

Supplementary Table 1. Genes, concepts, and themes associated with the ECM super cluster from DEGs upregulated in the AF. CompBio scores are shown in parenthesis.

Tissue	Theme	Gene			Concept	
AF - UP	ECM-Related (1843.33) 33 Concepts, 89 Genes	timp1 (612.227947) acvr2a (537.844593) mmp2 (352.562526) adamts5 (286.852662) mmp8 (280.699688) adamts1 (236.535003) acta2 (101.106559) col3a1 (82.885000) camp (76.450742) acta1 (68.285366) serpine1 (58.218303) adam10 (53.857835) id3 (44.748415) id2 (44.459548) adam8 (43.902986) car1 (42.519976) lcn2 (38.729749) nov (34.120957) pcolce (31.973806) myoz2 (31.137381) col5a2 (26.930686) col5a1 (23.860792) thsd4 (22.858018) thy1 (21.578509) krt19 (20.608352) cilp (18.910779) cd44 (18.829262) ceacam1 (18.463877) cd68 (18.279911) ptprc (17.380703)	nbl1 (16.824268) lrp1 (16.714537) col18a1 (15.273221) cxcr4 (14.098972) mt1 (13.570924) prg4 (12.378821) ccna2 (11.633536) gmfg (10.904592) ly6a (10.617937) cd53 (10.341455) gja1 (9.107612) cybb (8.910212) tnfrsf1a (8.787090) itgam (8.588916) nt5e (8.492694) slc4a1 (8.406977) lft (8.141345) fmln1 (8.140308) cdk2 (8.122184) itga11 (8.102874) s100a8 (7.788115) fndc4 (7.763835) mtor (7.396756) s100g (6.341115) anxa7 (6.313889) itgb2 (6.203705) mpo (5.993937) rbm15 (5.753340) cd177 (5.662562) prg2 (5.546844)	ncf1 (5.221649) csrp3 (5.118033) clec12a (5.026895) elane (4.955869) olfml2b (4.909754) aspn (4.841995) ceacam2 (4.751446) csf3r (4.663411) gypa (4.640726) prkcb (4.335864) ly6g (4.319558) fpr1 (4.313344) rac2 (4.166443) emcn (4.162347) lum (3.850878) spi1 (3.824567) s100a11 (3.709868) cd37 (3.638900) nfam1 (3.556899) ly6c1 (3.506441) cd33 (3.488967) ptpn6 (3.412393) lgals1 (3.409531) s100a9 (3.348135) des (3.246200) myb (3.240623) tmem173 (3.218413) prc1 (3.023227) cxcr2 (3.022913)	collagen (3.646197) tgf-beta (3.721052) factor-beta (3.742679) fibronectin (3.806666) ecm (3.936894) metalloproteinase (3.991639) metalloproteinases (4.133009) smad2 (4.246263) myofibroblasts (4.288810) timp (4.405909) smad (4.429273) smad3 (4.598823) morphogenetic (4.623340) myofibroblast (4.630659) tgfbeta (4.668659) basement (4.681120) collagenase (4.844961)	bmp (5.018716) activin (5.019449) superfamily (5.023064) gelatinase (5.036883) hydroxyproline (5.094928) type-i (5.204692) thrombospondin (5.271348) transdifferentiation (5.359269) hscs (5.363479) follistatin (5.543978) stromelysin (6.010261) inhibin (6.021328) type-ii (6.111235) metallopeptidase (6.138494) matrilysin (6.567857) alpha-defensins (8.213786)
	Amyloid Fibrils (1335.98) 9 Concepts, 69 Genes	gmfg (283.495788) saa2 (214.130815) saa1 (209.646000) col5a1 (129.945140) chil3 (122.699158) tyrobp (107.001631) pcolce (97.046803) col5a2 (96.707243) itgam (74.530176) adam10 (72.293998) cd68 (68.450531) cln5 (59.527633) cybb (36.976124) col3a1 (32.713914) ly6c1 (30.451364) ptprc (29.033897) lrp1 (26.657230) cllc1 (22.218654) kcnn4 (20.910989) cxcr4 (20.460192) ly6g (20.411731) lum (18.933472) anxa1 (17.017862)	gpnmb (16.943106) cxcr2 (16.360785) tnfrsf1a (14.944413) mmp8 (14.925052) timp1 (14.358748) gja1 (14.330784) lrp8 (13.944636) mmp2 (13.818302) slurp1 (12.491792) vcp (12.162038) elane (11.852324) acta1 (11.744921) ncf1 (11.505722) slc2a3 (10.536983) ackr3 (10.320303) hspb8 (9.101120) tuba4a (8.877054) s100a8 (8.475130) hspb6 (8.322914) dock2 (8.137158) cd33 (7.903601) slc1a4 (7.780038) lcn2 (7.318269)	keap1 (7.158345) lyz2 (6.700175) fcer1g (6.562978) htra2 (6.551572) s100a9 (6.204698) camkk2 (5.864645) itgb2 (5.863657) mtor (5.609613) irak4 (5.550643) thy1 (5.521960) hspa1a (5.406575) nov (4.950322) cables1 (4.933898) ndufa1 (4.616068) prdx2 (4.513970) ppp1r9b (4.154949) gpx1 (3.748461) ncf2 (3.536952) cd44 (3.520448) myh8 (3.451069) ptpn6 (3.371863) hist1h1c (3.255649) nt5e (3.164766)	amyloid (3.675113) microglia (3.678233) microglial (3.938665) neurodegenerative (4.131085) fibrils (4.370457)	glia (4.834059) fibrillar (4.866332) fibril (5.271661) fractalkine (5.970808)

Supplementary Table 2. Genes, concepts, and themes associated with the ECM super cluster from DEGs downregulated in the AF. CompBio scores are shown in parenthesis.

Tissue	Theme	Gene			Concept	
AF - DOWN	ECM-Related-1 (26396.29) 12 Concepts, 28 Genes	col11a1 (2098.882438) col2a1 (1630.599860) col11a2 (1277.967288) col10a1 (1083.481099) acan (917.538428) col9a2 (902.907770) col9a3 (274.739738) sox9 (234.729013) col27a1 (209.936683) hapln1 (115.385095)	snai2 (91.810780) lrp5 (54.800487) sox5 (35.346951) bmp5 (29.459357) itga6 (26.174950) fgfr3 (25.928760) krt8 (25.715599) trpc3 (22.293784) s100b (15.026250) fat1 (14.477513)	krtap5-1 (11.485184) frzb (11.217982) grem1 (10.484268) il6 (9.495524) gjb6 (9.112332) chst11 (7.658601) matn3 (6.776611) slc26a2 (3.209043)	col5a1 (1.859182) col5a2 (1.874813) col11a1 (1.930254) col3a1 (1.997060) col1a1 (2.093634) collagens (2.280152)	col1a2 (2.300814) col11a2 (2.521267) xi (2.745857) col6a1 (2.780897) fibrillar (2.803952) fn1 (3.013590)
	Cartilage, Articular (25744.45) 83 Concepts, 40 Genes	col2a1 (1128.017938) col10a1 (1080.111934) acan (860.307287) sox9 (815.726604) sox5 (437.338281) col9a2 (328.747043) col11a2 (276.562423) slc26a2 (256.343771) col11a1 (236.981555) fgfr3 (183.017668) matn3 (127.501777) hapln1 (111.513857) col9a3 (100.142952) sox8 (59.948448)	ucma (56.965981) wisp3 (49.854167) papss2 (46.153298) trpc3 (28.831117) col27a1 (27.622636) bmp5 (23.725537) lrp5 (23.174187) sgalnact1 (16.351351) trpv4 (15.743457) frzb (14.275226) chst11 (13.612511) sfrp5 (12.922046) il6 (12.912499) snai2 (12.391289)	chadl (10.556435) itga6 (9.523547) trpm7 (7.506775) scrg1 (7.463269) prrg4 (7.353324) clec4g (5.999290) grem1 (5.859621) gal3st2 (4.952021) etv5 (3.580243) fgfr1 (3.241588) tnr (3.136109) stc2 (3.045821)	chondrocytes (3.289268) cartilage (3.307109) chondrocyte (3.326771) col2a1 (3.338902) col10a1 (3.369533) sox9 (3.400894) chondrogenesis (3.415233) chondrogenic (3.460794) aggrecan (3.464150) hypertrophic (3.496752) articular (3.541992) ossification (3.628928) cartilaginous (3.701292) runx2 (3.706490) acan (3.709650) endochondral (3.713542) osteoarthritis (3.739690) ihh (3.952844) cartilage-specific (3.955506) oa (3.961725) comp (4.011701) chondrocytic (4.012494) mmp13 (4.102905) epiphyseal (4.111043) micromass (4.175520) alcian (4.207284) hyaline (4.209037) osteogenesis (4.239771) osteoarthritic (4.253466) cartilages (4.270364) chondrodysplasia (4.287202) dysplasia (4.297080) mscs (4.307354) atdc5 (4.348169) chondrocyte-specific (4.428309) col (4.454092) calcification (4.464701) runt-related (4.493386) pellet (4.499547) oligomeric (4.510336) osterix (4.612679) ix (4.618798)	dwarfism (4.636578) condylar (4.774255) alp (4.788202) col9a2 (4.798266) stature (4.859589) prehypertrophic (4.868729) dysplasias (4.903125) skeletogenesis (4.907638) intramembranous (4.910145) adamts5 (4.910365) hmscs (4.911215) chondrodysplasias (5.018934) cbfa1 (5.043626) mmp3 (5.052603) c3h10t1 (5.087190) fibrocartilage (5.114802) oa-like (5.149760) spondyloepiphyseal (5.171468) metaphyseal (5.202255) ocn (5.202709) mmp1 (5.270881) condensations (5.299069) osx (5.307061) adamts4 (5.337246) non-collagenous (5.347214) hmsc (5.364236) opn (5.386362) haploinsufficiency (5.422658) bm-mscs (5.584857) degradative (5.607887) radiographically (5.610724) runx3 (5.631284) mgp (5.639234) hif-2a (5.667425) patella (5.720246) osteocondrodysplasia (5.752396) sed (5.781078) gla (5.898991) osteoarthropathy (6.038257) co-culturing (6.107200) non-lethal (6.165223)

Supplementary Table 2. Continued

Tissue	Theme	Gene			Concept	
AF - DOWN	Intervertebral Disc (7447.58) 26 Concepts, 21 Genes	acan (439.145470) col2a1 (333.086640) col9a3 (329.640001) col10a1 (108.990959) sox9 (83.463072) col9a2 (69.342912) wisp3 (55.708591)	il6 (28.742186) slc35a3 (21.272618) krt8 (17.751198) col11a2 (12.073874) bcat1 (10.132739) col11a1 (9.631237) lrp5 (7.634491)	hapln1 (7.051835) sox5 (6.006319) fgfr3 (5.851093) trpc3 (4.067831) als2cr12 (3.923848) prrg4 (3.638312) slc27a1 (3.276362)	intervertebral (3.098914) catabolic (3.201843) mmp-13 (3.231700) disc (3.239936) pulposus (3.290450) mmp-3 (3.298470) anabolic (3.302926) ivd (3.585995) adamts-4 (3.591431) np (3.716188) fibrosus (3.824740) il-1b-induced (3.929351) adamts (4.322705)	catabolism (4.327264) matrix-degrading (4.353183) orthop (4.440543) metalloproteinase-13 (4.551878) anabolism (4.569259) endplate (4.573456) res (4.579345) motifs (4.587621) subchondral (4.624898) npcs (4.716056) vertebral (4.800218) meniscus (5.083920) ppd (6.753984)
	Wnt/B-Catenin Signaling (2623.14) 34 Concepts, 44 Genes	sfrp5 (1456.741692) lrp5 (933.530632) frzb (526.320025) rspo3 (227.275925) wisp3 (72.350683) nid2 (53.951897) sox9 (52.013862) col10a1 (39.635659) snai2 (39.458553) wnk2 (33.366337) trpc3 (31.489595) grem1 (31.135537) acan (21.556143) col2a1 (16.580297) gng7 (12.564949)	crisp3 (12.019394) cmtm5 (12.007081) bcat1 (11.877178) corin (11.570268) tdrd1 (11.013653) sox5 (9.960569) fgfr1 (9.015105) tnr (8.415435) fat1 (7.429845) il6 (7.105054) col11a1 (6.994276) st3gal6 (6.290501) epha1 (6.254263) rap1gap (5.969144) fgfr3 (5.937330)	atp10a (5.679341) chst11 (5.605750) krtap5-1 (5.012391) itga6 (4.652833) sox8 (4.252587) stc2 (4.221430) chrdl2 (3.925473) krt8 (3.923023) trpm7 (3.841549) azgp1 (3.661650) lbh (3.390774) fhl1 (3.244535) klrk1 (3.203263) vav3 (3.023654)	wnt (2.849254) sfrp1 (2.881782) sfrp2 (2.989890) frizzled-related (3.089474) sfrp4 (3.091842) dkk1 (3.125666) beta-catenin (3.262139) b-catenin (3.285141) frizzled (3.325955) sfrp (3.328173) dkk3 (3.367224) canonical (3.429486) methylation (3.457203) dickkopf (3.608469) wif1 (3.612718) epigenetic (3.643629) secreted (3.702506)	hypermethylation (3.758543) wnts (3.767718) silencing (3.953285) methylation-specific (3.964054) axin2 (4.018013) wnt3a (4.028198) methylated (4.128060) dkk (4.196777) lef1 (4.245415) 5-aza-2-deoxycytidine (4.324402) receptor-related (4.354817) sclerostin (4.534366) sost (4.544350) msp (4.834078) co-receptors (4.849295) silenced (5.045553) tcf4 (5.723785)
	Sox-Related 1 (4428.23) 14 Concepts, 24 Genes	sox9 (1097.437975) sox8 (751.562765) sox5 (228.369160) prrg4 (99.021026) dock8 (80.831015) tdrd1 (73.634575) itga6 (34.781206) col2a1 (32.233398)	snai2 (27.760488) etv5 (25.787928) acan (23.698189) cmtm5 (16.461623) atp10a (8.052100) hpgds (6.889043) tshr (5.967500) wisp3 (5.850102)	col10a1 (5.252615) fat1 (4.127250) il6 (3.803410) col9a2 (3.801224) vit (3.674874) s100b (3.503101) krt8 (3.189543) fga (3.178846)	sertoli (2.818841) gonads (2.835392) sry (2.919996) sex-determining (2.970243) amh (3.111122) gonad (3.203031) testes (3.249434)	wt1 (3.302998) dmrt1 (3.303239) anti-mullerian (3.397446) xy (3.525023) y-box (4.752868) transwell (6.244225) cck8 (6.617245)
	Sox-Related 2 (4320.37) 17 Concepts, 30 Genes	sox5 (1337.075779) sox8 (1233.034463) sox9 (1105.472865) col2a1 (441.897232) acan (386.170983) krt8 (212.306563) col10a1 (168.834048) col11a2 (91.637519) sfrp5 (76.942563) rspo3 (69.160925)	col9a2 (48.495728) itga6 (47.768198) snai2 (41.486594) fxyd3 (41.078834) corin (38.079511) avpr1a (29.181418) lrp5 (16.656286) kcnj6 (14.263510) fga (13.116907) npl (11.847700)	fgfr3 (11.803540) etv5 (10.009109) s100b (9.188300) rs1 (6.539457) atp10a (5.579282) frzb (3.796979) vav3 (3.454475) fam19a5 (3.326232) fat1 (3.308709) grem1 (3.064578)	sox5 (3.780091) sox6 (3.890635) sox17 (4.081493) sox (4.081561) sox13 (4.128322) hmg (4.297147) sox4 (4.342014) sox11 (4.381331) sox7 (4.689096)	hmg-box (4.746614) differentiating (5.169825) foxa2 (5.585035) trio (5.783954) krt19 (6.065990) gata6 (6.202158) trios (6.595608) family-based (6.660332)

Supplementary Table 2. Continued

Tissue	Theme	Gene			Concept	
AF - DOWN	BMP Signaling (2716.19) 15 Concepts, 25 Genes	bmp5 (1553.623224) grem1 (884.413269) col10a1 (278.503791) sox9 (231.508429) col2a1 (144.430751) chrdl2 (113.157899) acan (67.914182) lrp5 (31.788250) sox5 (31.627408)	snai2 (24.138709) frzb (20.016681) fgfr3 (16.288082) wisp3 (9.933986) etv5 (9.266946) il6 (8.438558) krt8 (6.850136) epha1 (6.250484) itga6 (5.833228)	ucma (5.757025) btbd3 (5.616615) hapln1 (4.954779) sfrp5 (4.469579) chst11 (4.224384) sox8 (3.803242) col11a2 (3.775045)	bmp (2.303506) bmps (2.366603) morphogenetic (2.423980) gremlin (2.629356) noggin (2.954818) bmp-4 (3.127434) bmp2 (3.183333)	smad1 (3.195307) bmp4 (3.287701) bmp7 (3.330544) morphogenic (3.413961) bmp-7 (3.621154) bmp-2 (3.632651) bmp6 (3.987768)
	Musculoskeletal Development (2528.37) 24 Concepts, 29 Genes	snai2 (1890.556804) krt8 (109.072525) nid2 (91.551024) sox9 (59.505064) wisp3 (51.712572) fgfr3 (41.351001) itga6 (40.545767) ppr5 (34.475651) sox5 (29.929998) etv5 (28.076578)	sfrp5 (17.631963) sox8 (17.137141) plekhh1 (9.761309) grem1 (9.468821) flg2 (9.247792) bmp5 (9.099204) col11a1 (8.604426) tubb2b (8.342068) rap1gap (8.212438) col2a1 (8.019902)	epha1 (6.695253) il6 (6.426786) fat1 (6.272435) lbh (5.748247) fxyd3 (5.676293) s100b (5.110721) stc2 (4.822166) trpm7 (4.427145) lrp5 (3.677255)	emt (2.597724) e-cadherin (2.653815) epithelial-mesenchymal (2.699951) zeb1 (2.859652) slug (2.947824) zeb2 (2.999858) snai1 (3.006083) n-cadherin (3.042434) epithelial-to-mesenchymal (3.05387) snail (3.074674) snail1 (3.170080) twist1 (3.179278)	cdh1 (3.271992) vimentin (3.297111) twist (3.363778) mesenchymal-like (3.677661) repressors (3.957374) migratory (4.170011) vim (4.173914) epithelial-like (4.457998) abilities (5.292244) hdac (5.432331) ctcs (5.740111) redundantly (6.779406)
	Receptor-Linked Signaling Pathways (2489.15) 24 Concepts, 21 Genes	fat1 (790.154755) fgfr3 (310.476772) als2cr12 (74.656645) nid2 (43.459538) rap1gap (39.810942) rspo3 (39.738371) snai2 (32.552946)	sfrp5 (30.560267) etv5 (20.631642) krt8 (18.733123) sox9 (17.303148) lrp5 (17.039307) itga6 (10.684787) col11a1 (7.096588)	tshr (7.070768) wisp3 (6.298762) col10a1 (4.115842) trpv4 (3.892836) fgfr1 (3.640222) fxyd3 (3.554194) il6 (3.520580)	pik3ca (3.317900) tp53 (3.370878) cdkn2a (3.414186) hras (3.494080) mutational (3.548852) notch1 (3.979337) nras (4.054667) casp8 (4.116906) ctnnb1 (4.299525) targetable (4.453009) ep300 (4.590126) hpv-negative (4.620245)	urothelial (4.654906) hnscc (4.887960) snapshot (4.964122) kdm6a (5.116073) oscc (5.126658) stratify (5.214842) tp63 (5.407127) fusions (5.592004) raf1 (5.723220) escc (6.106634) hematuria (6.111924) voided (6.434859)
	ECM-Related 2 (2293.94) 10 Concepts, 26 Genes	wisp3 (1667.098523) ucma (207.944154) tnr (202.489391) col2a1 (102.657771) col11a1 (96.692916) hapln1 (95.402725) acan (85.626622) col27a1 (66.716517) sox9 (48.045937)	nid2 (45.284384) itga6 (32.259187) col10a1 (23.223605) snai2 (18.483098) col9a3 (13.869674) sgalnact1 (10.310483) grem1 (9.022684) azgp1 (8.421314) il6 (7.653133)	chst11 (5.600756) bmp5 (4.642967) krt8 (4.238248) sfrp5 (4.193931) sox5 (3.926891) col9a2 (3.910873) fgfr3 (3.832928) fat1 (3.480678)	matricellular (3.107626) ctgf (3.141042) ccn (3.232633) matrix-associated (4.024893) ccn2 (4.156716)	ecm (4.229517) sparc (4.386490) tnrc (4.397243) nov (4.397504) tenascin (4.834538)
	Chondrogenesis, Wnt-Signaling (2275.69) 4 Concepts, 23 Genes	crisp3 (1710.852554) wisp3 (445.574896) scrg1 (141.768417) crisp1d1 (99.633005) chrdl2 (52.271158) rspo3 (26.773032) caps2 (26.666156) tnr (18.441720)	azgp1 (16.831110) lrp5 (15.902629) frzb (15.570485) krtap5-1 (14.004551) scin (13.518901) corin (13.498041) il6 (9.956003) hpgds (7.421620)	tshr (6.978162) ucma (6.933201) epha1 (6.600991) krt8 (5.878047) slc38a3 (5.560372) col2a1 (4.943332) vit (3.782643)	cysteine-rich (2.873740) secretory (3.350162)	protein-3 (3.399517) seminal (3.500861)

Supplementary Table 3. Genes, concepts, and themes associated with the ECM super cluster from DEGs upregulated in the NP. CompBio scores are shown in parenthesis.

Tissue	Theme	Gene			Concept	
NP - UP	Fibrosis (1759.04) 20 Concepts, 25 Genes	acta2(543.482127) tgfb1(328.721627) tagln(158.121278) cd68(108.087375) samd3(59.966126) kctd10(34.902421) lox(28.679216) dcn(26.434827) prg4(18.419191)	scgn(18.195443) adamts1(16.661173) igfbp7(16.592299) lcn2(13.956308) id2(12.712265) ly6c1(12.242559) serpine2(9.477135) sod3(8.671242)	gas1(6.607111) sdc1(6.267595) bgn(5.538995) cck(4.677438) apoe(3.929646) ackr3(3.269373) itgbl1(3.147234) pdlim1(3.113920)	myofibroblasts(2.222609) myofibroblast(2.299778) actin(2.360990) fibrotic(2.411990) a-sma(2.446208) tgfb1(2.496450) a-smooth(2.536581) asma(2.737290) antifibrotic(2.774928) profibrotic(2.816064)	pro-fibrotic(2.902964) tgf-b1(2.930241) anti-fibrotic(2.936146) ctgf(3.032073) alpha-smooth(3.115573) factor-b1(3.128643) ipf(3.446947) desmin(3.846418) proliferating(4.039757) pcna(4.280178)
	TGF-b (1412.27) 22 Concepts, 27 Genes	tgfb1(1399.798764) acvr2a(533.754538) samd3(261.819470) acta2(120.642216) id2(101.298345) tagln(88.349069) prg4(76.315109) skor1(54.994660)	bgn(28.849510) lox(16.334643) spns2(15.740377) cd68(10.350145) igfbp7(9.899773) dcn(7.943128) sdc1(7.686828) ackr3(6.289405)	serpine2(5.473657) nupr1(4.743388) gas1(4.305821) defb14(4.269271) slurp1(4.227742) lcn2(3.454714)	smad2(2.315423) smad(2.320045) transforming(2.378728) smad3(2.402950) tgfb(2.463918) smad4(2.599408) smads(2.907649) smad7(3.009349) tgf-b(3.066623) factor-beta(3.115825) sb431542(3.163900)	factor-b(3.187115) canonical(3.227526) tgfbeta(3.263062) decapentaplegic(3.348883) alk5(3.381910) smad6(3.599656) alk1(3.654841) homolog(3.660054) crosstalk(3.882857) tgf-b-induced(4.517347) il11(5.583286)
	Smooth Muscle-Related (1324.78) 19 Concepts, 12 Genes	tagln(2096.651344) acta2(361.256258) tgfb1(31.361910) cd68(28.033877)	apoe(18.767829) prg4(16.211574) cck(12.940126) lox(11.770680)	id2(9.728464) hspb7(6.873854) sod3(5.926330) clu(4.090956)	smooth(2.456770) sm22(2.638581) calponin(2.802465) alpha-actin(2.827005) myocardin(2.888935) smcs(2.924173) smc(2.925993) srf(2.982518) vsmc(3.115737) vsmcs(3.169627)	muscle-specific(3.262970) carg(3.274315) dedifferentiated(3.436226) sm22a(3.715338) caldesmon(3.786593) dedifferentiation(4.049818) 10t1(4.183518) redifferentiation(4.982690) gizzard(5.814655)
	Transdifferentiation (1221.40) 4 Concepts, 10 Genes	acta2(1201.777668) tagln(1185.170385) bgn(173.286795) tgfb1(167.485548)	vcn(55.351273) igfbp7(15.618597) id2(10.688672) cd68(7.710427)	lox(7.512100) gcg(7.204661)	transgelin(2.978616) tagln(3.087059)	transdifferentiated(3.235273) transdifferentiation(3.248468)
	ECM-Related 1 (1190.28) 12 Concepts, 23 Genes	adamts1(440.271904) acta2(277.456040) tgfb1(166.858693) bgn(148.396875) lcn2(63.277083) igfbp7(55.321603) lox(49.950387) itgbl1(43.821205)	sdc1(34.431466) dcn(29.377189) prg4(24.495480) tagln(22.555833) clu(20.088853) apoe(16.178455) serpine2(14.976139) vcn(12.868949)	cd68(11.676116) sod3(9.970021) id2(6.748853) ackr3(6.232635) ogn(6.093047) cck(5.915860) gas1(5.713139)	mmp9(2.849815) timp1(3.017778) mmp3(3.107565) mmp2(3.113644) mmp10(3.115669) mmp1(3.118569)	mmp13(3.283269) timp4(3.396869) timp3(3.442019) serpina1(5.630654) auroc(5.814984)
	ECM-Related 2 (883.72) 13 Concepts, 19 Genes	acta2(1262.680517) bgn(779.041887) dcn(230.610606) tgfb1(226.878857) serpine2(137.289976) vcn(136.838323) lox(108.371968) tagln(74.939099)	adamts1(43.938890) prg4(21.874914) clu(16.670202) ogn(15.956992) lcn2(14.992418) sdc1(11.655266) nupr1(11.137976) id2(8.399842)	sdc1(11.655266) nupr1(11.137976) id2(8.399842) apoe(7.702383) ackr3(7.058911) cd68(4.771356)	col1a1(2.670793) col3a1(2.691863) col1a2(3.037582) col5a1(3.054936) col11a1(3.236537) col4a1(3.423685) thbs2(3.480202)	fn1(3.505812) col5a2(3.551780) col6a3(3.610670) serpine1(4.383907) pdgfa(5.025298) col6a1(5.106879)

Supplementary Table 3. Continued

Tissue	Theme	Gene			Concept	
NP - UP	Signaling (819.07) 6 Concepts, 40 Genes	cck(1265.035925) tppp3(56.289035) tgfb1(37.539936) ackr3(35.793361) itgbl1(28.001653) ddit4(26.288177) id2(21.366805) samd3(19.725052) acta2(18.605096) gas1(16.611856) serpine2(16.236403) phlda1(16.124154) nupr1(14.832093) tagln(14.207048)	lox(13.421290) ubxn10(12.290339) acvr2a(12.255481) adamts1(11.898321) ly6c1(10.956534) spns2(9.072666) clu(8.424992) sdc1(8.172304) gcg(7.487287) lcn2(7.444048) apoe(7.433287) cd68(7.166558) htra4(7.044545) sh3gl2(6.316121)	senp8(6.195442) sod3(5.857229) vcan(5.600875) igfbp7(5.385919) lrp8(4.620362) prg4(4.403925) bgn(4.352893) slc6a6(4.290901) clip1(3.984210) dcn(3.784045) pdlim1(3.762330) slurp1(3.306712)	cck8(3.167105) knockdown(3.177897) regulating(3.420846)	promoting(3.618110) rt-qpcr(3.731739) mtt(4.056493)
	ECM-Related 3 (802.91) 6 Concepts, 18 Genes	tgfb1(1356.765903) acta2(652.433641) tagln(200.977770) acvr2a(141.942900) dcn(140.696523) gas1(87.478387)	adamts1(63.513933) bgn(45.083365) nupr1(41.450740) lox(23.598303) igfbp7(20.170268) clu(15.991197)	id2(11.406870) cd68(9.790247) ogn(7.511690) nptx2(6.335244) vcan(5.724098) lcn2(4.654188)	tgfb2(3.232275) tgfb3(3.534521) tgfb3(3.595887)	sparc(3.924471) osteonectin(3.971362)
	ECM Formation (760.29) 9 Concepts, 12 Genes	acta2(2115.127347) tagln(881.061611) tgfb1(530.331038) acvr2a(372.990823)	bgn(60.037487) dcn(48.670771) lox(40.199123) cd68(25.540694)	ogn(9.197675) vcan(7.595531) apoe(6.997491) sod3(3.704063)	myh11(2.759659) acta2(2.869817) fbn1(3.315965) dissections(3.316387) tgfb1(3.369713)	tgfb2(3.450191) bicuspid(4.220093) a-actin(4.772665) multisystemic(5.131694)

Supplementary Table 4. Genes, concepts, and themes associated with the ECM super cluster from DEGs downregulated in the NP. CompBio scores are shown in parenthesis

Tissue	Theme	Gene			Concept	
NP - DOWN	Articular Cartilage (5237.08) 68 Concepts, 36 Genes	acan(979.269576)	oaf(37.386938)	azgp1(5.869103)	col2a1(3.028827)	mmp3(4.125722)
		sox9(721.126969)	lrp5(28.221855)	arrdc4(5.692985)	aggrecan(3.036804)	ivd(4.150318)
		hapln1(258.270544)	krt8(24.788770)	lrig1(5.259064)	sox9(3.070992)	sulfated(4.259454)
		col11a1(250.999527)	fbxo32(20.204360)	fasn(4.518206)	cartilage(3.073792)	cartilage-specific(4.331201)
		chst3(72.894356)	p4ha3(20.168536)	sema3d(4.202030)	chondrocytes(3.112391)	chondroitin(4.333844)
		frzb(71.168042)	sox12(15.678582)	s100b(3.667279)	acan(3.118336)	sulfate(4.339159)
		fzd2(69.634257)	creb3l2(10.941130)	sik3(3.643213)	articular(3.127973)	gags(4.355755)
		fgfr3(69.251393)	gas7(10.193341)	cd36(3.558735)	chondrocyte(3.162398)	degenerated(4.444788)
		slc26a2(66.797074)	kcnip3(8.743618)	nr2f2(3.498712)	proteoglycan(3.232657)	versican(4.450733)
		wnt16(50.144751)	igfbp1(7.866324)	krt20(3.293930)	chondrogenic(3.236732)	ihh(4.467454)
		gpc4(49.409809)	etv5(6.145413)	epha2(3.182975)	mmp13(3.395868)	fibrosus(4.492794)
		spp1(38.644301)	h2-q4(5.935605)	slc38a2(3.170989)	ecm(3.398651)	mmp-3(4.549018)
					osteoarthritis(3.404458)	mmp9(4.662965)
					oa(3.553580)	heparan(4.687490)
					chondrogenesis(3.558764)	pericellular(4.733570)
					osteoarthritic(3.645061)	gdf5(4.758046)
					col10a1(3.654130)	notochordal(4.799123)
					adamts5(3.688935)	frzb(4.836488)
					cartilaginous(3.703124)	anabolism(4.882784)
					proteoglycans(3.714567)	annulus(4.886569)
					intervertebral(3.765803)	matrix-degrading(4.891543)
					mmp-13(3.842129)	mmp2(4.947659)
					safranin(3.876110)	vcan(4.949059)
					pulposus(3.977786)	pthrp(5.003931)
					endochondral(3.997455)	timp1(5.106374)
					meniscus(4.021928)	sulfation(5.120412)
					pellet(4.032542)	npcs(5.310798)
					anabolic(4.050971)	nscs(5.328656)
			mmp1(4.070421)	timp3(5.382248)		
			alcian(4.071255)	frizzled-related(5.528478)		
			micromass(4.083292)	cytoarchitecture(5.734467)		
			catabolic(4.104601)	wingless-type(5.745214)		
			hyaluronan(4.107871)	mmp7(5.769034)		
			subchondral(4.116266)	neuropil(6.028149)		

Supplementary Table 4. Continued

Tissue	Theme	Gene			Concept	
NP - DOWN	Chondrogenic Regulation 1 (2934.92) 34 Concepts, 30 Genes	spp1(1142.847146)	nr2f2(10.550128)	caskin1(4.757372)	osteocalcin(2.826012)	col(3.960904)
		sox9(302.096019)	hapln1(9.933787)	cd80(4.163214)	osteogenic(2.867198)	bmp-2(3.962073)
		acan(178.523570)	etv5(8.914981)	igfbp1(4.092491)	runx2(2.910324)	mc3t3-e1(4.172151)
		lrp5(59.399570)	plcb4(8.202968)	gas7(4.092242)	opn(3.004970)	scaffold(4.271630)
		wnt16(45.482908)	oaf(7.747307)	slc26a2(4.071627)	ocn(3.013820)	cbfa1(4.286769)
		lmo4(45.394951)	slc44a2(7.036027)	krt8(3.583942)	runt-related(3.050723)	dlx5(4.360384)
		frzb(33.848578)	arrdc4(6.885272)	slc25a14(3.578921)	osterix(3.127429)	col1(4.368243)
		fgfr3(29.682851)	il7(6.046551)	myh11(3.221717)	osteopontin(3.152872)	bmp4(4.523177)
		ubtd2(17.484032)	rgma(5.422780)	col11a1(3.187964)	alizarin(3.255732)	protein-2(4.531577)
		wdr83(11.310384)	mid1(4.916818)	fzd2(3.016568)	bsp(3.277159)	bmsc(4.548817)
					sialoprotein(3.369443)	msx2(4.840270)
					osteoblastic(3.394882)	calvaria(4.932179)
					bmp2(3.530151)	multilineage(4.935040)
					osx(3.604891)	bmp7(5.239681)
					mineralized(3.643335)	cell-derived(5.454350)
					mscs(3.780796)	bm-mscs(5.639325)
					bmscs(3.853095)	msx1(5.744151)
	Mesenchyme Morphogenesis (2764.70) 32 Concepts, 43 Genes	sox9(965.022677)	sik3(21.660849)	plcb4(7.337551)	embryos(3.834227)	morpholino(5.110370)
		acan(464.414839)	gpc4(21.636583)	plet1(7.047377)	morphogenesis(4.206942)	ectoderm(5.186358)
		sox12(235.031933)	wnt16(25.954594)	slc12a7(6.585805)	mesenchyme(4.214995)	sry-related(5.218199)
		cdc42se1(148.808710)	slc26a2(19.510742)	atp1a1(8.002270)	embryogenesis(4.231860)	endoderm(5.250290)
		nr2f2(107.091619)	epha3(17.847310)	frzb(6.360604)	sox(4.270485)	gastrulation(5.302402)
		fgfr3(83.153218)	s100b(17.807652)	mid1(6.345077)	specification(4.359953)	cooperatively(5.404704)
		chst3(74.966214)	sh3tc2(17.529598)	krt8(5.399472)	bud(4.373879)	trio(5.453748)
		rgma(60.273225)	creb3l2(13.432193)	spp1(5.279942)	patterning(4.377381)	chondrocytic(5.477692)
		slco3a1(56.264387)	hoxd10(12.392281)	dhrs3(4.355529)	sox5(4.455757)	atdc5(5.556001)
		etv5(51.740829)	mgat4a(12.022728)	plxna2(4.332246)	sox6(4.465105)	fgf10(5.595562)
		sema3d(36.705984)	lrp5(12.002836)	gas7(4.324903)	zebrafish(4.505183)	branching(5.605023)
		celsr1(34.288792)	fzd2(11.250505)	nck2(3.669056)	craniofacial(4.508340)	alpha1(5.791300)
		rdh10(31.422267)	orc6(8.820331)	krt20(3.240671)	hmg(4.924500)	stature(5.955483)
		lmo4(28.863496)	dmrta1(8.237332)	epha2(3.102100)	arches(4.967528)	shox(6.373351)
		col11a1(24.958204)			sox10(5.009034)	spondyloepiphyseal(6.644939)
					chondrocyte-specific(5.069558)	15q26(6.902245)
	Proteoglycan-Related (2615.64) 17 Concepts, 28 Genes	acan(832.648632)	wnt16(64.352947)	abr(8.518360)	sparc(3.506177)	dcn(4.831851)
		col11a1(827.848613)	tspan7(40.773364)	fhl1(8.395059)	col3a1(3.529294)	sp7(4.889848)
		spp1(496.548817)	fkbp14(39.417158)	masp1(7.087041)	col1a1(3.545889)	tnc(4.912705)
		sparcl1(325.088076)	fzd2(29.225721)	igfbp1(6.293580)	spp1(3.800689)	thbs1(5.122691)
		sox9(214.843419)	nid2(24.037694)	creb3l2(5.622775)	fn1(3.819515)	bone-related(5.283941)
		hapln1(113.984761)	cd36(19.938055)	azgp1(4.953714)	alpl(4.145434)	bgn(5.458915)
		frzb(111.601840)	reln(16.763203)	tshr(4.664321)	col1a2(4.236811)	eng(5.810089)
		myh11(81.240501)	fasn(12.981217)	epha2(3.377696)	bglap(4.535495)	matricellular(5.997198)
		lrp5(79.643585)	fgfr3(11.088998)		postn(4.619479)	
		pxn(67.122952)	krt8(9.446436)			

Supplementary Table 4. Continued

Tissue	Theme	Gene			Concept	
NP - DOWN	Cell Proliferation (2041.96) 20 Concepts, 42 Genes	fgfr3(1525.548436)	snx10(19.834352)	gpc4(6.084653)	414(5.238578)	dwarfism(4.738539)
		gcdh(152.472373)	fzd2(18.846392)	nck2(6.078230)	fibroblast(3.444906)	syndromic(4.876667)
		nid2(132.476042)	inpp4a(16.706031)	s100b(5.487875)	fgfr3(3.475395)	twist1(5.122779)
		orc6(116.339476)	oaf(15.287090)	krt8(5.261698)	fgf(3.565767)	fgf-2(5.163702)
		etv5(96.196498)	epha2(15.255464)	myh11(4.902799)	fgfr2(3.641585)	ccnd1(5.267434)
		gjc3(69.314718)	epha3(14.041058)	atp1a1(4.828203)	fgfr(3.687335)	nonsyndromic(5.312449)
		sox9(61.932313)	spp1(13.772386)	fasn(4.387618)	fgfr1(3.699220)	macrocephaly(5.805964)
		acan(35.660583)	lrp5(10.537150)	rxfp2(4.272634)	craniosynostosis(4.091315)	maf(5.902357)
		gas7(29.946328)	frzb(9.906477)	arf2(3.606769)	fgf2(4.372765)	mgus(6.320143)
		col11a1(28.740631)	sik3(9.645166)	igfbp1(3.496204)	fgfs(4.462144)	post-natal(6.615423)
		slc9a7(28.707243)	wnt16(9.367909)	tshr(3.271951)		
		tspan7(24.055831)	krt20(9.138376)	abr(3.229060)		
		sox12(23.689190)	hoxd10(9.054512)	nr2f2(3.219847)		
		slc26a2(20.018878)	cdkl5(7.284404)	dsc2(3.073734)		
	Chondrogenic Regulation 2 (1808.37) 6 Concepts, 18 Genes	sox9(359.631350)	acan(49.756819)	slc26a2(24.017946)	nkx3(3.879572)	skeletogenesis(5.275678)
		krt20(226.962318)	fgfr3(47.460462)	lrp5(23.521571)	c3h10t1(5.014052)	cribriform(5.654027)
		sox12(183.102048)	nr2f2(28.772398)	spp1(22.828696)	shh(5.187445)	amacr(5.690433)
		krt8(112.424610)	hoxd10(28.262805)	etv6(9.178086)		
		sik3(94.898494)	etv5(26.101850)	epha3(8.328017)		
		fasn(68.953575)	mid1(25.697878)	wnt16(5.338947)		