **Supplementary Table 4**).

Supplementary Table 1:

Differentially Distributed Subpopulation Genes

<i>CD55</i>	$p < 10^{-8}$
<i>PROCR</i>	$p < 10^{-6}$
<i>ACE</i>	$p < 10^{-4}$
<i>DPP4</i>	$p < 10^{-4}$
<i>ITGB3</i>	$p < 10^{-3}$
<i>IL4R</i>	$p < 10^{-2}$
<i>CD34</i>	$p < 10^{-2}$
<i>CD99</i>	$p < 10^{-2}$
<i>CD73</i>	$p < 0.05$
<i>PTGFRN</i>	$p < 0.05$
<i>GGT1</i>	$p < 0.05$

Significance determined via Kolmogorov-Smirnov analysis.

Supplementary Table 2:

Gene list for initial hASC single-cell analysis

Assay ID	Gene Name	Assay ID	Gene Name
Hs00184500	m1 ABCB1	Hs00364603	m1 IGSF8
Hs00174179	m1 ACE	Hs00609817	m1 IL13RA1
Hs00153853	m1 ADAM10	Hs00166237	m1 IL4R
Hs01041915	m1 ADAM17	Hs01075667	m1 IL6R
Hs00174265	m1 ANPEP	Hs00961554	m1 INSR
Hs00740857	mH ATP1B3	Hs00168433	m1 ITGA4
Hs00936295	m1 BSG	Hs01547673	m1 ITGA5
Hs00171632	m1 BST2	Hs00233808	m1 ITGAV
Hs99999919	m1 CCR4	Hs01127543	m1 ITGB1
Hs01033303	m1 CD200	Hs01001469	m1 ITGB3
Hs00987207	m1 CD276	Hs01070036	m1 JAG1
Hs00174796	m1 CD28	Hs01022013	m1 JAM2
Hs00994886	m1 CD302	Hs00358836	m1 KLF4
Hs00213164	m1 CD320	Hs00233844	m1 KLRD1
Hs00233544	m1 CD33	Hs00174497	m1 LEPR
Hs02576480	m1 CD34	Hs00174838	m1 MCAM
Hs00169627	m1 CD36	Hs00195551	m1 MFI2
Hs00374176	m1 CD40	Hs01032443	m1 MKI67
Hs00179953	m1 CD47	Hs00153510	m1 MME
Hs00892618	m1 CD55	Hs00609976	m1 NGFR
Hs00174141	m1 CD59	Hs00826128	m1 NRP1
Hs00198752	m1 CD6	Hs01573922	m1 NT5E
Hs00156390	m1 CD63	Hs00228839	m1 PDCD1LG2
Hs00154355	m1 CD68	Hs00998018	m1 PDGFRA
Hs00233564	m1 CD72	Hs01065282	m1 PECAM1
Hs00269961	m1 CD74	Hs00182181	m1 PLAUR
Hs00174717	m1 CD81	Hs00955621	m1 PLXNC1
Hs01017982	m1 CD82	Hs00175591	m1 PRNP
Hs00188486	m1 CD83	Hs00941182	m1 PROCR
Hs00233521	m1 CD9	Hs01385989	m1 PTGFRN
Hs00173542	m1 CD97	Hs00898488	m1 PTPRC
Hs00365982	m1 CD99	Hs01071562	m1 PVRL2
Hs00219699	m1 CRTAM	Hs00210043	m1 PVRL3
Hs00426981	m1 CSPG4	Hs00374243	m1 SLC3A2
Hs00175210	m1 DPP4	Hs00223114	m1 SLC44A1
Hs00923996	m1 ENG	Hs00951083	m1 TFRC
Hs00969559	m1 ENTPD1	Hs00174816	m1 THY1
Hs01001580	m1 ERBB2	Hs01551078	m1 TLR3
Hs01076029	m1 F3	Hs00152939	m1 TLR4
Hs00531110	m1 FAS	Hs01042313	m1 TNFRSF1
Hs01552926	m1 FGFR2	Hs00366278	m1 TNFRSF10B
Hs00201853	m1 FZD4	Hs00388742	m1 TNFRSF10D
Hs00934682	m1 GATA6	Hs01042313	m1 TNFRSF1A
Hs00980756	m1 GGT1	Hs00205419	m1 TNFRSF21
Hs00164932	m1 ICAM1	Hs00921974	m1 TNFSF10
Hs00609563	m1 ICAM2	Hs00198106	m1 TNFSF13B
Hs00609566	m1 IGF1R	Hs01003372	m1 VCAM1
Hs00974474	m1 IGF2R	Hs00998537	m1 WNT5A

Supplementary Table 3:

Gene list for functionalized single-cell analyses
of unsorted and enriched hASCs

Assay ID	Gene Name	Assay ID	Gene Name
Hs00174179	<i>ACE</i>	Hs00181813	<i>HB-EGF</i>
Hs99999903	<i>ACTB</i>	Hs00300159	<i>HGF</i>
Hs00153853	<i>ADAM10</i>	Hs01547656	<i>IGF1</i>
Hs00375822	<i>ANGPT1</i>	Hs01040719	<i>IGFBP2</i>
Hs01048042	<i>ANGPT2</i>	Hs00609817	<i>IL13RA1</i>
Hs99999018	<i>BCL2</i>	Hs00166237	<i>IL4R</i>
Hs00236329	<i>BCL2L1</i>	Hs01075667	<i>IL6R</i>
Hs00153353	<i>BIRC5</i>	Hs01547673	<i>ITGA5</i>
Hs00154192	<i>BMP2</i>	Hs01001469	<i>ITGB3</i>
Hs00171632	<i>BST2</i>	Hs01070036	<i>JAG1</i>
Hs00234140	<i>CCL2</i>	Hs00176676	<i>KDR</i>
Hs00234142	<i>CCL3</i>	Hs00358836	<i>KLF4</i>
Hs00765553	<i>CCND1</i>	Hs00174497	<i>LEPR</i>
Hs01033303	<i>CD200</i>	Hs01554597	<i>MEF2C</i>
Hs00535586	<i>CD248</i>	Hs00153510	<i>MME</i>
Hs00213164	<i>CD320</i>	Hs00905030	<i>MYC</i>
Hs02576480	<i>CD34</i>	Hs00609976	<i>NGFR</i>
Hs01075861	<i>CD44</i>	Hs01574659	<i>NOS3</i>
Hs00179953	<i>CD47</i>	Hs01573922	<i>NTSE</i>
Hs00892618	<i>CD55</i>	Hs00696862	<i>PCNA</i>
Hs00174141	<i>CD59</i>	Hs00964426	<i>PDGFA</i>
Hs00156390	<i>CD63</i>	Hs00998018	<i>PDGFRA</i>
Hs00154355	<i>CD68</i>	Hs01019580	<i>PDGFRB</i>
Hs00269961	<i>CD74</i>	Hs00169777	<i>PECAM1</i>
Hs00174717	<i>CD81</i>	Hs00182176	<i>PGF</i>
Hs00362607	<i>CD93</i>	Hs00182181	<i>PLAUR</i>
Hs00365982	<i>CD99</i>	Hs00955621	<i>PLXNC1</i>
Hs00174344	<i>CDH5</i>	Hs00941182	<i>PROCR</i>
Hs00153439	<i>CFLAR</i>	Hs00383235	<i>PTN</i>
Hs00355049	<i>CTNNB1</i>	Hs00898488	<i>PTPRC</i>
Hs00930455	<i>CXCL12</i>	Hs00161050	<i>PVRL1</i>
Hs00222859	<i>CXCL16</i>	Hs01071562	<i>PVRL2</i>
Hs00175210	<i>DPP4</i>	Hs99999901	<i>R18S</i>
Hs00174961	<i>EDN1</i>	Hs01109068	<i>STAB1</i>
Hs01076078	<i>EGFR</i>	Hs00945146	<i>TEK</i>
Hs00923996	<i>ENG</i>	Hs00608187	<i>TGFA</i>
Hs01001580	<i>ERBB2</i>	Hs00998133	<i>TGFB1</i>
Hs01076029	<i>F3</i>	Hs00234244	<i>TGFB2</i>
Hs00531110	<i>FAS</i>	Hs00174816	<i>THY1</i>
Hs00266645	<i>FGF2</i>	Hs00178500	<i>TIE1</i>
Hs00999691	<i>FGF4</i>	Hs00152939	<i>TLR4</i>
Hs00940253	<i>FGF7</i>	Hs99999043	<i>TNF</i>
Hs00181829	<i>FGF9</i>	Hs01042313	<i>TNFRSF1</i>
Hs01552926	<i>FGFR2</i>	Hs00237054	<i>TNFRSF25</i>
Hs01052961	<i>FLT1</i>	Hs00157317	<i>TYMP</i>
Hs00201853	<i>FZD4</i>	Hs00174239	<i>VCAM1</i>
Hs00934682	<i>GATA6</i>	Hs00900055	<i>VEGFA</i>
Hs00980756	<i>GGT1</i>	Hs00236913	<i>XIAP</i>

Supplementary Table 4:

Gene list for single-cell gene distribution analyses of mASCs

Assay ID	Gene Name	Assay ID	Gene Name
Mm00802048_m1	<i>Ace</i>	Mm00492322_m1	<i>Ggt1</i>
Mm00607939_s1	<i>Actb</i>	Mm00439306_m1	<i>Hg-egf</i>
Mm00545742_m1	<i>Adam10</i>	Mm01135193_m1	<i>Hgf</i>
Mm00456503_m1	<i>Angpt1</i>	Mm00439560_m1	<i>Igf1</i>
Mm00545822_m1	<i>Angpt2</i>	Mm00492632_m1	<i>Igfbp2</i>
Mm00437762_m1	<i>B2m</i>	Mm00516037_m1	<i>Igfbp5</i>
Mm00477631_m1	<i>Bcl2</i>	Mm00446726_m1	<i>Il13ra1</i>
Mm00437783_m1	<i>Bcl2l1</i>	Mm01275139_m1	<i>Il4r</i>
Mm00599749_m1	<i>Birc5</i>	Mm00439653_m1	<i>Il6r</i>
Mm01340178_m1	<i>Bmp2</i>	Mm00439797_m1	<i>Itga5</i>
Mm01609165_g1	<i>Bst2</i>	Mm00443980_m1	<i>Itgb3</i>
Mm00441242_m1	<i>Ccl2</i>	Mm00496902_m1	<i>Jag1</i>
mm00441259_g1	<i>Ccl3</i>	Mm01222421_m1	<i>Kdr</i>
Mm00432359_m1	<i>Ccnd1</i>	Mm00445212_m1	<i>Kit</i>
Mm00487740_m1	<i>Cd200</i>	Mm00516104_m1	<i>Klf4</i>
Mm00547485_s1	<i>Cd248</i>	Mm00440181_m1	<i>Lepr</i>
Mm00507988_m1	<i>Cd320</i>	Mm01340842_m1	<i>Mef2c</i>
Mm00519283_m1	<i>Cd34</i>	Mm00485028_m1	<i>Mme</i>
Mm00681165_m1	<i>Cd44</i>	Mm00487803_m1	<i>Myc</i>
Mm00495005_m1	<i>Cd47</i>	Mm00446296_m1	<i>Ngfr</i>
Mm00438377_m1	<i>Cd55</i>	Mm00440502_m1	<i>Nos2</i>
Mm00483149_m1	<i>Cd59</i>	Mm00501910_m1	<i>Nt5e</i>
Mm01966817_g1	<i>Cd63</i>	Mm00448100_g1	<i>Pcna</i>
Mm03047340_m1	<i>Cd68</i>	Mm01205760_m1	<i>Pdgfa</i>
Mm00658576_m1	<i>Cd74</i>	Mm00440701_m1	<i>Pdgfra</i>
Mm00504869_m1	<i>Cd81</i>	Mm00435546_m1	<i>Pdgfrb</i>
Mm00440239_g1	<i>Cd93</i>	Mm01242584_m1	<i>Pecam1</i>
Mm04214669_u1	<i>Cd99</i>	Mm01302896_m1	<i>Pgf</i>
Mm00486938_m1	<i>Cdh5</i>	Mm00440911_m1	<i>Plaur</i>
Mm01255578_m1	<i>Cflar</i>	Mm01236713_m1	<i>Plxnc1</i>
Mm00517812_m1	<i>Ctnnb1</i>	Mm00440992_m1	<i>Procr</i>
Mm00445552_m1	<i>Cxcl12</i>	Mm01132688_m1	<i>Ptn</i>
Mm00469712_m1	<i>Cxcl16</i>	Mm01292575_m1	<i>Ptprc</i>
Mm00494538_m1	<i>Dpp4</i>	Mm00445392_m1	<i>Pvrl1</i>
Mm00438656_m1	<i>Edn1</i>	Mm00436144_m1	<i>Pvrl2</i>
Mm00433023_m1	<i>Egfr</i>	Mm03928990_g1	<i>R18s</i>
Mm00468256_m1	<i>Eng</i>	Mm00443243_m1	<i>Tek</i>
Mm00658541_m1	<i>ErbB2</i>	Mm00446232_m1	<i>Tgfa</i>
mm00438853_m1	<i>F3</i>	Mm01178820_m1	<i>Tgfb1</i>
mm01204974_m1	<i>Fas</i>	Mm00436955_m1	<i>Tgfb2</i>
Mm00433287_m1	<i>Fg2</i>	Mm00493681_m1	<i>Thy1</i>
Mm00438917_m1	<i>Fg4</i>	Mm00441786_m1	<i>Tie2</i>
Mm00433291_m1	<i>Fg7</i>	Mm00445273_m1	<i>Tlr4</i>
Mm00442795_m1	<i>Fg9</i>	Mm00443258_m1	<i>Tnf</i>
Mm01269930_m1	<i>Fgfr2</i>	Mm00441875_m1	<i>Tnfrsf1</i>
Mm00438980_m1	<i>Flt1</i>	Mm01263821_m1	<i>Tnfrsf25</i>
Mm00433382_m1	<i>Fzd4</i>	Mm01320970_m1	<i>Vcam1</i>
Mm01235633_m1	<i>Gata6</i>	Mm01281447_m1	<i>Vegfa</i>