

Supplemental Data

Supplementary Table 1. Differentially expressed genes in elderly vs. young HSC. SAM significant genes (FDR < 30%); age-up-regulated genes are in red, and age-down-regulated genes are in green.

Gene ID	Gene Name	Fold Change
242828_at	FIGN: fidgetin	12.84
239710_at	FIGN: fidgetin	9.40
228863_at	PCDH17: protocadherin 17	4.69
220518_at	ABI3BP: ABI gene family, member 3 (NESH) binding protein	4.25
1560698_a_at	LOC283392: hypothetical protein LOC283392	4.13
238964_at	FIGN: fidgetin	4.05
234074_at	---: CDNA FLJ10946 fis, clone PLACE1000005	3.97
220014_at	PRR16: proline rich 16	3.87
241470_x_at	---: Transcribed locus	3.84
227289_at	PCDH17: protocadherin 17	3.79
236193_at	HIST1H2BC /// HIST1H2BE /// HIST1H2BF /// HIST1H2BG /// HIST1H2BI: histone cluster 1, H2bg /// histone cluster 1, H2bf /// histone cluster 1, H2be /// histone cluster 1, H2bf /// histone cluster 1, H2bi /// histone cluster 1, H2bc	3.75
220679_s_at	CDH7: cadherin 7, type 2	3.45
243882_at	---: ---	3.37
241845_at	---: ---	3.33
1554007_at	---: CDNA clone IMAGE:5303689	3.31
1553808_a_at	NKX2-3: NK2 transcription factor related, locus 3 (Drosophila)	3.27
209369_at	ANXA3: annexin A3	3.27
223395_at	ABI3BP: ABI gene family, member 3 (NESH) binding protein	3.14
237009_at	---: ---	3.11
233611_at	---: CDNA FLJ12106 fis, clone HEMBB1002702	3.06
228195_at	MGC13057: hypothetical protein MGC13057	2.96
1554592_a_at	SLC1A6: solute carrier family 1 (high affinity aspartate/glutamate transporter), member 6	2.96
228373_at	C16orf72: chromosome 16 open reading frame 72	2.94
219937_at	TRHDE: thyrotropin-releasing hormone degrading enzyme	2.93
230192_at	TRIM13: tripartite motif-containing 13	2.91
230836_at	ST8SIA4: ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 4	2.88
231969_at	STOX2: storkhead box 2	2.87
1554593_s_at	SLC1A6: solute carrier family 1 (high affinity aspartate/glutamate transporter), member 6	2.87
205656_at	PCDH17: protocadherin 17	2.84
244414_at	---: ---	2.82
226977_at	LOC492311: similar to bovine IgA regulatory protein	2.78
244674_at	---: Transcribed locus	2.77
1565913_at	---: Full length insert cDNA clone YR04D03	2.75
228821_at	ST6GAL2: ST6 beta-galactosamide alpha-2,6-sialyltransferase 2	2.74
1557756_a_at	C14orf145: chromosome 14 open reading frame 145	2.72
236548_at	GIPC2: GIPC PDZ domain containing family, member 2	2.72
1559401_a_at	---: CDNA clone IMAGE:5267013	2.71
236495_at	---: Transcribed locus	2.70
227874_at	EMCN: Endomucin	2.68
202431_s_at	MYC: v-myc myelocytomatosis viral oncogene homolog (avian)	2.65
237409_at	---: Transcribed locus	2.64
238937_at	ZNF420: zinc finger protein 420	2.63
225838_at	EPC2: enhancer of polycomb homolog 2 (Drosophila)	2.63
231979_at	---: CDNA FLJ13266 fis, clone OVARC1000960	2.63
203739_at	ZNF217: zinc finger protein 217	2.62
218979_at	RMI1: RMI1, RecQ mediated genome instability 1, homolog (S. cerevisiae)	2.60
1556931_at	---: Full length insert cDNA clone ZD58F06	2.59
230703_at	---: Transcribed locus	2.57
1565602_at	---: Full length insert cDNA clone YN67C05	2.56
204712_at	WIF1: WNT inhibitory factor 1	2.55
234033_at	---: Clone IMAGE:110218 mRNA sequence	2.54
206049_at	SELP: selectin P (granule membrane protein 140kDa, antigen CD62)	2.50
216456_at	---: MRNA; cDNA DKFZp761L0812 (from clone DKFZp761L0812); partial cds	2.49

209189_at	FOS: v-fos FBJ murine osteosarcoma viral oncogene homolog	2.49
208891_at	DUSP6: dual specificity phosphatase 6	2.48
243528_at	---: Transcribed locus	2.47
240574_at	---: CDNA clone IMAGE:5262677	2.47
208893_s_at	DUSP6: dual specificity phosphatase 6	2.45
220777_at	KIF13A: kinesin family member 13A	2.43
235052_at	ZNF792: zinc finger protein 792	2.40
212225_at	EIF1: eukaryotic translation initiation factor 1	2.40
231985_at	MICAL3: microtubule associated monooxygenase, calponin and LIM domain containing 3	2.39
236846_at	LOC284757: hypothetical protein LOC284757	2.39
241471_at	LOC730236: hypothetical LOC730236	2.39
1559042_at	NDUFB6: NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 6, 17kDa	2.38
232504_at	LOC285628: hypothetical protein LOC285628	2.38
229298_at	KBTBD7: kelch repeat and BTB (POZ) domain containing 7	2.37
235811_at	---: ---	2.37
239208_s_at	C21orf57: Chromosome 21 open reading frame 57	2.36
214945_at	FAM153A /// FAM153B /// FAM153C: family with sequence similarity 153, member B /// family with sequence similarity 153, member A /// family with sequence similarity 153, member C	2.34
208792_s_at	CLU: clusterin	2.33
226360_at	ZNRF3: zinc and ring finger 3	2.32
1557472_a_at	FLJ30838: hypothetical gene supported by AL832565	2.32
228372_at	C10orf128: chromosome 10 open reading frame 128	2.32
239847_at	---: CDNA clone IMAGE:6186815	2.31
213005_s_at	KANK1: KN motif and ankyrin repeat domains 1	2.30
1563963_at	---: Transcribed locus	2.30
232912_at	GPR180: G protein-coupled receptor 180	2.30
240601_at	---: Transcribed locus	2.29
224956_at	NUFIP2: nuclear fragile X mental retardation protein interacting protein 2	2.29
237865_x_at	---: ---	2.29
227693_at	WDR20: WD repeat domain 20	2.29
238669_at	PTGS1: prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	2.29
243521_at	---: Transcribed locus	2.28
212286_at	ANKRD12: ankyrin repeat domain 12	2.28
212327_at	LIMCH1: LIM and calponin homology domains 1	2.27
240728_at	PLCB4: Phospholipase C, beta 4	2.25
212065_s_at	USP34: ubiquitin specific peptidase 34	2.25
204310_s_at	NPR2: natriuretic peptide receptor B/guanylate cyclase B (atriuretic peptide receptor B)	2.24
213849_s_at	PPP2R2B: protein phosphatase 2 (formerly 2A), regulatory subunit B, beta isoform	2.23
210218_s_at	SP100: SP100 nuclear antigen	2.22
231747_at	CYSLTR1: cysteinyl leukotriene receptor 1	2.22
234605_at	CDC14B: CDC14 cell division cycle 14 homolog B (S. cerevisiae)	2.22
226298_at	RUNDC1: RUN domain containing 1	2.22
205128_x_at	PTGS1: prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	2.21
234986_at	---: Transcribed locus	2.21
240154_at	---: Transcribed locus	2.20
218534_s_at	AGGF1: angiogenic factor with G patch and FHA domains 1	2.20
236031_x_at	---: CDNA FLJ30128 fis, clone BRACE1000124	2.20
235532_at	PIGM: phosphatidylinositol glycan anchor biosynthesis, class M	2.20
235255_at	ATP6V0A2: ATPase, H+ transporting, lysosomal V0 subunit a2	2.19
204545_at	PEX6: peroxisomal biogenesis factor 6	2.19
226782_at	SLC25A30: solute carrier family 25, member 30	2.19
1563364_at	---: Homo sapiens, clone IMAGE:4272847, mRNA	2.19
242878_at	---: ---	2.18
241438_at	---: Transcribed locus	2.18
213506_at	F2RL1: coagulation factor II (thrombin) receptor-like 1	2.18
215388_s_at	CFH /// CFHR1: complement factor H /// complement factor H-related 1	2.17
215813_s_at	PTGS1: prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)	2.17
204720_s_at	DNAJC6: DnaJ (Hsp40) homolog, subfamily C, member 6	2.17
1560697_at	LOC283392: hypothetical protein LOC283392	2.16
226189_at	ITGB8: integrin, beta 8	2.16
227404_s_at	EGR1: Early growth response 1	2.15
219738_s_at	PCDH9: protocadherin 9	2.14
236160_at	---: Transcribed locus	2.13

242579_at	BMPR1B: bone morphogenetic protein receptor, type IB	2.13
219615_s_at	KCNK5: potassium channel, subfamily K, member 5	2.13
210377_at	ACSM3: acyl-CoA synthetase medium-chain family member 3	2.12
239449_at	---: Transcribed locus	2.12
226109_at	C21orf91: chromosome 21 open reading frame 91	2.12
204071_s_at	TOPORS: topoisomerase I binding, arginine/serine-rich	2.12
223263_s_at	FGFR10P2: FGFR1 oncogene partner 2	2.11
219737_s_at	PCDH9: protocadherin 9	2.11
226483_at	TMEM68: transmembrane protein 68	2.10
220577_at	GVIN1: GTPase, very large interferon inducible 1	2.09
218294_s_at	NUP50: nucleoporin 50kDa	2.09
205942_s_at	ACSM3: acyl-CoA synthetase medium-chain family member 3	2.09
221524_s_at	RRAGD: Ras-related GTP binding D	2.09
239901_at	---: Transcribed locus	2.08
240777_at	SYNE2: Spectrin repeat containing, nuclear envelope 2	2.07
1554665_at	ZNF586: zinc finger protein 586	2.07
235342_at	SPOCK3: sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 3	2.07
237590_at	---: ---	2.06
238744_at	---: Transcribed locus	2.06
232150_at	---: CDNA clone IMAGE:4792085	2.06
227506_at	SLC16A9: solute carrier family 16, member 9 (monocarboxylic acid transporter 9)	2.06
220235_s_at	C1orf103: chromosome 1 open reading frame 103	2.06
219504_s_at	RPAP2: RNA polymerase II associated protein 2	2.05
205140_at	FPGT: fucose-1-phosphate guanylyltransferase	2.05
241399_at	FAM19A2: family with sequence similarity 19 (chemokine (C-C motif)-like), member A2	2.05
239466_at	LOC344595: hypothetical LOC344595	2.04
234326_at	---: CDNA: FLJ21248 fis, clone COL01235	2.04
1554806_a_at	FBXO8: F-box protein 8	2.04
240247_at	---: ---	2.03
203869_at	USP46: ubiquitin specific peptidase 46	2.02
1562648_at	CCDC88A: Coiled-coil domain containing 88A	2.01
1562406_at	---: CDNA clone IMAGE:5278001	2.01
217536_x_at	---: Transcribed locus	2.01
230411_at	---: CDNA FLJ41934 fis, clone PERIC2005111	2.01
209795_at	CD69: CD69 molecule	2.01
206118_at	STAT4: signal transducer and activator of transcription 4	2.00
1552735_at	PCDHGA4: protocadherin gamma subfamily A, 4	1.99
238170_at	---: Transcribed locus	1.99
239429_at	---: Transcribed locus	1.98
220572_at	DKFZp547G183: hypothetical protein DKFZp547G183	1.98
232301_at	UBE3B: ubiquitin protein ligase E3B	1.98
214713_at	YLPM1: YLP motif containing 1	1.98
204739_at	CENPC1: centromere protein C 1	1.97
235264_at	HCFC2: host cell factor C2	1.97
235044_at	CYYR1: cysteine/tyrosine-rich 1	1.96
222156_x_at	CCPG1: cell cycle progression 1	1.96
230881_at	CCDC42: coiled-coil domain containing 42	1.96
204700_x_at	C1orf107: chromosome 1 open reading frame 107	1.95
243331_at	---: Transcribed locus	1.95
209006_s_at	C1orf63: chromosome 1 open reading frame 63	1.95
218614_at	C12orf35: chromosome 12 open reading frame 35	1.94
205159_at	CSF2RB: colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	1.94
226998_at	NARG1: NMDA receptor regulated 1	1.94
212979_s_at	FAM115A: family with sequence similarity 115, member A	1.94
209757_s_at	MYCN: v-myc myelocytomatosis viral related oncogene, neuroblastoma derived (avian)	1.93
243319_at	---: Transcribed locus	1.93
206861_s_at	CGGBP1: CGG triplet repeat binding protein 1	1.92
218929_at	CDKN2AIP: CDKN2A interacting protein	1.91
238609_at	C7orf38: chromosome 7 open reading frame 38	1.91
1569345_at	---: Transcribed locus	1.91
218472_s_at	PELO: pelota homolog (Drosophila)	1.90
227980_at	ZNF322A: zinc finger protein 322A	1.90
234081_at	---: CDNA FLJ11986 fis, clone HEMBB1001364	1.88

1559485_at	ATG2B: ATG2 autophagy related 2 homolog B (<i>S. cerevisiae</i>)	1.88
235014_at	LOC147727: hypothetical LOC147727	1.88
206109_at	FUT1: fucosyltransferase 1 (galactoside 2-alpha-L-fucosyltransferase, H blood group)	1.88
242565_x_at	C21orf57: Chromosome 21 open reading frame 57	1.88
209585_s_at	MINPP1: multiple inositol polyphosphate histidine phosphatase, 1	1.87
201143_s_at	EIF2S1: eukaryotic translation initiation factor 2, subunit 1 alpha, 35kDa	1.87
218604_at	LEMD3: LEM domain containing 3	1.85
1564175_at	LOC401074: Hypothetical LOC401074	1.85
218520_at	TBK1: TANK-binding kinase 1	1.85
226956_at	MTMR3: myotubularin related protein 3	1.84
234597_at	---: CDNA: FLJ20914 fis, clone ADSE00646	1.84
223215_s_at	C14orf100: chromosome 14 open reading frame 100	1.84
225236_at	RBM18: RNA binding motif protein 18	1.82
207128_s_at	ZNF223: zinc finger protein 223	1.81
227559_at	---: Transcribed locus	1.81
229373_at	---: Transcribed locus	1.79
238725_at	---: Transcribed locus	1.79
227410_at	FAM43A: family with sequence similarity 43, member A	1.79
241116_at	---: Transcribed locus	1.79
1560274_at	LOC100132279 /// WTAP: Wilms tumor 1 associated protein /// hypothetical protein LOC100132279	1.79
1555486_a_at	FLJ14213: protor-2	1.79
1554501_at	TSC22D4: TSC22 domain family, member 4	1.79
239081_at	---: Transcribed locus	1.78
201694_s_at	EGR1: early growth response 1	1.78
218535_s_at	RIOK2: RIO kinase 2 (yeast)	1.77
204447_at	ProSAPIP1: ProSAPIP1 protein	1.76
224628_at	C2orf30: chromosome 2 open reading frame 30	1.76
236360_at	FLJ42875: hypothetical LOC440556	1.76
206016_at	CCDC22: coiled-coil domain containing 22	1.76
215525_at	---: ---	1.75
219383_at	FLJ14213: protor-2	1.75
202097_at	NUP153: nucleoporin 153kDa	1.75
228753_at	LOC100128737: hypothetical protein LOC100128737	1.74
213109_at	TNIK: TRAF2 and NCK interacting kinase	1.74
238355_at	RBM39: RNA binding motif protein 39	1.74
222893_s_at	RPAP2: RNA polymerase II associated protein 2	1.73
219436_s_at	EMCN: endomucin	1.73
213376_at	ZBTB1: zinc finger and BTB domain containing 1	1.72
233226_at	PTPN9: Protein tyrosine phosphatase, non-receptor type 9	1.71
203761_at	SLA: Src-like-adaptor	1.71
225132_at	FBXL3: F-box and leucine-rich repeat protein 3	1.71
226280_at	---: CDNA FLJ43545 fis, clone PROST2011631	1.70
244613_at	---: ---	1.69
209193_at	PIM1: pim-1 oncogene	1.69
236128_at	ZNF91: zinc finger protein 91	1.67
216465_at	---: MRNA; cDNA DKFZp586N2022 (from clone DKFZp586N2022)	1.67
223470_at	PIGM: phosphatidylinositol glycan anchor biosynthesis, class M	1.67
205928_at	ZNF443: zinc finger protein 443	1.66
221025_x_at	PUS7L: pseudouridylate synthase 7 homolog (<i>S. cerevisiae</i>)-like	1.65
201236_s_at	BTG2: BTG family, member 2	1.64
232265_at	ATXN7L1: ataxin 7-like 1	1.64
225005_at	PHF13: PHD finger protein 13	1.62
225445_at	tcag7.1228: hypothetical protein FLJ25778	1.61
222312_s_at	---: CDNA clone IMAGE:6186815	1.61
200881_s_at	DNAJA1: DnaJ (Hsp40) homolog, subfamily A, member 1	1.61
213233_s_at	KLHL9: kelch-like 9 (<i>Drosophila</i>)	1.60
241445_at	---: Transcribed locus	1.59
214651_s_at	HOXA9: homeobox A9	1.57
227066_at	MOBK12C: MOB1, Mps One Binder kinase activator-like 2C (yeast)	1.56
230520_at	AIG1: androgen-induced 1	1.56
238279_x_at	---: ---	1.55
1569098_s_at	TP53BP1: tumor protein p53 binding protein 1	1.55
225490_at	ARID2: AT rich interactive domain 2 (ARID, RFX-like)	1.54

223377_x_at	CISH: cytokine inducible SH2-containing protein	1.54
242761_s_at	ZNF420: zinc finger protein 420	1.52
201041_s_at	DUSP1: dual specificity phosphatase 1	1.51
228445_at	AIFM2: apoptosis-inducing factor, mitochondrion-associated, 2	1.50
218079_s_at	GGNBP2: gametogenetin binding protein 2	1.50
226504_at	FAM109B: family with sequence similarity 109, member B	1.48
225121_at	TBC1D23: TBC1 domain family, member 23	1.48
225912_at	TP53INP1: tumor protein p53 inducible nuclear protein 1	-1.70
226419_s_at	FLJ44342: hypothetical LOC645460	-1.73
206674_at	FLT3: fms-related tyrosine kinase 3	-1.76
224606_at	KLF6: Kruppel-like factor 6	-1.78
241353_s_at	LOC100129105: similar to hCG1821214	-1.86
225673_at	MYADM: myeloid-associated differentiation marker	-1.93
204639_at	ADA: adenosine deaminase	-1.98
208763_s_at	TSC22D3: TSC22 domain family, member 3	-2.03
244080_at	---: Transcribed locus, strongly similar to XP_001151823.1 PREDICTED: hypothetical protein [Pan troglodytes]	-2.04
36829_at	PER1: period homolog 1 (Drosophila)	-2.07
214176_s_at	---: Transcribed locus	-2.11
226525_at	---: Transcribed locus	-2.17
215671_at	PDE4B: phosphodiesterase 4B, cAMP-specific (phosphodiesterase E4 dunce homolog, Drosophila)	-2.34
230986_at	KLF8: Kruppel-like factor 8	-2.36
213665_at	SOX4: SRY (sex determining region Y)-box 4	-2.39
236253_at	---: Transcribed locus	-2.49
229178_at	LOC145786: hypothetical protein LOC145786	-2.56
223708_at	C1QTNF4: C1q and tumor necrosis factor related protein 4	-2.64
228983_at	---: Transcribed locus	-2.78
231508_s_at	---: Transcribed locus	-2.79
214043_at	PTPRD: protein tyrosine phosphatase, receptor type, D	-2.80
201324_at	EMP1: epithelial membrane protein 1	-2.81
207735_at	RNF125: ring finger protein 125	-2.82
1552803_a_at	C1orf215: chromosome 1 open reading frame 215	-2.82
202861_at	PER1: period homolog 1 (Drosophila)	-2.96
222044_at	PCIF1: PDX1 C-terminal inhibiting factor 1	-2.96
204784_s_at	MLF1: myeloid leukemia factor 1	-3.03
228188_at	FOSL2: FOS-like antigen 2	-3.15
230233_at	---: Transcribed locus	-3.21
242051_at	---: Transcribed locus	-3.22
239476_at	---: CDNA FLJ36491 fis, clone THYMU2018197	-3.26
1561079_at	ANKRD28: ankyrin repeat domain 28	-3.29
206726_at	PGDS: prostaglandin D2 synthase, hematopoietic	-3.50
203708_at	PDE4B: phosphodiesterase 4B, cAMP-specific (phosphodiesterase E4 dunce homolog, Drosophila)	-3.79
239809_at	---: Transcribed locus	-4.17
205239_at	AREG /// LOC727738: amphiregulin (schwannoma-derived growth factor) /// similar to Amphiregulin precursor (AR) (Colorectum cell-derived growth factor) (CRDGF)	-7.56
215446_s_at	LOX: lysyl oxidase	-10.59

Supplementary Table 2. Selected list of genes that have been implicated in hematopoietic malignancies and are differentially expressed between elderly and young human HSC; age-up-regulated genes are in red, and age-down-regulated genes are in green.

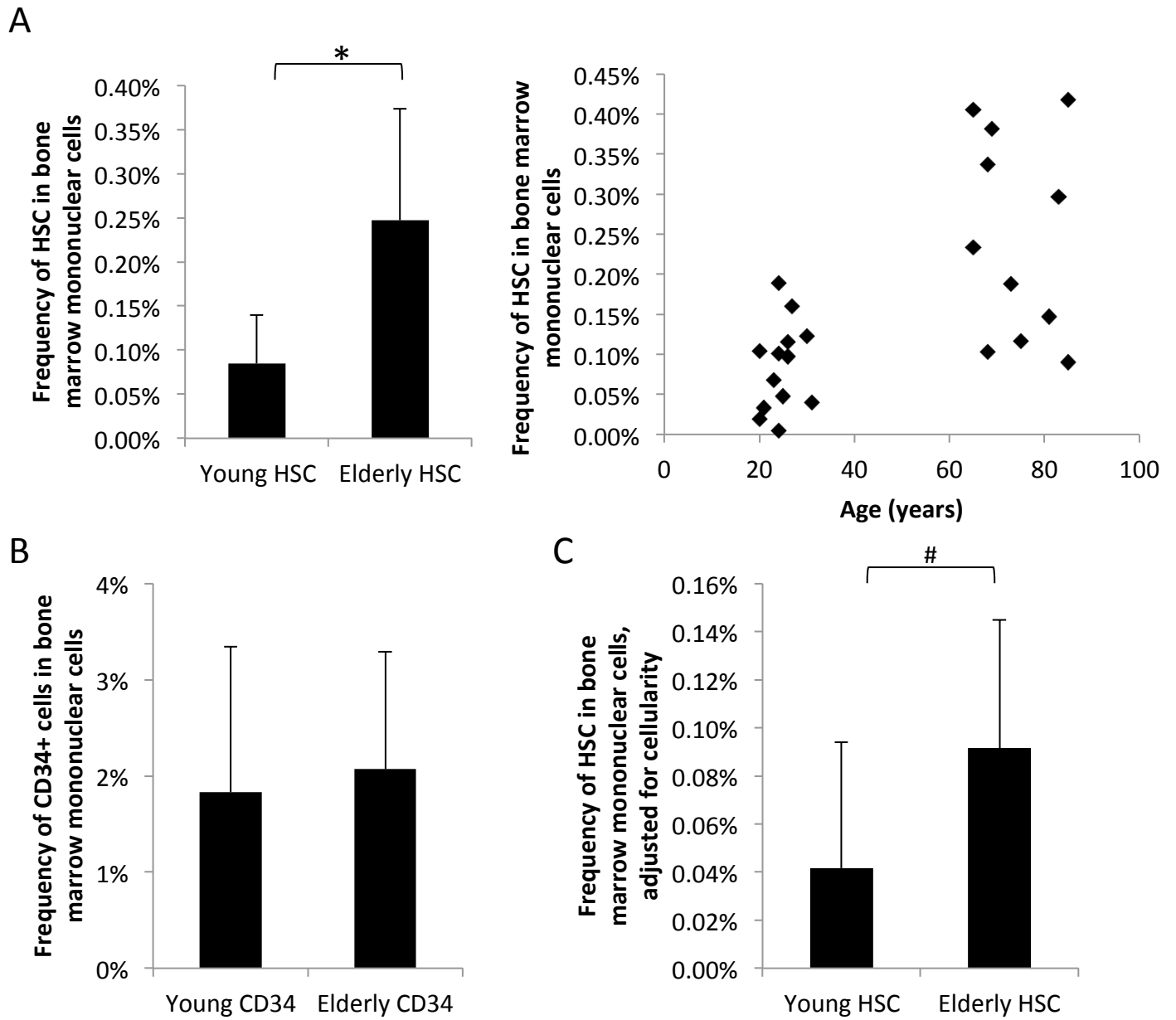
Gene ID	Gene Name	Fold Change
208079_s_at	AURKA: aurora kinase A	1.81
209189_at	FOS: v-fos FBJ murine osteosarcoma viral oncogene homolog	2.49
209905_at	HOXA9: homeobox A9	1.62
202431_s_at	MYC: v-myc myelocytomatosis viral oncogene homolog (avian)	2.65
230192_at	TRIM13: tripartite motif-containing 13	2.91
36711_at	MAFF: v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)	-2.06
206674_at	FLT3: fms-related tyrosine kinase 3	-1.76

Supplementary Table 3. Complete blood count (CBC) values from matching peripheral blood of bone marrow samples used for this study (data available for subset of samples only).

		Complete Blood Count						
Age	Gender	WBC	Hb	HCT	PLT	MCV	RDW	RBC
24	Male	5.3	14.1	39.8	225	87.2	13.1	4.57
24	Female	8.5	13.1	37.6	269	93.7	12.5	4.01
26	Female	4.5	14	14.3	198	94.6	13.7	4.36
26	Male	4.3	14.4	41.8	200	89.5	13.5	4.67
27	Female	7.3	15.9	45.4	224	87.7	12.9	5.18
30	Female	6.3	13.1	37.8	191	89.3	13.6	4.23
31	Male	8.1	14.4	40.8	274	93.8	14.4	4.35
65	Male	5.2	14.6	43	195	91	13.9	4.72
65	Male	4.7	15.1	43.6	184	91	14.1	4.78
68	Male	7	14.8	42.8	236	92	13.1	4.68
68	Male	8.1	13.2	38.4	230	98	12.1	3.92
73	Male	5.6	13.4	38.4	295	87	13.1	4.41
75	Male	7.3	15.1	44	219	89.5	13.8	4.91
81	Male	9.4	15.4	44.9	188	89.5	14.7	5.02
83	Female	7.1	13.3	39.4	250	89.9	14.1	4.38
85	Female	5.1	12.7	37	215	100.5	13.7	3.68
85	Female	6.2	13.8	41.1	163	87.4	15.3	4.7

Supplementary Figure 1. Increased frequency of HSC out of total mononuclear cells isolated from normal elderly bone marrow compared to young.

(A) Summary of HSC as frequency of total bone marrow mononuclear cell population from multiple young (n=13) and elderly (n=11) bone marrow samples. * = $p < 0.002$. (B) CD34+ cells as frequency of total bone marrow mononuclear cell population from multiple young (n=13) and elderly (n=11) bone marrow samples. (C) Relative HSC as frequency of total bone marrow mononuclear cell population from multiple young (n=13) and elderly (n=11) bone marrow samples, adjusted for bone marrow cellularity, as estimated from bone marrow core biopsies. # = $p < 0.02$. Error bars represent standard deviation.

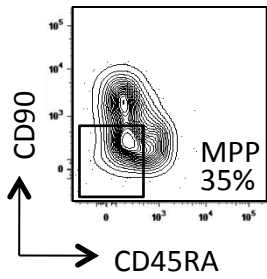


Supplementary Figure 1

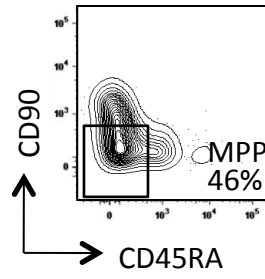
Supplementary Figure 2. Frequency of MPP in normal elderly bone marrow compared to young.

(A) Gating strategy and flow cytometric profile of MPP (Lin^- , CD34^+ , CD38^- , CD90^- , CD45RA^-) in representative hematopoietically normal young (left) and elderly (right) bone marrow samples. The panels for each sample are gated on $\text{Lin}^- \text{CD34}^+ \text{CD38}^-$ live cells. (B) Summary of MPP as frequency of total $\text{Lin}^- \text{CD34}^+$ population from multiple young (n=13) and elderly (n=11) bone marrow samples. (C) Summary of MPP as frequency of total bone marrow mononuclear cell population from multiple young (n=13) and elderly (n=11) bone marrow samples. Error bars represent standard deviation.

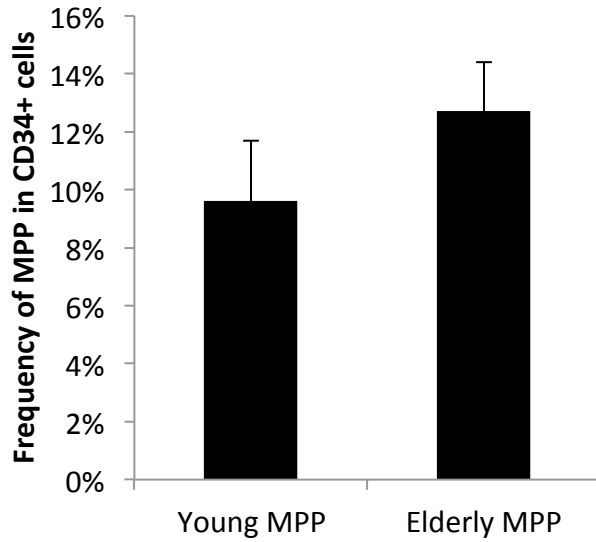
A Young Bone Marrow (31 year old, male):
Live, Lin-CD34+CD38-:



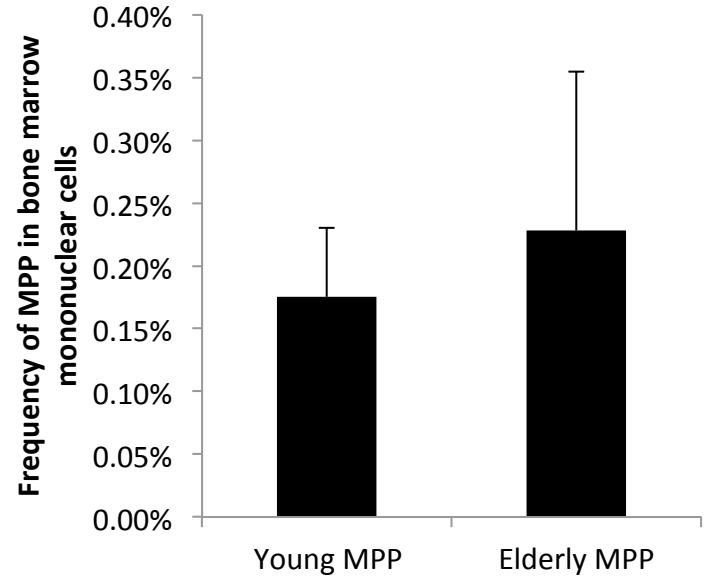
Elderly Bone Marrow (83 year old, female):
Live, Lin-CD34+CD38-:



B



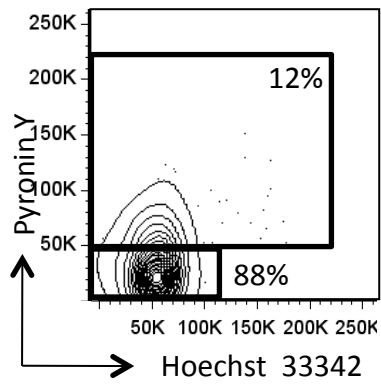
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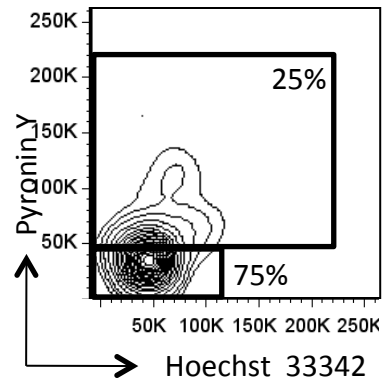
Supplementary Figure 3. Gating strategy and cell cycle flow cytometric profile of live, Lin⁻ CD34⁺ cells.

(A) Gating strategy and flow cytometric profile of quiescent G₀ (Hoechst 33342^{low}, Pyronin Y^{low}, correlating with 2N DNA and low levels of RNA) and non-G₀ (Pyronin Y^{high}, correlating with 2N to 4N DNA and higher levels of RNA) populations in representative elderly and young HSC from hematopoietically normal bone marrow samples. The panels for each sample are gated on Lin-CD34+CD38-CD90+CD45RA- live cells. (B) Quiescent G₀ (Hoechst 33342^{low}, Pyronin Y^{low}, correlating with 2N DNA and low levels of RNA) and non-G₀ (Pyronin Y^{high}, correlating with 2N to 4N DNA and higher levels of RNA) populations in representative elderly and young Lin⁻ CD34⁺ population from hematopoietically normal bone marrow samples. The panel is gated on Lin-CD34+CD38-CD90+CD45RA- live cells. This profile was used to set gates for Hoechst 33342 and Pyronin Y in (A).

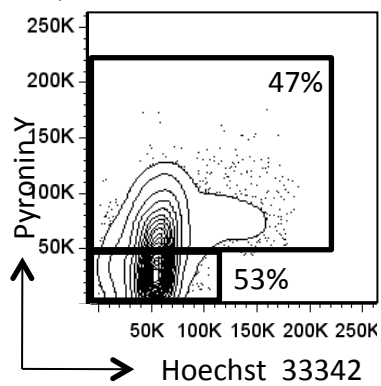
A Young Bone Marrow (31 year old, male):
Live, Lin-CD34+CD38-CD90+:



Elderly Bone Marrow (83 year old, female):
Live, Lin-CD34+CD38-CD90+:

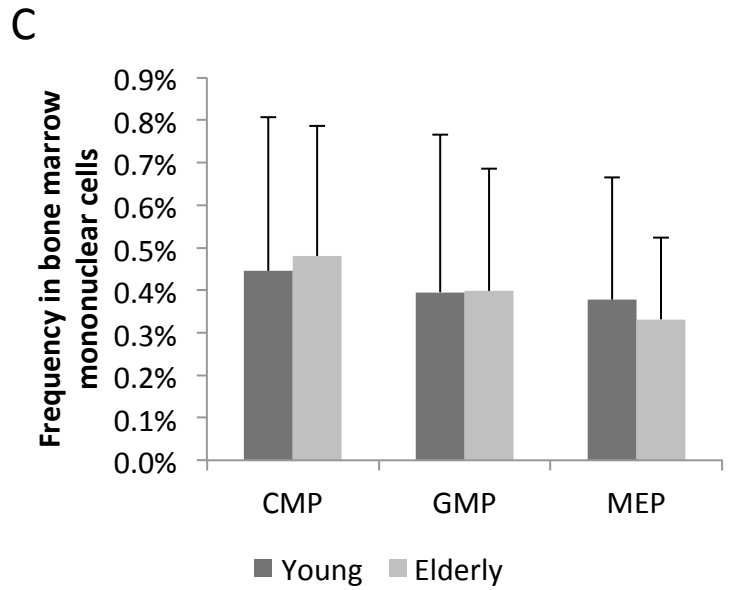
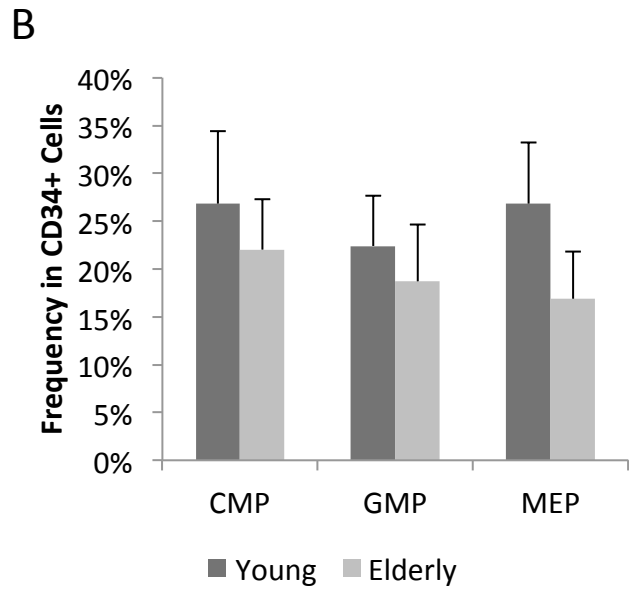
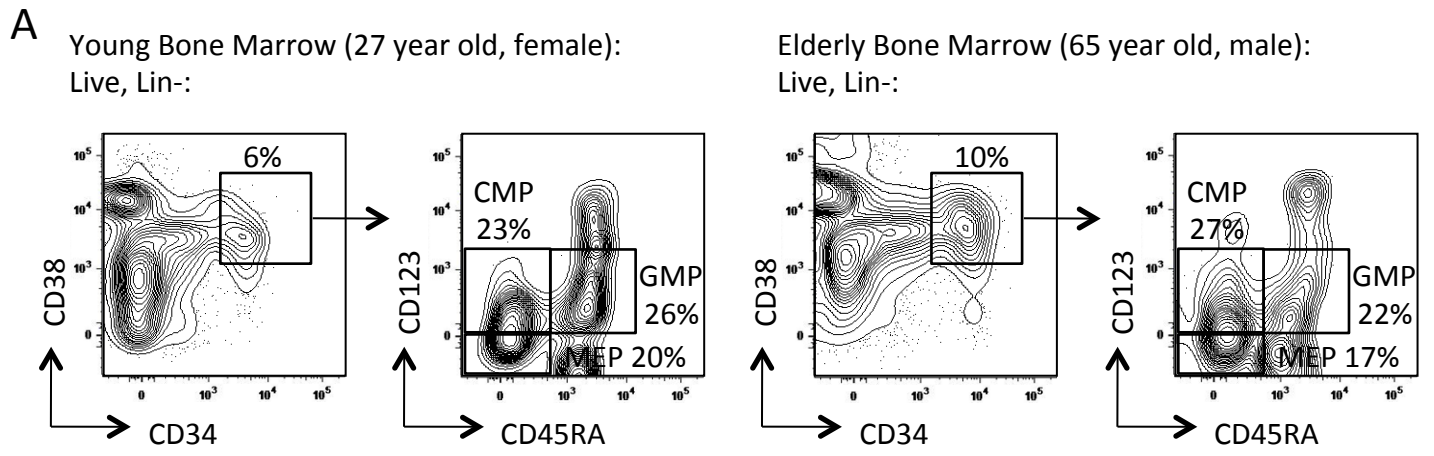


B Live, Lin-CD34+:



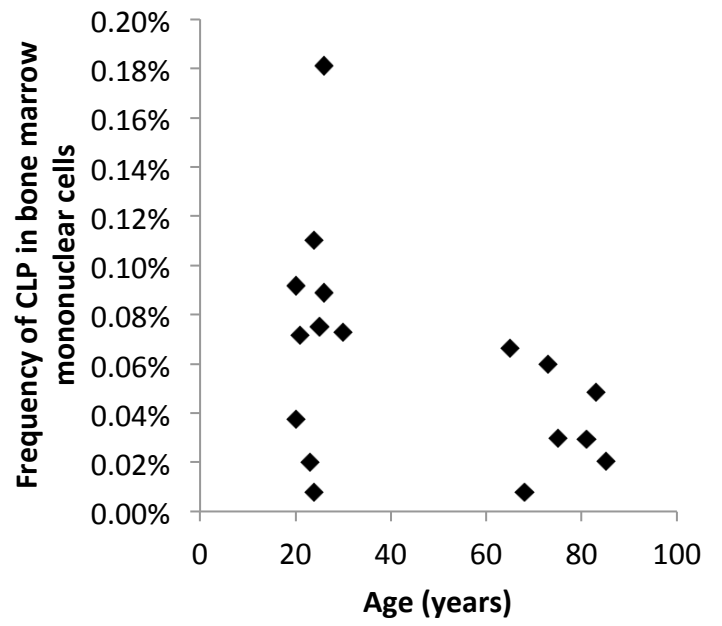
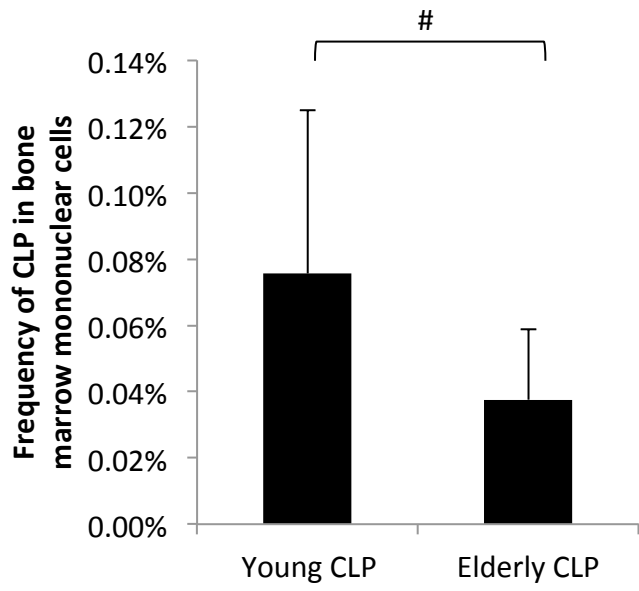
Supplementary Figure 4. Similar myeloid progenitor frequencies in normal elderly and young bone marrow.

(A) Gating strategy and flow cytometric profile of CMP ($\text{Lin}^- \text{CD34}^+ \text{CD38}^+ \text{CD123}^+ \text{CD45RA}^-$), GMP ($\text{Lin}^- \text{CD34}^+ \text{CD38}^+ \text{CD123}^+ \text{CD45RA}^+$), and MEP ($\text{Lin}^- \text{CD34}^+ \text{CD38}^+ \text{CD123}^- \text{CD45RA}^-$) in representative hematopoietically normal young and elderly bone marrow samples. The left panels for each sample are gated on lineage negative (Lin^-) live cells, and the right panels are gated on $\text{Lin}^- \text{CD34}^+ \text{CD38}^+$ live cells. (B) Summary of myeloid progenitor (CMP, GMP, and MEP) frequencies as total of $\text{Lin}^- \text{CD34}^+$ population from multiple young ($n=13$) and elderly ($n=11$) bone marrow samples. (C) Summary of myeloid progenitor (CMP, GMP, and MEP) frequencies as total of bone marrow mononuclear cell population from multiple young ($n=13$) and elderly ($n=11$) bone marrow samples. Error bars represent standard deviation.



Supplementary Figure 5. Decreased frequency of CLP out of total mononuclear cells isolated from normal elderly bone marrow compared to young.

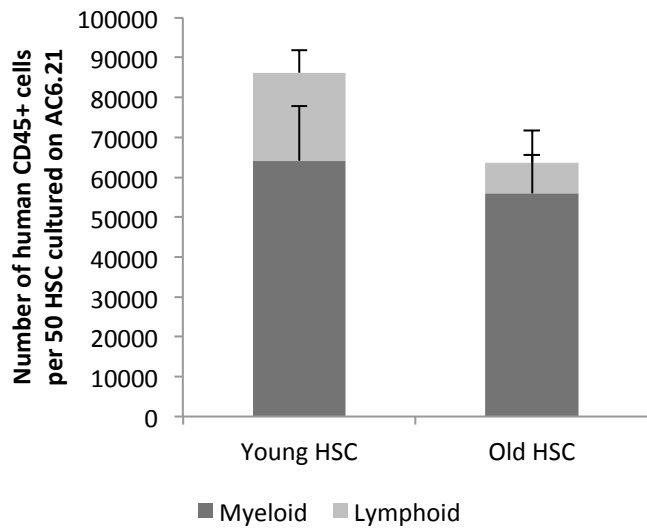
Summary of CLP as frequency of total bone marrow mononuclear cell population from multiple young (n=10) and elderly (n=7) bone marrow samples. # = $p < 0.05$. Error bars represent standard deviation.



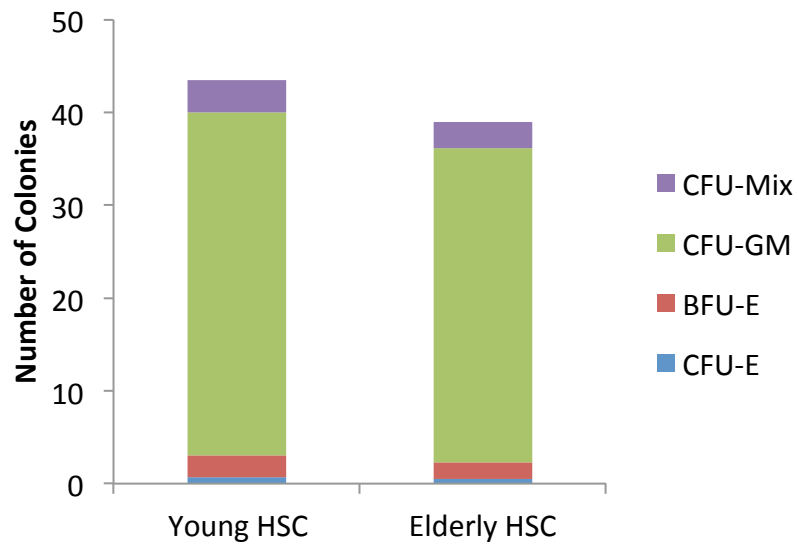
Supplementary Figure 6. Generation of lymphoid and myeloid progeny *in vitro* by HSC from normal young and elderly bone marrow.

(A) Summary of numbers and types of cells produced per 50 HSC from multiple normal young (n=8) and elderly (n=6) bone marrow samples co-cultured with AC6.2.1 stromal cell line. (B) Summary of numbers and types of colonies produced by 300 HSC from multiple normal young (n=6) and elderly (n=6) bone marrow samples cultured in methylcellulose medium. Error bars represent standard deviation.

A

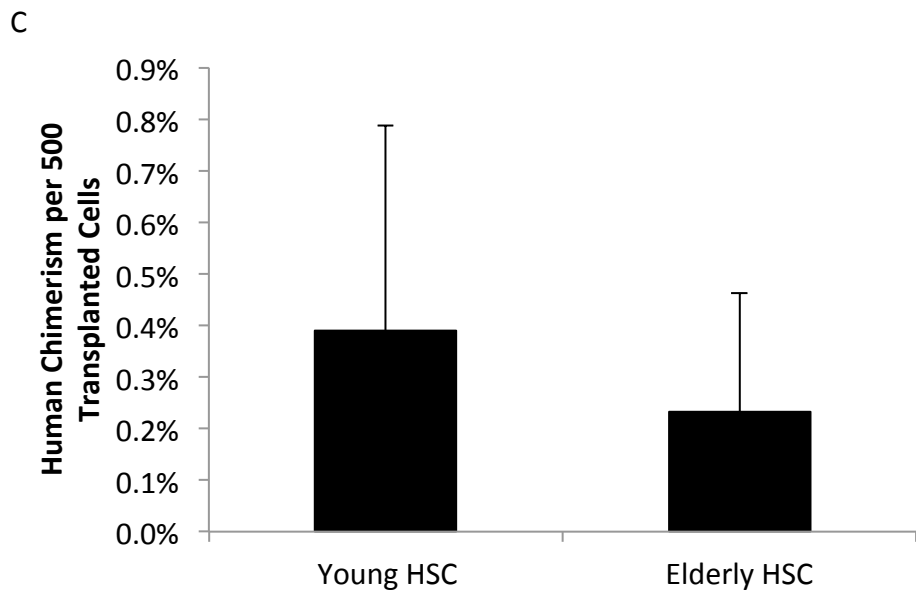
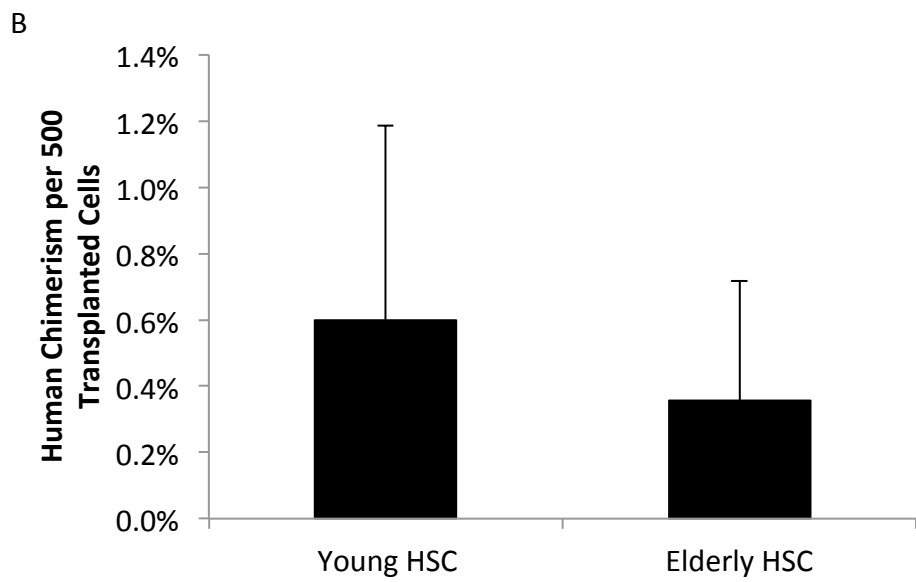
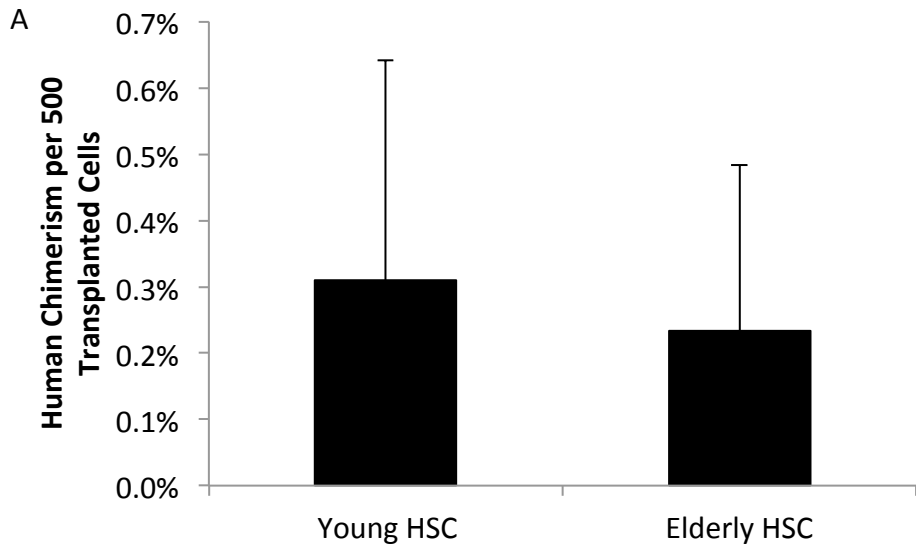


B



Supplementary Figure 7. Engraftment of human T cells, erythroid cells, and platelets

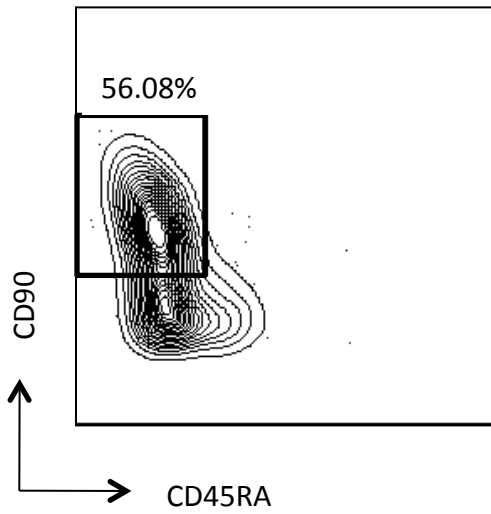
(A) Summary of spleen engraftment of human CD45⁺CD3⁺ T cells as measured by percent human chimerism per 500 transplanted HSC from unique young (n=10) and elderly (n=9) bone marrow samples. (B) Summary of bone marrow engraftment of human glycophorin A⁺ erythroid cells. (C) Summary of bone marrow engraftment of human CD41/61⁺ platelets. Error bars represent standard deviation.



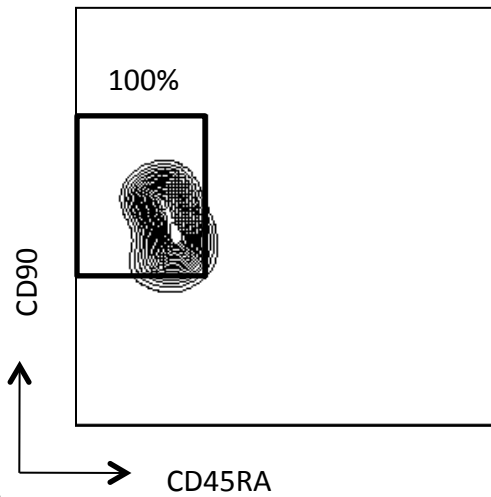
Supplementary Figure 8. Purification of HSC from bone marrow by FACS

(A) Representative flow cytometric profile of HSC prior to sorting. (B) Representative flow cytometric profile of sorted HSC which were re-analyzed to assess purity. (C) Summary of sort purity of sorted HSC from multiple young (n=11) and elderly (n=8) bone marrow samples.

A Pre-sort:
Live, Lin⁻, CD34⁺, CD38⁻:



B Post-sort:
Live:



C

Samples	Post-sort purity (range)
Elderly HSC (8 samples)	96.55%-100.00%
Young HSC (11 samples)	95.25%-100.00%

Supplementary Figure 9. Ingenuity Pathways Analysis of age-regulated genes.

(A) The “Cell Cycle, Connective Tissue Development and Function, Cellular Development” network and (B) the “Gene Expression, Hematological System Development and Function, Tissue Morphology” network are identified by IPA, based on the age-regulated genes from SAM, as the most significantly affected during human HSC aging. Selection of (B) biological functions and (C) molecular pathways identified by IPA as significantly enriched in the age-regulated HSC geneset.

