SUPPLEMENTAL FIGURE AND TABLE LEGENDS

SUPPLEMENTAL FIGURE 1: (A). Synectin expression was detected by qPCR from a hepatocyte cell line (HepG2), a normal human cholangiocyte (NHC) cell line, and human HSC cell line (LX2), N=3. (B). Synectin protein expression was assessed by Western blot from the hepatocyte cell line Huh7, human HSC (hHSC), human umbilical vein endothelial cells (HUVEC), and human hepatic sinusoidal endothelial cells. We observed similar levels of synectin in all cell types, N=3. (C). Primary hepatocytes, HSC and liver endothelial cells were isolated from mice and protein expression was analyzed by Western blot. Synectin expression was ubiquitous among the cell types, but PDGFR expression was HSC selective. The lysate was prepared from pools of multiple isolations of each cell type. (D). HSC were isolated from Synectin$^{fl/fl}$ mice and transduced *in vitro* with AdCre-eGFP. AdLacZ was used as a control. Cell lysates were harvested and analyzed by Western blot (densitometry of PDGFRα, PDGFRβ and synectin is shown in adjacent graphs), N=3. (E). Mice were treated with olive oil or CCL_4 twice a week for 4 weeks. HSCs were isolated from these mice, lysed, and analyzed by Western blot. The isolated HSCs showed increased expression of PDGFRs and synectin in CCL_4 compared to control, N=3. Densitometric analysis for PDGFRα, PDGFRβ and synectin are shown in the adjacent graphs. Error bars represent SEM. Student’s unpaired t test was used to analyze the differences between two groups (**$p < 0.001$, ***$p < 0.0001$).

SUPPLEMENTAL FIGURE 2: Quantitation of the immunohistochemistry and Western blots from Figure 1. Sirius Red staining and immunohistochemistry were quantified using ImageJ and are depicted in the graphs. The graphs A – E correspond to the panels in Figure 1C as follows: (A) Sirius red, (B) collagen I, (C) PDGFR-α, (D) PDGFR-β, and (E) α-SMA, N=3-5. (F). Densitometry of Western blots from whole mouse liver lysates for PDGFRα, PDGFRβ and synectin levels (Figure 1D), N=3-4. Error bars are SEM. One-way ANOVA with Bonferroni's multiple comparison test was used to analyze groups for statistical significance (*$p<0.05$, **$p < 0.001$, ***$p < 0.0001$).

SUPPLEMENTAL FIGURE 3: (A). Mice with HSC selective deletion of synectin (Col^{cre}/Synectin$^{fl/fl}$) and littermate controls (Synectin$^{fl/fl}$) underwent sham surgery or bile duct ligation (BDL). Mice were sacrificed 3 weeks after surgery and livers were harvested for analysis. mRNA was harvested and analyzed by qPCR, which showed a decrease in collagen-1 mRNA in Col^{cre}/Synectin$^{fl/fl}$ mice after BDL compared to littermate controls, N=3-6 per group. (B). Hepatic collagen content was reduced in Col^{cre}/Synectin$^{fl/fl}$ mice after BDL as demonstrated by hydroxyproline analysis, N=3-6 per group. (C). Lysates from whole mouse liver were harvested and analyzed by Western Blot to assess protein levels of PDGFR-α, PDGFR-β, and synectin in Col^{cre}/Synectin$^{fl/fl}$ mice after BDL, N=3-4. (D). 5μm liver sections were stained with antibodies against collagen-1 or PDGFR-α (green), and co-stained with DAPI to visualize the nucleus. Staining for PDGFR-α and collagen-1 were reduced in Col^{cre}/Synectin$^{fl/fl}$ mice after BDL when compared to control littermates, N=3-5. Data are expressed as mean ± SEM. One-way ANOVA with Bonferroni's multiple comparison test was used to analyze groups for statistical significance (*$p<0.05$, **$p < 0.001$, ***$p<0.0001$).

SUPPLEMENTAL FIGURE 4: (A). Ingenuity pathway analysis (IPA) of mRNAseq data from synectin knockdown hHSCs compared to wild type hHSCs reveals an established gene network of PDGFR-β signaling. The green circles are genes that were downregulated in this network in synectin knockdown hHSCs. (B). Levels of PDGF ligands (A, B, C, and D isoforms) were analyzed from the RNAseq data set. There was no significant difference in mRNA levels of PDGF ligands between control cells and synectin knockdown cells. One-way ANOVA with Bonferroni's multiple comparison test was used to analyze groups for statistical significance (***$p < 0.0001$).

SUPPLEMENTAL FIGURE 5: (A). Densitometry analysis of western blotting of H3K27Ac in control and synectin knockdown hHSC (Western blots from Figure 3B), N=3. H3K27Ac reduction with synectin knockdown was statistically significant in both whole cell lysate and the nuclear fraction. (B).

Densitometry analysis of the Western blot showing H3K27Ac and p300 protein levels in control and p300 knockdown hHSC (Western blots from Figure 3C), N=3. p300 was efficiently knocked down represented by graph along with a reduction in H3K27Ac levels. Error bars are SEM. Student's unpaired t test was used to analyze the differences between two groups (**$p < 0.001$, ***$p < 0.0001$).

SUPPLEMENTAL FIGURE 6: A receptor tyrosine kinase array was performed to assess specified target protein levels in an unbiased manner. Lysates were obtained from hHSC with-shRNA-mediated synectin knockdown with and without PDGF stimulation. hHSC were serum starved overnight and treated with PDGF-bb for 15 minutes before cells were lysed for analysis.

SUPPLEMENTAL FIGURE 7: (A). hHSCs were transfected with shRNA against synectin or a control, and treated with PDGF-bb in conjunction with 3MA (1 μM) or bafilomycin (10 μM). Western blot analysis of the cell lysates showed that PDGFR-α levels were increased by inhibition of autophagy by 3-MA or bafilomycin in both control and synectin knockdown hHSC, N=3. (B). Western blots showing PDGFR-β expression from Figures 4C and 4D were quantified by ImageJ. Student's unpaired t test was used to analyze the differences between two groups (*$p<0.05$, **$p < 0.001$).

SUPPLEMENTAL FIGURE 8: (A). LOGO depicting sequence homology of PDGFR-α from six species (Xenopus laevis, Gallus gallus, Homo sapiens, Mus musculus, Rattus norvgicus, Fugu rubripes, and Danio rerio) for lysine 606 and lysine 971 is shown. (B). Mass spectrometry results of PDGFR-α showing three peptides with ubiquitination modification following PDGF stimulation. This confirmed PDGF-stimulated ubiquitination at lysine 971 (peptide outline with red box and lysine 971 highlighted in green).

SUPPLEMENTAL FIGURE 9: Ingenuity Pathway Analysis (IPA) of pathways differentially regulated in synectin knockdown HSCs compared to wild type HSC following PDGF-bb treatment. The IPA revealed the hepatic fibrosis/hepatic stellate cell activation pathway is the most significantly downregulated pathway in synectin knockdown hHSCs.

SUPPLEMENTAL FIGURE 10: (A-C). Synectin was knocked down in hHSCs using shRNA, and mRNA and whole cell lysate were harvested. (A). mRNA expression of α-SMA and collagen I were analyzed by qPCR, and showed reduced expression of both genes after synectin knockdown compared to control hHSC, N=3. (B and C) Analysis of the whole cell lysate by Western blot showed reduced Fibronectin (B) and Collagen (C) expression in hHSC after synectin knockdown, N=3. (D). hHSC with synectin knockdown were plated in various cell concentrations and assessed for proliferation by BrdU assay. Two separate wells were analyzed at each of four different cell concentrations, and two independent experiments were performed. (E). A peptide that blocks the PDZ domain of synectin was incubated with hHSC in a microfluidic chamber system and migration was assessed in response to PDGF stimulation. In the presence of blocking peptide the rate of migration was reduced in response to PDGF, N=3 (E). Error bars are SEM. Student's unpaired t test was used to analyze the differences between two groups (*$P < 0.05$, **$p < 0.001$). One-way ANOVA with Bonferroni's multiple comparison test was used to analyze groups for statistical significance (*$p<0.05$, **$p < 0.001$, ***$p < 0.0001$).

SUPPLEMENTAL FIGURE 11: (A). Synectin-knockdown hHSCs were serum starved overnight and stimulated with PDGF for 15 minutes. Lysates were harvested, and PDGFR and AKT phosphorylation were assessed by Western blot. AKT showed similar levels of phosphorylation after PDGF treatment for 15 minutes in synectin knockdown cells compared to controls, N=3 (A). hHSCs with shRNA mediated synectin knockdown were treated with PDGF for 0, 15, or 30 minutes, after which they were fixed and co-stained for EEA (a marker of early endosomes) and phosphor-PDGFRα/β. Imaging of phosphorylated

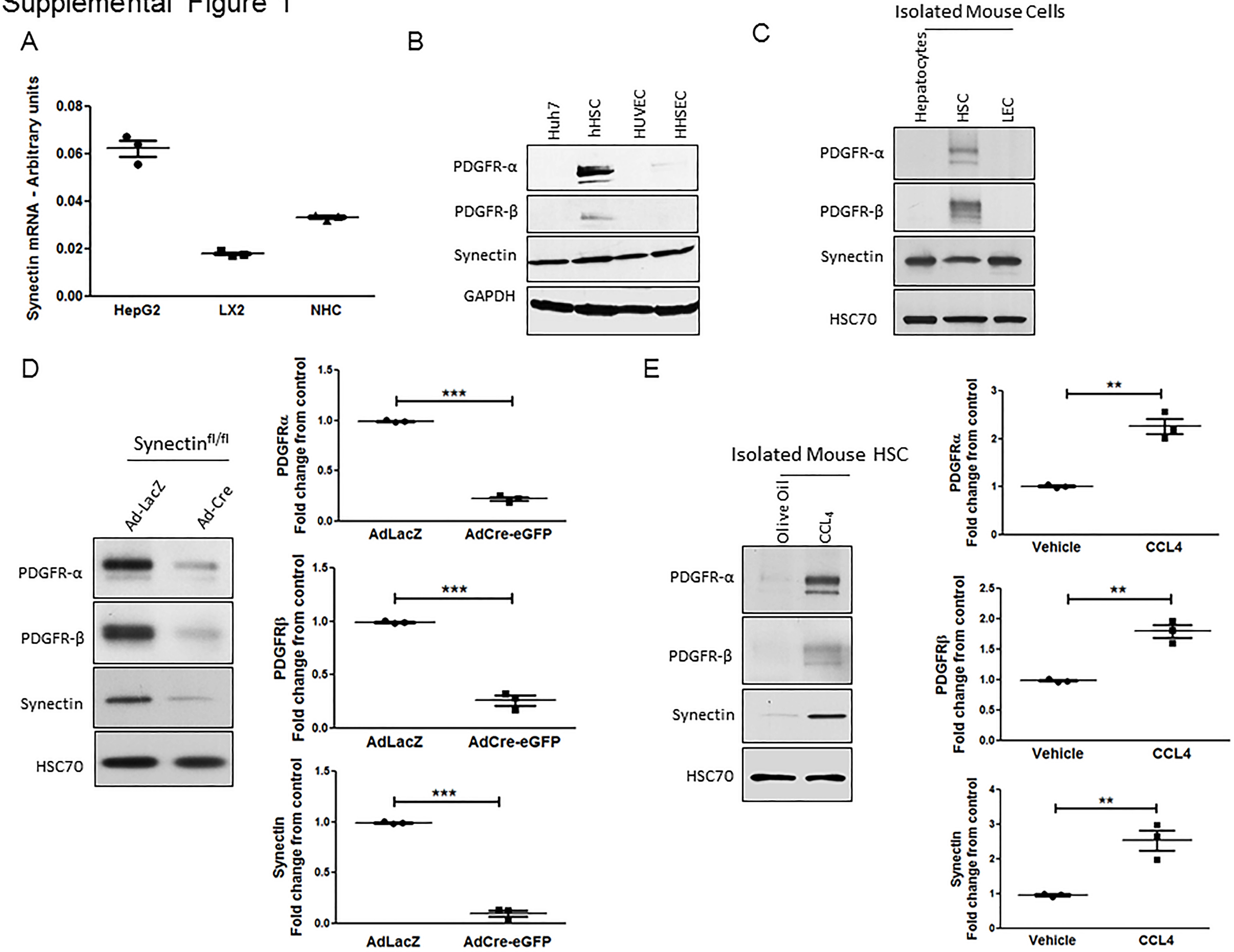
PDGFR with EEA showed PDGFR phosphorylation in control and synectin knockdown hHSC with localization to EEA positive vesicles, N=3. (C). Lysates were harvested from synectin-knockdown hHSCs or control cells following PDGF treatment for 3 minutes. Western blot was used to assess active Rac1 levels. Densitometric analysis was performed from Western blots of active Rac1 and values are represented as fold change, N=3. Error bars are SEM, * p-value < 0.05, statistical test used was One-way ANOVA. For two group comparisons, 2-tailed Student's t test was used (* p-value < 0.05).

SUPPLEMENTAL TABLE 1: All genes with logFC >1.5 or <-1.5 from the RNAseq analysis of wild type vs. synectin knockdown hHSC are shown in this file.

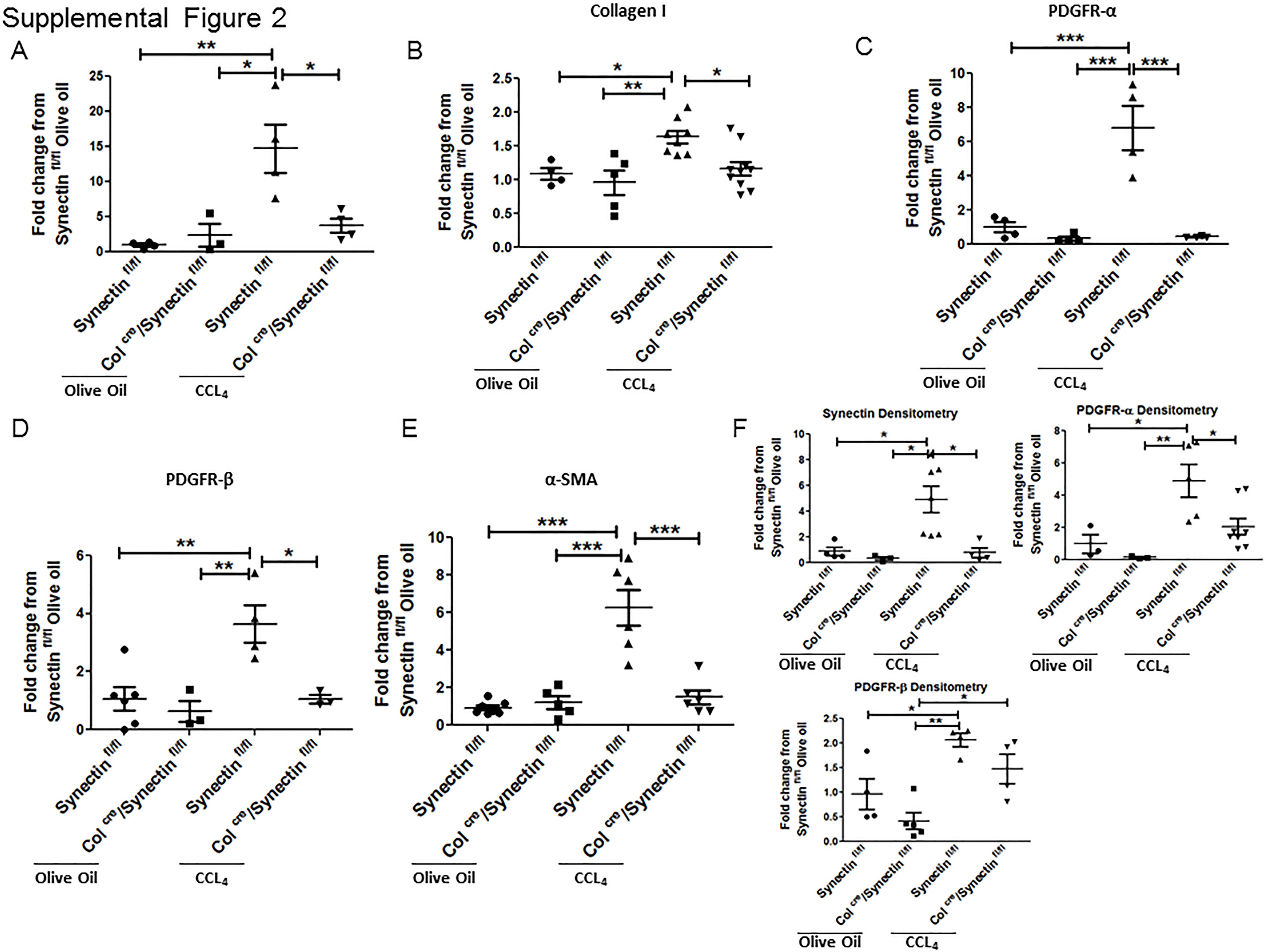
SUPPLEMENTAL TABLE 2: Summary of Ingenuity pathway analysis (IPA) for affected canonical pathways and enriched genes in synectin knockdown hepatic stellate cells (hHSC) compared to wild type hHSC without PDGF-bb treatment.

SUPPLEMENTAL TABLE 3: Summary of Ingenuity pathway analysis (IPA) for affected canonical pathways and enriched genes in synectin knockdown hepatic stellate cells (hHSCs) compared to wild type hHSCs with PDGF-bb treatment.

Supplemental Figure 1



Supplemental Figure 2



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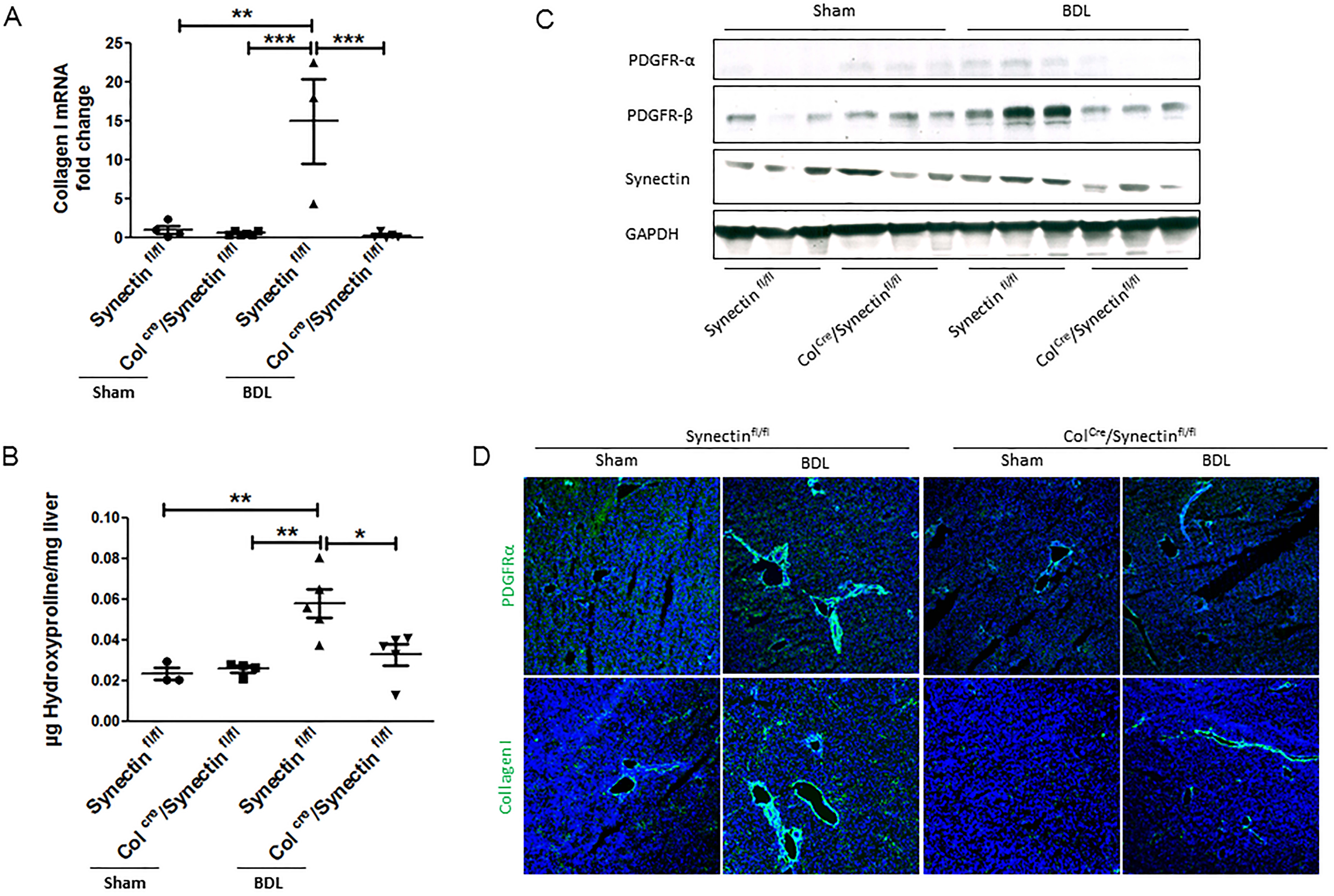
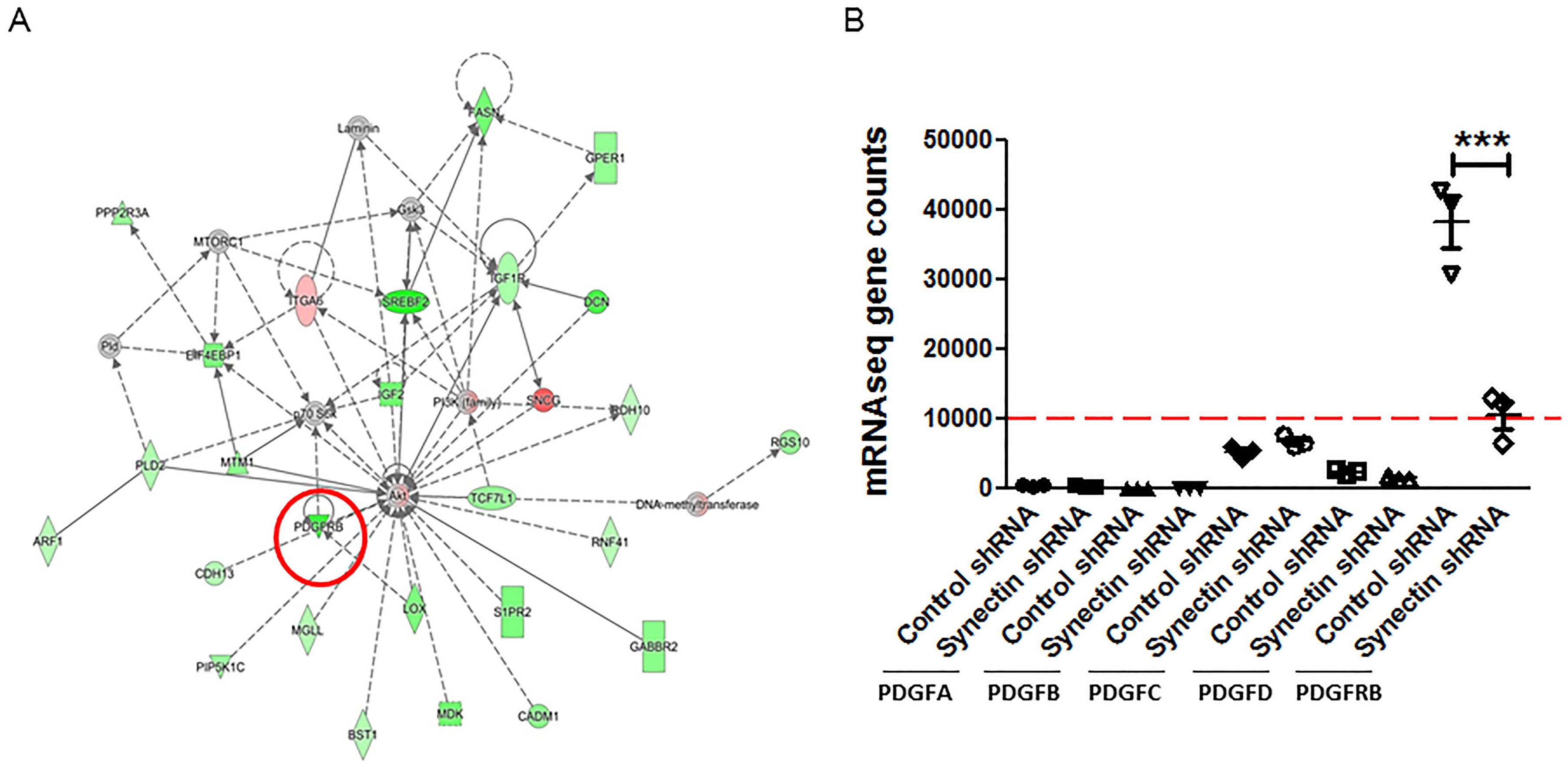


Supplemental Figure 4



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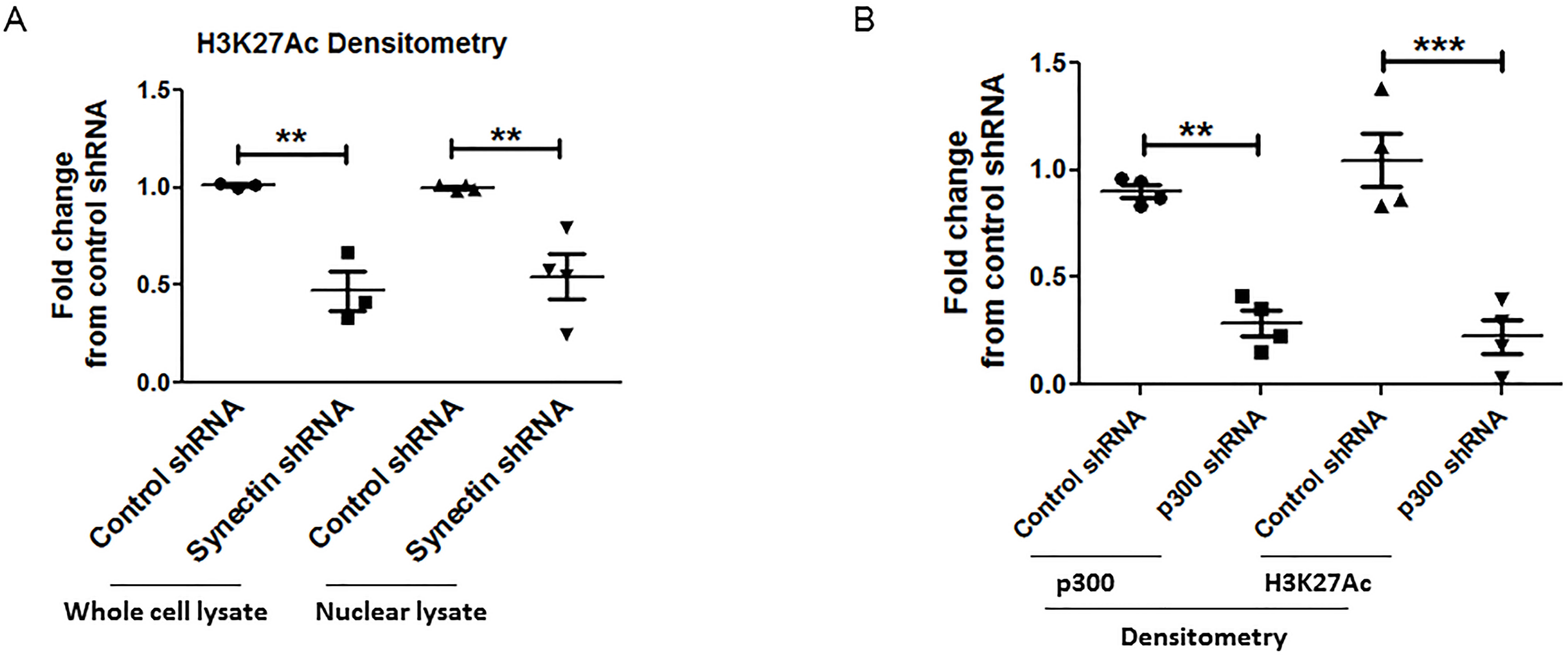

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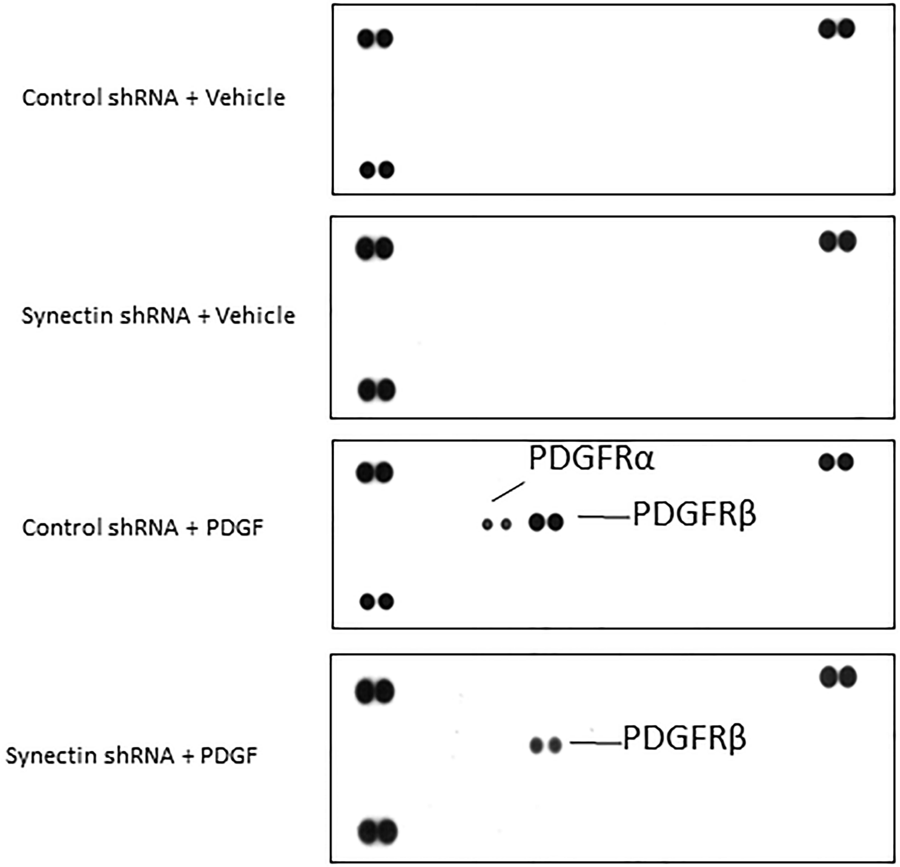

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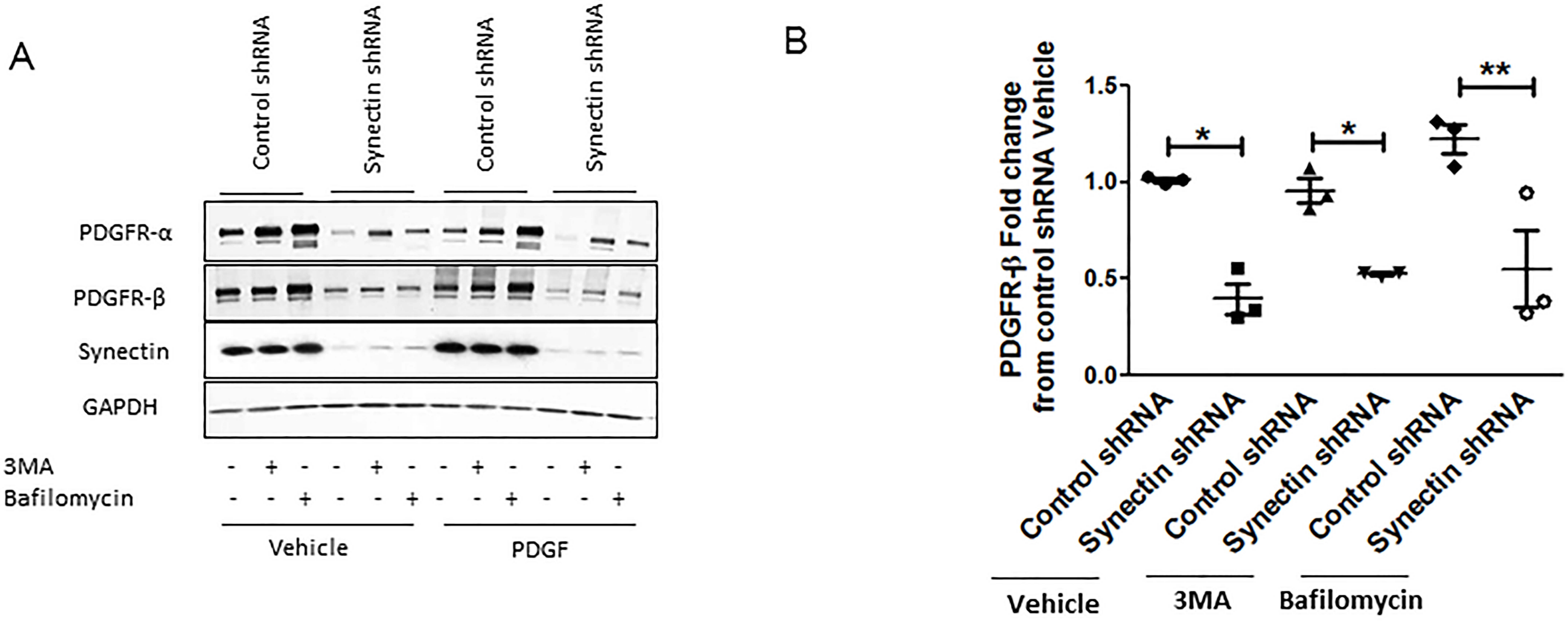
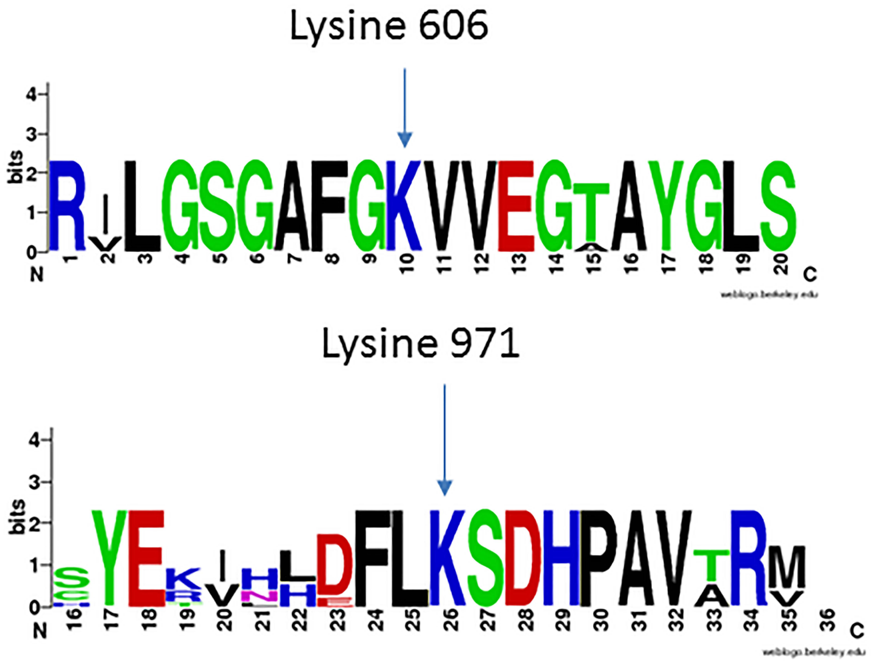


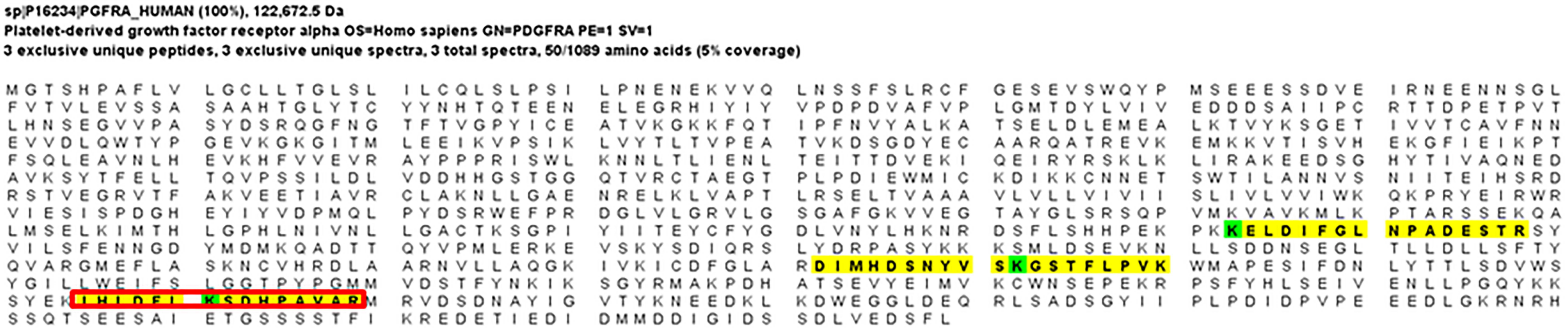
Supplemental Figure 8

A


Lysine 606

Lysine 971

B



sp|P16234|PGFRA_HUMAN (100%), 122,672.5 Da
Platelet-derived growth factor receptor alpha OS=Homo sapiens GN=PDGFRA PE=1 SV=1
3 exclusive unique peptides, 3 exclusive unique spectra, 3 total spectra, 50/1089 amino acids (5% coverage)

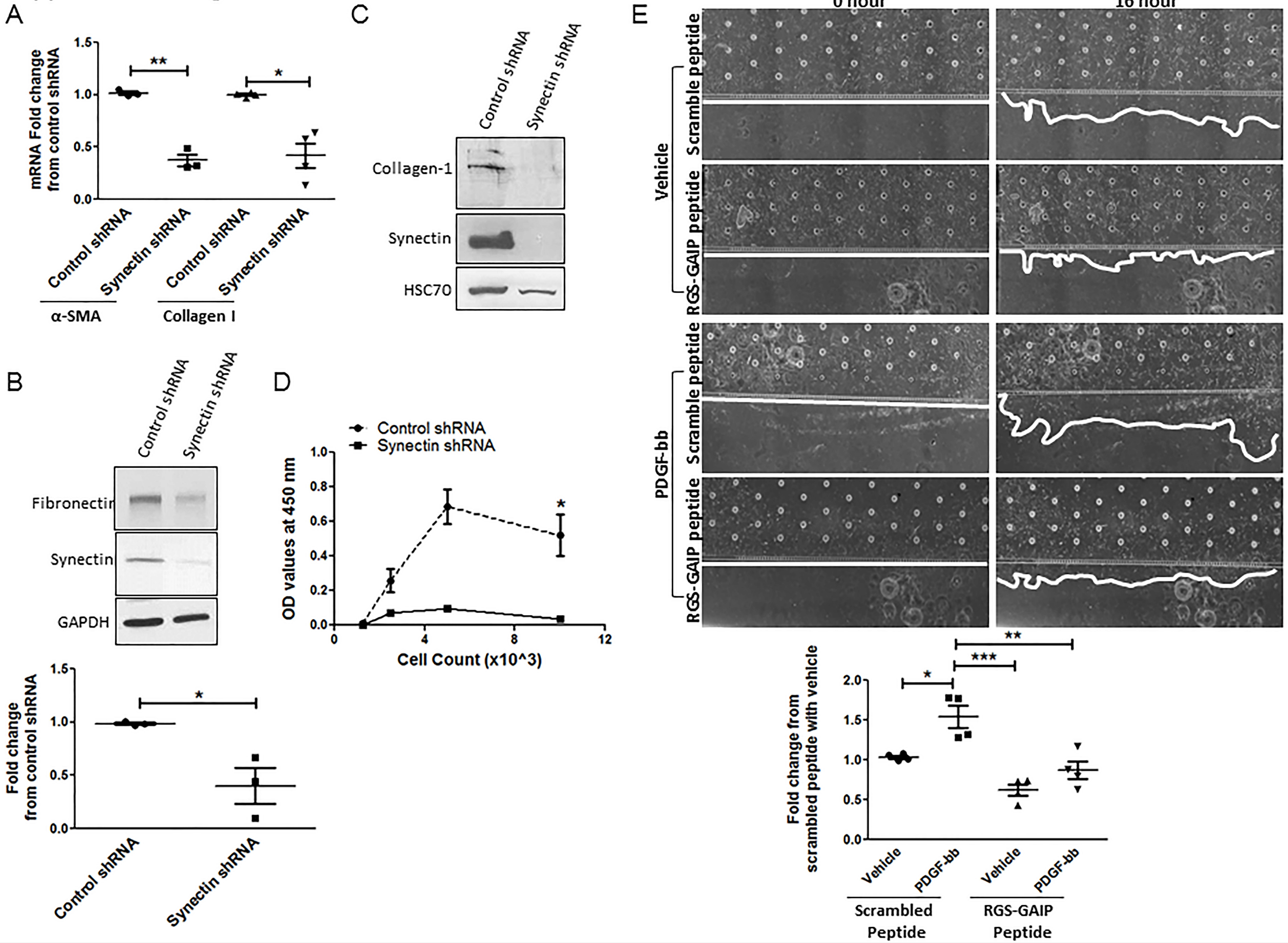
MGTSHPAFLV LGCLLTGLSL ILCQLSLPSI LPNENEKVVQ LNSSFSLRCF GESEVSWQYP MSEEESSDVE IRNEENNSGL
FVTVLEVSSA SAAHTGLYTC YYNHTQTEEN ELEGRHIYIY VPDPDVAFVP LGMTDYLVIV EDDDSAIIPC RTTDPETPVT
LHNSEGVVPA SYDSRQGFNG TFTVGPYICE ATVKGKKFQT IPFNVYALKA TSELDLEMEA LKTVYKSGET IVVTCAVFNN
EVVDLQWTYP GEVKGKGITM LEEIKVPSIK LVYTLTVPEA TVKDSGDYEC AARQATREVK EMKKVTISVH EKGFIEIKPT
FSQLEAVNLH EVKHFVVEVR AYPPPRISWL KNNLTLIENL TEITTDVEKI QEIRYRSKLK LIRAKEEDSG HYTIVAQNED
AVKSYTFELL TQVPSSILDL VDDHHGSTGG QTVRCTAEGT PLPDIEWMIC KDIKKCNNET SWTILANNVS NIITEIHSRD
RSTVEGRVTF AKVEETIAVR CLAKNLLGAE NRELKLVAPT LRSELTVAAA VLVLLVIVII SLIVLVVIWK QKPRYEIRWR
VIESISPDGH EYIYVDPMQL PYDSRWEFPR DGLVLGRVLG SGAFGKVVEG TAYGLSRSQP VMKVAVKMLK PTARSSEKQA
LMSELKIMTH LGPHLNIVNL LGACTKSGPI YIITEYCFYG DLVNYLHKNR DSFLSHHPEK PK**KELDIFGL** **NPADESTR**SY
VILSFENNGD YMDMKQADTT QYVPMLERKE VSKYSDIQRS LYDRPASYKK KSMLDSEVKN LLSDDNSEGL TLLDLLSFTY
QVARGMEFLA SKNCVHRDLA ARNVLLAQGK IVKICDFGLA R**DIMHDSNYV** **SKGSTFLPVK** WMAPESIFDN LYTTLSDVWS
YGILLWEIFS LGGTPYPGMM VDSTFYNKIK SGYRMAKPDH ATSEVYEIMV KCWNSEPEKR PSFYHLSEIV ENLLPGQYKK
SYEK**IHLDFL** **KSDHPAVAR**M RVDSDNAYIG VTYKNEEDKL KDWEGGLDEQ RLSADSGYII PLPDIDPVPE EEDLGKRNRH
SSQTSEESAI ETGSSSSTFI KREDETIEDI DMMDDIGIDS SDLVEDSFL

Lysine 971

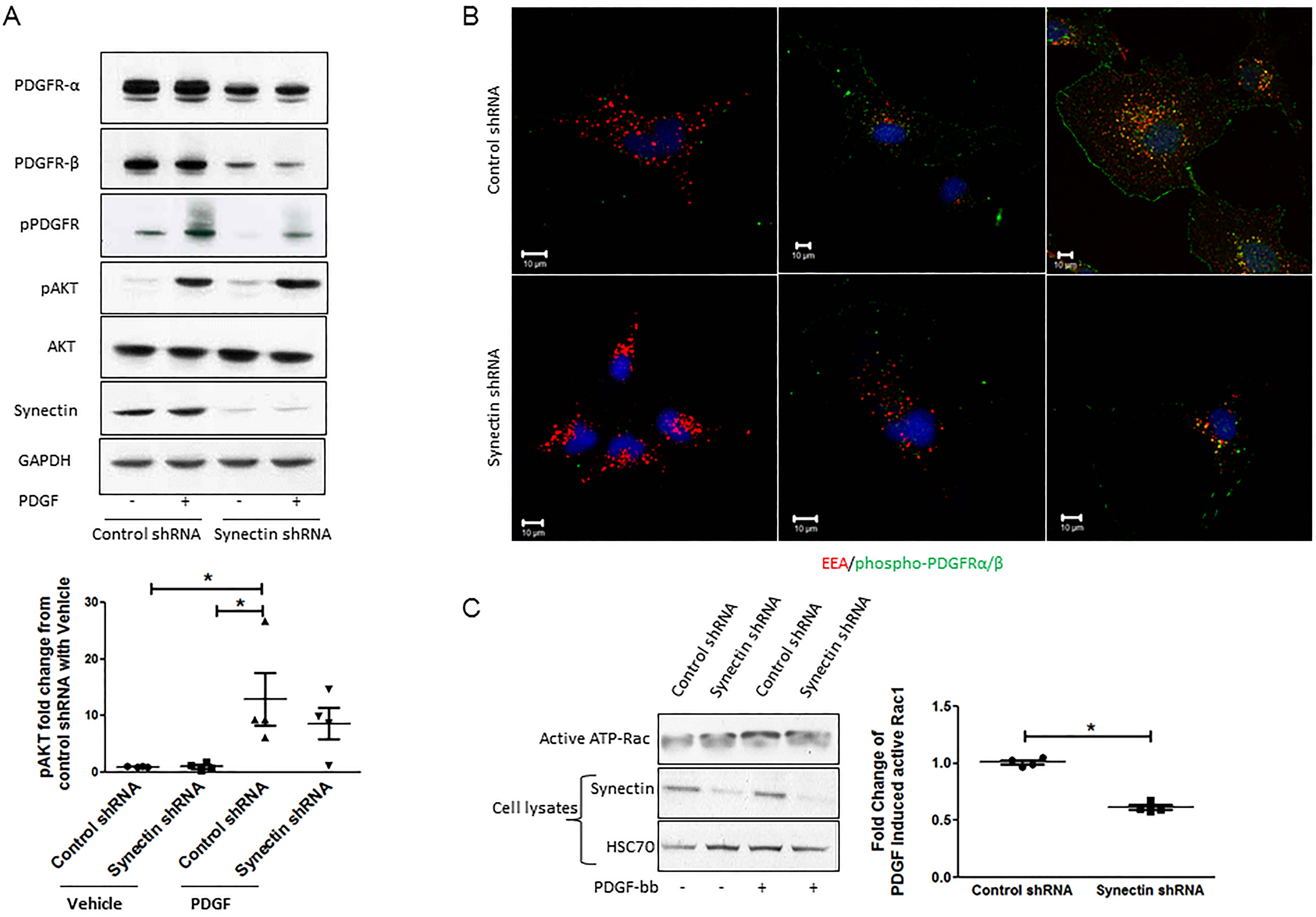
Supplemental Figure 9

Analysis: ctl PDGF vs shSyn PDGF LogFC1.4-2016-12-13 11:15 AM

Supplemental Figure 10



Supplemental Figure 11



Supplementary Table 1. Top regulated genes in RNAseq analysis (control vs synectin KD, absolute value of log FC >1.5; False Discovery Rate [FDR] <0.05 and P<0.05)

Gene		logFC	PValue	FDR
ENSG00000196517	SLC6A9	-3.568440737	8.10E-44	1.29E-39
ENSG00000112977	DAP	-3.374558958	6.91E-41	5.52E-37
ENSG00000169756	LIMS1	-3.073975444	1.64E-35	8.72E-32
ENSG00000106366	SERPINE1	-3.110843125	4.60E-33	1.84E-29
ENSG00000010610	CD4	-2.880621201	3.00E-32	9.60E-29
ENSG00000103888	KIAA1199	-3.969095749	1.79E-28	4.78E-25
ENSG00000130164	LDLR	-3.035104889	5.54E-28	1.26E-24
ENSG00000167772	ANGPTL4	3.426100027	6.31E-28	1.26E-24
ENSG00000187990	HIST1H2BG	4.004345462	2.16E-27	3.84E-24
ENSG00000206625	RNU6-1	6.291497881	3.99E-27	6.37E-24
ENSG00000171951	SCG2	3.558720129	8.59E-27	1.25E-23
ENSG00000073712	FERMT2	-2.603245721	9.88E-27	1.32E-23
ENSG00000172819	RARG	-2.4741929	5.39E-26	6.62E-23
ENSG00000143786	CNIH3	2.539693875	5.81E-26	6.63E-23
ENSG00000163431	LMOD1	-2.812039623	9.10E-26	9.70E-23
ENSG00000269378	ITGB1P1	-2.408082065	2.85E-25	2.85E-22
ENSG00000131238	PPT1	-2.451623043	5.50E-25	5.17E-22
ENSG00000184678	HIST2H2BE	2.349389524	9.30E-25	8.26E-22
ENSG00000186480	INSIG1	-2.367723227	2.24E-24	1.89E-21
ENSG00000214517	PPME1	-2.445736212	5.59E-24	4.47E-21
ENSG00000116133	DHCR24	-2.399743718	1.14E-23	8.68E-21
ENSG00000150093	ITGB1	-2.423864966	2.19E-23	1.59E-20
ENSG00000102802	MEDAG	2.61620716	4.15E-23	2.88E-20
ENSG00000272324	CTD-2154B17.4	-3.461549307	1.42E-22	9.40E-20
ENSG00000198911	SREBF2	-2.605199025	1.47E-22	9.40E-20
ENSG00000259546	RP11-351M8.2	-3.598815012	2.60E-22	1.60E-19
ENSG00000157601	MX1	3.288079084	5.80E-22	3.43E-19
ENSG00000147027	TMEM47	-2.328681693	2.07E-21	1.18E-18
ENSG00000223774	RP11-307B6.3	-2.773549002	1.31E-20	7.19E-18
ENSG00000137959	IFI44L	3.178721806	1.98E-20	1.06E-17
ENSG00000127241	MASP1	-2.417072577	2.09E-20	1.08E-17
ENSG00000102893	PHKB	-2.20339166	2.84E-20	1.42E-17
ENSG00000106688	SLC1A1	-2.53605608	5.93E-20	2.87E-17
ENSG00000125144	MT1G	6.300191997	8.04E-20	3.78E-17
ENSG00000149596	JPH2	-2.696939608	8.58E-20	3.92E-17
ENSG00000166923	GREM1	-2.180173898	1.20E-19	5.34E-17
ENSG00000078081	LAMP3	-3.792677067	1.47E-19	6.34E-17
ENSG00000146674	IGFBP3	-2.264087541	1.56E-19	6.55E-17
ENSG00000132031	MATN3	-3.328377126	1.65E-19	6.74E-17
ENSG00000072163	LIMS2	-2.375770974	1.96E-19	7.82E-17
ENSG00000139269	INHBE	-2.652877253	2.42E-19	9.44E-17
ENSG00000111424	VDR	-2.257966276	2.82E-19	1.07E-16

ENSG00000137273	FOXF2	-2.180909951	4.61E-19	1.71E-16
ENSG00000158406	HIST1H4H	2.253464641	5.00E-19	1.82E-16
ENSG00000162692	VCAM1	-2.052076477	5.64E-19	2.00E-16
ENSG00000204941	PSG5	2.304133671	1.08E-18	3.74E-16
ENSG00000157766	ACAN	-2.854970361	1.10E-18	3.74E-16
ENSG00000204291	COL15A1	-3.119297657	1.86E-18	6.16E-16
ENSG00000138642	HERC6	2.670032243	2.49E-18	7.97E-16
ENSG00000213626	LBH	-2.168188223	2.96E-18	9.26E-16
ENSG00000139289	PHLDA1	2.15600508	3.76E-18	1.14E-15
ENSG00000183160	TMEM119	-2.077680445	3.81E-18	1.14E-15
ENSG00000107731	UNC5B	-2.127201634	3.85E-18	1.14E-15
ENSG00000129353	SLC44A2	-2.149777689	5.25E-18	1.53E-15
ENSG00000135842	FAM129A	-2.191239655	5.66E-18	1.61E-15
ENSG00000120875	DUSP4	2.033581943	1.14E-17	3.15E-15
ENSG00000183671	GPR1	-3.088779135	1.51E-17	4.08E-15
ENSG00000185745	IFIT1	2.728088628	3.08E-17	8.21E-15
ENSG00000197409	HIST1H3D	2.8365294	7.42E-17	1.94E-14
ENSG00000189221	MAOA	-2.541392786	7.93E-17	2.02E-14
ENSG00000107796	ACTA2	-2.190979741	7.96E-17	2.02E-14
ENSG00000111335	OAS2	3.195930064	1.19E-16	2.97E-14
ENSG00000124635	HIST1H2BJ	2.659335058	1.34E-16	3.24E-14
ENSG00000197977	ELOVL2	-2.464342663	2.40E-16	5.64E-14
ENSG00000256261	AC104698.1	-2.066800987	2.64E-16	6.12E-14
ENSG00000054356	PTPRN	-2.208416806	3.57E-16	8.14E-14
ENSG00000162695	SLC30A7	-2.122643395	6.57E-16	1.48E-13
ENSG00000159658	EFCAB14	-2.065048218	8.65E-16	1.92E-13
ENSG00000171812	COL8A2	-2.284715406	1.14E-15	2.50E-13
ENSG00000161243	FBXO27	-2.51710169	1.34E-15	2.88E-13
ENSG00000151892	GFRA1	-2.08895422	1.54E-15	3.23E-13
ENSG00000171502	COL24A1	2.346797662	2.39E-15	4.89E-13
ENSG00000203813	HIST1H3H	2.881047068	2.42E-15	4.89E-13
ENSG00000128510	CPA4	2.01082674	2.85E-15	5.70E-13
ENSG00000141540	TTYH2	-2.469141169	3.06E-15	6.03E-13
ENSG00000163017	ACTG2	-2.200719066	4.65E-15	9.06E-13
ENSG00000072952	MRVI1	-2.692063578	5.43E-15	1.03E-12
ENSG00000150636	CCDC102B	2.073519772	5.95E-15	1.11E-12
ENSG00000196866	HIST1H2AD	3.021652355	6.02E-15	1.11E-12
ENSG00000135114	OASL	3.484354308	7.77E-15	1.38E-12
ENSG00000240476	LINC00973	2.768657763	9.87E-15	1.73E-12
ENSG00000091129	NRCAM	-3.036165943	1.77E-14	3.07E-12
ENSG00000137965	IFI44	2.280070428	1.81E-14	3.11E-12
ENSG00000089127	OAS1	3.214970468	1.86E-14	3.15E-12
ENSG00000228318	AP001610.5	3.062847639	2.11E-14	3.53E-12
ENSG00000104415	WISP1	-2.252187086	2.12E-14	3.53E-12
ENSG00000157368	IL34	-2.746105075	2.17E-14	3.57E-12
ENSG00000229400	RP11-3L21.2	2.703352992	2.19E-14	3.57E-12

ENSG00000231924	PSG1	2.190216333	2.93E-14	4.64E-12
ENSG00000131386	GALNT15	2.15134155	3.60E-14	5.42E-12
ENSG00000187193	MT1X	2.925727206	3.62E-14	5.42E-12
ENSG00000255701	AC090953.1	2.195201607	7.73E-14	1.12E-11
ENSG00000261655	CTD-3064M3.3	-2.543393439	1.16E-13	1.61E-11
ENSG00000164106	SCRG1	-2.525597324	1.62E-13	2.23E-11
ENSG00000136275	C7orf69	-2.50982856	2.09E-13	2.76E-11
ENSG00000111846	GCNT2	2.66941309	2.15E-13	2.82E-11
ENSG00000223477	LINC00842	-2.66097047	3.57E-13	4.58E-11
ENSG00000183486	MX2	2.463966639	3.58E-13	4.58E-11
ENSG00000180596	HIST1H2BC	2.108921394	4.26E-13	5.36E-11
ENSG00000267194	RP1-193H18.2	2.094677256	4.53E-13	5.61E-11
ENSG00000134201	GSTM5	-2.285542803	4.75E-13	5.79E-11
ENSG00000153234	NR4A2	2.642968004	5.12E-13	6.15E-11
ENSG00000189143	CLDN4	2.222674256	5.77E-13	6.88E-11
ENSG00000169432	SCN9A	-2.397010101	6.15E-13	7.22E-11
ENSG00000251257	CTD-2263F21.1	3.223134905	7.32E-13	8.48E-11
ENSG00000112294	ALDH5A1	-2.19827483	8.72E-13	9.96E-11
ENSG00000117600	LPPR4	-2.147970421	1.22E-12	1.35E-10
ENSG00000180139	ACTA2-AS1	-2.139254496	1.24E-12	1.36E-10
ENSG00000166292	TMEM100	2.956092717	1.43E-12	1.54E-10
ENSG00000123159	GIPC1	-2.035320155	1.79E-12	1.85E-10
ENSG00000166165	CKB	2.173197624	1.79E-12	1.85E-10
ENSG00000136205	TNS3	-2.179324958	2.13E-12	2.17E-10
ENSG00000130303	BST2	3.397559041	3.06E-12	3.04E-10
ENSG00000257207	LIMS3	-2.408502943	3.69E-12	3.57E-10
ENSG00000260912	RP11-363E7.4	2.180044421	4.00E-12	3.82E-10
ENSG00000259827	RP11-343H19.2	2.831032098	4.69E-12	4.43E-10
ENSG00000102271	KLHL4	2.062712511	5.28E-12	4.93E-10
ENSG00000204882	GPR20	-2.806846529	5.42E-12	5.04E-10
ENSG00000118194	TNNT2	-3.195499924	6.50E-12	6.01E-10
ENSG00000169715	MT1E	2.641428295	6.64E-12	6.10E-10
ENSG00000154639	CXADR	2.13399855	8.00E-12	7.27E-10
ENSG00000169184	MN1	-2.298663292	8.55E-12	7.63E-10
ENSG00000185885	IFITM1	2.052944921	1.48E-11	1.25E-09
ENSG00000166387	PPFIBP2	-2.144959492	2.11E-11	1.76E-09
ENSG00000108932	SLC16A6	2.462480791	2.61E-11	2.12E-09
ENSG00000134326	CMPK2	3.054176585	3.47E-11	2.79E-09
ENSG00000138646	HERC5	2.720486034	3.57E-11	2.85E-09
ENSG00000004799	PDK4	2.935462614	3.83E-11	3.01E-09
ENSG00000196611	MMP1	2.139691181	4.25E-11	3.30E-09
ENSG00000196557	CACNA1H	-2.12089051	7.13E-11	5.25E-09
ENSG00000134321	RSAD2	2.799674565	7.45E-11	5.44E-09
ENSG00000236107	AC010127.3	-2.411258139	7.96E-11	5.76E-09
ENSG00000270132	WISP1-OT1	-2.259671632	8.11E-11	5.83E-09
ENSG00000184005	ST6GALNAC3	-2.174971477	8.75E-11	6.24E-09

ENSG00000124212	PTGIS	-2.340141871	8.91E-11	6.33E-09
ENSG00000129295	LRRC6	2.625013171	9.13E-11	6.45E-09
ENSG00000124875	CXCL6	-2.115337829	9.70E-11	6.83E-09
ENSG00000243978	RGAG1	-2.883707858	1.09E-10	7.59E-09
ENSG00000173894	CBX2	-2.03278702	1.28E-10	8.78E-09
ENSG00000112981	NME5	2.407876147	1.37E-10	9.32E-09
ENSG00000170006	TMEM154	-2.035843581	1.74E-10	1.16E-08
ENSG00000003989	SLC7A2	-2.125942421	2.04E-10	1.33E-08
ENSG00000124171	PARD6B	2.068093848	2.21E-10	1.44E-08
ENSG00000069482	GAL	2.13743292	3.71E-10	2.34E-08
ENSG00000164318	EGFLAM	2.337719719	4.58E-10	2.84E-08
ENSG00000165983	PTER	-2.080485971	5.26E-10	3.20E-08
ENSG00000165949	IFI27	2.678027075	6.22E-10	3.75E-08
ENSG00000169248	CXCL11	2.405151307	7.01E-10	4.19E-08
ENSG00000123329	ARHGAP9	-2.082461864	7.55E-10	4.48E-08
ENSG00000089041	P2RX7	-2.517052617	8.47E-10	5.01E-08
ENSG00000198518	HIST1H4E	2.411335408	9.71E-10	5.58E-08
ENSG00000133640	LRRIQ1	2.710214395	1.05E-09	6.01E-08
ENSG00000172361	CCDC11	2.223799785	1.33E-09	7.42E-08
ENSG00000124942	AHNAK	-2.820456161	1.38E-09	7.71E-08
ENSG00000183578	TNFAIP8L3	2.303526958	1.46E-09	8.03E-08
ENSG00000126709	IFI6	2.462236522	2.26E-09	1.20E-07
ENSG00000184408	KCND2	2.31215947	2.59E-09	1.35E-07
ENSG00000156453	PCDH1	-2.320497893	3.05E-09	1.57E-07
ENSG00000233384	RP11-100E13.1	2.388518839	3.58E-09	1.82E-07
ENSG00000158683	PKD1L1	-2.530368181	4.07E-09	2.05E-07
ENSG00000261425	RP11-709B3.2	-2.150257459	4.49E-09	2.25E-07
ENSG00000242396	RP11-67L3.5	-2.496455311	5.31E-09	2.62E-07
ENSG00000137809	ITGA11	-2.067877655	7.16E-09	3.49E-07
ENSG00000178752	FAM132B	-2.035832768	7.26E-09	3.53E-07
ENSG00000161896	IP6K3	-2.0223315	8.81E-09	4.20E-07
ENSG00000169933	FRMPD4	-2.207246203	1.03E-08	4.85E-07
ENSG00000177112	MRVI1-AS1	-2.499903295	1.38E-08	6.34E-07
ENSG00000136002	ARHGEF4	-2.234814936	1.39E-08	6.36E-07
ENSG00000134463	ECHDC3	-2.07410765	1.41E-08	6.40E-07
ENSG00000270919	RP11-379K22.3	-2.292882199	1.83E-08	8.07E-07
ENSG00000185920	PTCH1	-2.041372614	1.87E-08	8.17E-07
ENSG00000185567	AHNAK2	-2.17148886	2.22E-08	9.53E-07
ENSG00000125148	MT2A	2.119511659	2.52E-08	1.06E-06
ENSG00000259721	RP11-758N13.1	-2.40133867	3.30E-08	1.37E-06
ENSG00000223609	HBD	-2.330184728	3.53E-08	1.45E-06
ENSG00000228237	EFCAB14-AS1	-2.318291189	3.94E-08	1.59E-06
ENSG00000152527	PLEKHH2	-2.041885191	4.36E-08	1.73E-06
ENSG00000255282	WTAPP1	2.007835985	5.56E-08	2.14E-06
ENSG00000153253	SCN3A	-2.421015095	5.70E-08	2.19E-06
ENSG00000187608	ISG15	2.287889016	5.72E-07	1.76E-05

ENSG00000176928	GCNT4	-2.039364865	1.67E-06	4.51E-05
ENSG00000103175	WFDC1	-2.116001583	2.88E-06	7.21E-05
ENSG00000149506	ZP1	2.014841477	3.24E-06	7.93E-05
ENSG00000154262	ABCA6	2.123620719	4.47E-06	0.000106098
ENSG00000165323	FAT3	-2.48640352	5.18E-06	0.000120754
ENSG00000254453	NAV2-AS2	-2.202650752	6.69E-06	0.000151562
ENSG00000205181	LINC00654	-2.110002086	3.92E-05	0.000693747
ENSG00000196743	GM2A	-1.996006361	1.89E-18	6.16E-16
ENSG00000010292	NCAPD2	-1.979643494	7.75E-18	2.17E-15
ENSG00000011105	TSPAN9	-1.872212477	1.33E-16	3.24E-14
ENSG00000166448	TMEM130	-1.883838542	1.84E-16	4.38E-14
ENSG00000112658	SRF	-1.777701568	1.53E-15	3.23E-13
ENSG00000134882	UBAC2	-1.983021792	1.74E-15	3.62E-13
ENSG00000255292	SDHD	-1.874375507	5.44E-15	1.03E-12
ENSG00000128294	TPST2	-1.965202813	6.01E-15	1.11E-12
ENSG00000256545	AL139819.1	-1.903299568	7.08E-15	1.28E-12
ENSG00000109107	ALDOC	-1.978412674	7.12E-15	1.28E-12
ENSG00000167191	GPRC5B	-1.825099792	2.50E-14	4.03E-12
ENSG00000082641	NFE2L1	-1.873371163	2.60E-14	4.15E-12
ENSG00000110108	TMEM109	-1.807910623	3.11E-14	4.86E-12
ENSG00000141469	SLC14A1	1.911179758	3.13E-14	4.86E-12
ENSG00000099194	SCD	-1.94433566	3.41E-14	5.24E-12
ENSG00000113269	RNF130	-1.748578399	3.63E-14	5.42E-12
ENSG00000128165	ADM2	-1.877631445	4.44E-14	6.57E-12
ENSG00000124920	MYRF	-1.998306016	5.85E-14	8.58E-12
ENSG00000117394	SLC2A1	-1.766133282	8.06E-14	1.16E-11
ENSG00000116584	ARHGEF2	-1.76806344	9.02E-14	1.29E-11
ENSG00000083454	P2RX5	-1.913995693	9.51E-14	1.35E-11
ENSG00000113578	FGF1	-1.930583187	1.13E-13	1.59E-11
ENSG00000092969	TGFB2	-1.692553529	1.73E-13	2.35E-11
ENSG00000018625	ATP1A2	-1.972757906	1.73E-13	2.35E-11
ENSG00000175215	CTDSP2	-1.95312869	1.78E-13	2.38E-11
ENSG00000149089	APIP	-1.992573253	1.98E-13	2.63E-11
ENSG00000184557	SOCS3	1.66321302	2.94E-13	3.83E-11
ENSG00000121743	GJA3	-1.982207819	4.08E-13	5.18E-11
ENSG00000049239	H6PD	-1.744413008	4.52E-13	5.61E-11
ENSG00000130707	ASS1	-1.719906243	4.64E-13	5.70E-11
ENSG00000172936	MYD88	-1.735382683	5.02E-13	6.07E-11
ENSG00000168394	TAP1	-1.654137529	6.02E-13	7.12E-11
ENSG00000029364	SLC39A9	-1.651120567	7.07E-13	8.25E-11
ENSG00000055211	GINM1	-1.667588391	8.34E-13	9.59E-11
ENSG00000119280	C1orf198	-1.727911771	9.05E-13	1.03E-10
ENSG00000103174	NAGPA	-1.717974634	1.03E-12	1.16E-10
ENSG00000145244	CORIN	-1.636932753	1.08E-12	1.20E-10
ENSG00000160013	PTGIR	1.745541626	1.08E-12	1.20E-10
ENSG00000011465	DCN	-1.817570348	1.34E-12	1.46E-10

ENSG00000186106	ANKRD46	1.630730821	1.44E-12	1.54E-10
ENSG00000129422	MTUS1	1.922391206	1.53E-12	1.63E-10
ENSG00000103257	SLC7A5	-1.766654601	1.60E-12	1.69E-10
ENSG00000089060	SLC8B1	-1.63250175	1.62E-12	1.70E-10
ENSG00000101265	RASSF2	-1.966039479	1.63E-12	1.70E-10
ENSG00000109814	UGDH	-1.626374687	2.07E-12	2.13E-10
ENSG00000213949	ITGA1	-1.84504102	2.44E-12	2.47E-10
ENSG00000110880	CORO1C	-1.675154295	2.60E-12	2.61E-10
ENSG00000136159	NUDT15	-1.781962478	2.92E-12	2.91E-10
ENSG00000147041	SYTL5	1.827828553	3.44E-12	3.39E-10
ENSG00000171992	SYNPO	-1.78486614	3.47E-12	3.39E-10
ENSG00000133110	POSTN	1.649848791	3.48E-12	3.39E-10
ENSG00000011198	ABHD5	1.72203066	3.98E-12	3.82E-10
ENSG00000102316	MAGED2	-1.730047579	4.02E-12	3.82E-10
ENSG00000151233	GXYLT1	1.676858583	4.96E-12	4.67E-10
ENSG00000119392	GLE1	-1.630588928	7.03E-12	6.42E-10
ENSG00000247556	OIP5-AS1	1.620194981	8.22E-12	7.42E-10
ENSG00000111087	GLI1	-1.914263497	8.28E-12	7.43E-10
ENSG00000133243	BTBD2	-1.544881657	9.09E-12	8.07E-10
ENSG00000184068	RP5-821D11.7	-1.825342155	9.29E-12	8.20E-10
ENSG00000216775	RP1-152L7.5	-1.689125755	1.03E-11	9.07E-10
ENSG00000107130	NCS1	-1.574117685	1.11E-11	9.70E-10
ENSG00000115884	SDC1	-1.551491622	1.13E-11	9.83E-10
ENSG00000256235	SMIM3	1.731309514	1.22E-11	1.05E-09
ENSG00000269636	AC010441.1	1.730072354	1.31E-11	1.13E-09
ENSG00000135744	AGT	1.909807903	1.39E-11	1.19E-09
ENSG00000063660	GPC1	-1.598408128	1.48E-11	1.25E-09
ENSG00000115902	SLC1A4	-1.61455744	1.71E-11	1.44E-09
ENSG00000100439	ABHD4	-1.59771505	1.79E-11	1.50E-09
ENSG00000026559	KCNG1	-1.716626862	2.24E-11	1.85E-09
ENSG00000101255	TRIB3	-1.628999305	2.28E-11	1.88E-09
ENSG00000126950	TMEM35	1.623688263	2.41E-11	1.97E-09
ENSG00000249992	TMEM158	1.809039279	2.43E-11	1.98E-09
ENSG00000214455	RCN1P2	-1.555181046	3.58E-11	2.85E-09
ENSG00000266341	RP5-890E16.4	-1.610326567	3.81E-11	3.01E-09
ENSG00000112685	EXOC2	-1.646271476	3.98E-11	3.12E-09
ENSG00000113721	PDGFRB	-1.922440123	4.00E-11	3.12E-09
ENSG00000002834	LASP1	-1.573366169	4.34E-11	3.32E-09
ENSG00000172795	DCP2	1.551431582	4.34E-11	3.32E-09
ENSG00000121236	TRIM6	-1.907889177	4.41E-11	3.36E-09
ENSG00000144218	AFF3	-1.899800352	4.71E-11	3.57E-09
ENSG00000172893	DHCR7	-1.681391079	4.81E-11	3.62E-09
ENSG00000255252	RP1-65P5.3	-1.679938739	5.15E-11	3.86E-09
ENSG00000147394	ZNF185	-1.575096252	5.36E-11	4.00E-09
ENSG00000204370	SDHD	-1.688840195	6.99E-11	5.17E-09
ENSG00000070831	CDC42	-1.629711782	7.41E-11	5.43E-09

ENSG00000057019	DCBLD2	1.681645084	7.80E-11	5.66E-09
ENSG00000198168	SVIP	1.565912746	8.43E-11	6.04E-09
ENSG00000183044	ABAT	-1.606417532	1.08E-10	7.56E-09
ENSG00000165914	TTC7B	-1.559247984	1.09E-10	7.59E-09
ENSG00000119917	IFIT3	1.692766358	1.10E-10	7.61E-09
ENSG00000173705	SUSD5	-1.61289843	1.11E-10	7.67E-09
ENSG00000071575	TRIB2	1.500605832	1.45E-10	9.81E-09
ENSG00000129965	INS-IGF2	-1.649827312	1.47E-10	9.92E-09
ENSG00000083444	PLOD1	-1.541751691	1.59E-10	1.07E-08
ENSG00000159399	HK2	-1.556373931	1.72E-10	1.15E-08
ENSG00000080573	COL5A3	-1.670301312	1.95E-10	1.29E-08
ENSG00000117228	GBP1	-1.700710843	2.82E-10	1.82E-08
ENSG00000204516	MICB	-1.538809554	2.83E-10	1.82E-08
ENSG00000186469	GNG2	1.510248497	2.89E-10	1.84E-08
ENSG00000145604	SKP2	-1.580075332	3.49E-10	2.22E-08
ENSG00000197879	MYO1C	-1.977639666	3.60E-10	2.28E-08
ENSG00000108984	MAP2K6	1.65508856	3.65E-10	2.31E-08
ENSG00000162595	DIRAS3	1.787098359	3.99E-10	2.50E-08
ENSG00000180573	HIST1H2AC	1.615892682	4.14E-10	2.57E-08
ENSG00000135069	PSAT1	-1.537511118	4.89E-10	3.01E-08
ENSG00000105989	WNT2	-1.93546416	4.95E-10	3.03E-08
ENSG00000198732	SMOC1	1.940008257	6.07E-10	3.68E-08
ENSG00000162390	ACOT11	-1.985026322	7.03E-10	4.19E-08
ENSG00000138650	PCDH10	-1.825390701	8.66E-10	5.09E-08
ENSG00000211445	GPX3	1.783254414	9.24E-10	5.39E-08
ENSG00000267283	AC005306.3	-1.539504866	9.48E-10	5.48E-08
ENSG00000104881	PPP1R13L	-1.729796585	1.05E-09	6.00E-08
ENSG00000125848	FLRT3	-1.823156796	1.24E-09	6.98E-08
ENSG00000021645	NRXN3	-1.895758234	1.27E-09	7.14E-08
ENSG00000239332	LINC01119	1.859761979	1.53E-09	8.41E-08
ENSG00000185483	ROR1	-1.831871659	1.67E-09	9.06E-08
ENSG00000259007	RP11-463J10.3	1.541269679	1.83E-09	9.89E-08
ENSG00000100889	PCK2	-1.691635418	1.95E-09	1.05E-07
ENSG00000168453	HR	-1.961162764	2.00E-09	1.07E-07
ENSG00000166394	CYB5R2	-1.831025056	2.02E-09	1.08E-07
ENSG00000150540	HNMT	-1.58556106	2.30E-09	1.21E-07
ENSG00000145391	SETD7	-1.91679128	2.30E-09	1.21E-07
ENSG00000049449	RCN1	-1.597483248	2.60E-09	1.36E-07
ENSG00000162551	ALPL	-1.536027325	2.97E-09	1.53E-07
ENSG00000265168	RP11-192H23.5	-1.849788644	3.27E-09	1.68E-07
ENSG00000149485	FADS1	-1.673794387	3.52E-09	1.80E-07
ENSG00000178814	OPLAH	-1.68303198	4.50E-09	2.25E-07
ENSG00000244675	AC108676.1	1.878672981	5.10E-09	2.53E-07
ENSG00000150938	CRIM1	-1.786465859	5.12E-09	2.53E-07
ENSG00000178550	AC010170.1	1.510919885	5.95E-09	2.91E-07
ENSG00000257453	RP11-290L1.3	1.716511937	6.36E-09	3.11E-07

ENSG00000110660	SLC35F2	-1.503572801	7.63E-09	3.69E-07
ENSG00000112531	QKI	-1.538487603	8.47E-09	4.08E-07
ENSG00000172379	ARNT2	-1.617630869	9.66E-09	4.58E-07
ENSG00000112414	GPR126	-1.900570774	1.12E-08	5.22E-07
ENSG00000173041	ZNF680	1.521526489	1.22E-08	5.68E-07
ENSG00000148288	GBGT1	-1.946192412	1.25E-08	5.77E-07
ENSG00000171246	NPTX1	-1.670493457	1.30E-08	5.99E-07
ENSG00000175084	DES	-1.77982925	1.46E-08	6.62E-07
ENSG00000237350	CDC42P6	-1.683677006	1.52E-08	6.81E-07
ENSG00000198074	AKR1B10	1.74384279	1.67E-08	7.40E-07
ENSG00000145777	TSLP	1.579789495	1.82E-08	8.02E-07
ENSG00000205710	C17orf107	-1.675528276	1.90E-08	8.24E-07
ENSG00000261625	RP11-554A11.4	-1.883163995	1.99E-08	8.61E-07
ENSG00000153993	SEMA3D	-1.554848553	2.24E-08	9.60E-07
ENSG00000116741	RGS2	1.657029042	2.25E-08	9.63E-07
ENSG00000167972	ABCA3	1.647569349	2.42E-08	1.03E-06
ENSG00000179295	PTPN11	-1.543465622	2.44E-08	1.03E-06
ENSG00000105855	ITGB8	1.815524637	2.93E-08	1.23E-06
ENSG00000169245	CXCL10	1.570975576	2.98E-08	1.25E-06
ENSG00000115738	ID2	-1.601307818	3.20E-08	1.33E-06
ENSG00000106123	EPHB6	-1.75593928	3.79E-08	1.55E-06
ENSG00000138435	CHRNA1	1.624102919	3.81E-08	1.55E-06
ENSG00000158125	XDH	1.775441064	3.94E-08	1.59E-06
ENSG00000113805	CNTN3	-1.755124603	3.95E-08	1.59E-06
ENSG00000187800	PEAR1	-1.508172241	4.60E-08	1.81E-06
ENSG00000154930	ACSS1	-1.586913098	4.62E-08	1.82E-06
ENSG00000254894	NAV2-AS1	-1.749124338	4.78E-08	1.87E-06
ENSG00000055118	KCNH2	-1.924444322	5.04E-08	1.96E-06
ENSG00000102755	FLT1	-1.866016286	5.93E-08	2.27E-06
ENSG00000247271	ZBED5-AS1	1.588907371	6.26E-08	2.38E-06
ENSG00000151364	KCTD14	-1.72775679	6.65E-08	2.52E-06
ENSG00000164251	F2RL1	-1.719539675	6.78E-08	2.56E-06
ENSG00000088882	CPXM1	-1.763621955	6.78E-08	2.56E-06
ENSG00000118849	RARRES1	1.518119192	6.91E-08	2.58E-06
ENSG00000148848	ADAM12	1.672497447	7.65E-08	2.85E-06
ENSG00000131620	ANO1	-1.863210008	7.79E-08	2.89E-06
ENSG00000198846	TOX	-1.709988068	7.96E-08	2.95E-06
ENSG00000169594	BNC1	-1.906402344	1.23E-07	4.41E-06
ENSG00000111907	TPD52L1	-1.6032069	1.25E-07	4.47E-06
ENSG00000232358	RP5-955M13.4	-1.637058751	1.35E-07	4.79E-06
ENSG00000260466	RP4-536B24.2	-1.85806217	1.52E-07	5.34E-06
ENSG00000031691	CENPQ	-1.705679234	1.90E-07	6.57E-06
ENSG00000167600	CYP2S1	-1.759316013	1.91E-07	6.59E-06
ENSG00000174945	AMZ1	-1.639463801	2.14E-07	7.30E-06
ENSG00000013619	MAMLD1	-1.572326151	2.18E-07	7.41E-06
ENSG00000116962	NID1	-1.630529646	2.44E-07	8.25E-06

ENSG00000186088	GSAP	-1.538799381	2.84E-07	9.46E-06
ENSG00000203780	FANK1	1.658475838	3.24E-07	1.07E-05
ENSG00000185742	C11orf87	-1.503455414	3.38E-07	1.11E-05
ENSG00000156795	WDYHV1	-1.51795924	3.40E-07	1.11E-05
ENSG00000146555	SDK1	1.595777282	3.54E-07	1.16E-05
ENSG00000254545	RP11-84A19.3	-1.576398364	3.62E-07	1.18E-05
ENSG00000155511	GRIA1	-1.745022318	3.77E-07	1.22E-05
ENSG00000162267	ITIH3	-1.802531393	3.82E-07	1.23E-05
ENSG00000214447	FAM187A	1.550197162	4.31E-07	1.38E-05
ENSG00000165659	DACH1	1.864373357	4.78E-07	1.51E-05
ENSG00000181072	CHRM2	-1.652313575	6.06E-07	1.85E-05
ENSG00000159167	STC1	1.648936141	6.10E-07	1.86E-05
ENSG00000136546	SCN7A	-1.558737016	7.43E-07	2.22E-05
ENSG00000125968	ID1	1.717493833	7.44E-07	2.22E-05
ENSG00000251664	PCDHA12	1.732036705	8.29E-07	2.46E-05
ENSG00000113594	LIFR	1.577490612	8.35E-07	2.48E-05
ENSG00000111331	OAS3	1.670558508	8.71E-07	2.57E-05
ENSG00000121858	TNFSF10	1.8363745	9.91E-07	2.88E-05
ENSG00000204965	PCDHA5	1.753448819	1.02E-06	2.95E-05
ENSG00000168961	LGALS9	1.586275232	1.03E-06	2.98E-05
ENSG00000165716	FAM69B	-1.649300796	1.08E-06	3.10E-05
ENSG00000132846	ZBED3	-1.729663405	1.20E-06	3.42E-05
ENSG00000243232	PCDHAC2	1.74261413	1.23E-06	3.50E-05
ENSG00000250120	PCDHA10	1.742618163	1.24E-06	3.51E-05
ENSG00000169851	PCDH7	-1.672730236	1.25E-06	3.54E-05
ENSG00000163531	NFASC	-1.808967554	1.27E-06	3.56E-05
ENSG00000134250	NOTCH2	-1.909307794	1.27E-06	3.56E-05
ENSG00000154175	ABI3BP	-1.802407323	1.32E-06	3.67E-05
ENSG00000249158	PCDHA11	1.710032409	1.39E-06	3.84E-05
ENSG00000225614	ZNF469	-1.761828661	1.83E-06	4.90E-05
ENSG00000164542	KIAA0895	1.55625211	1.88E-06	5.01E-05
ENSG00000239389	PCDHA13	1.711358662	2.09E-06	5.50E-05
ENSG00000204962	PCDHA8	1.621245806	2.15E-06	5.64E-05
ENSG00000204967	PCDHA4	1.537624055	2.29E-06	5.92E-05
ENSG00000166833	NAV2	-1.710559863	2.30E-06	5.94E-05
ENSG00000273081	RP4-813F11.4	1.646960211	2.73E-06	6.92E-05
ENSG00000204963	PCDHA7	1.533291189	2.81E-06	7.08E-05
ENSG00000228313	CTD-2555K7.4	-1.81489336	2.87E-06	7.20E-05
ENSG00000134780	DAGLA	-1.660607837	3.07E-06	7.61E-05
ENSG00000104783	KCNN4	1.67945676	3.12E-06	7.71E-05
ENSG00000137203	TFAP2A	-1.548516557	3.13E-06	7.73E-05
ENSG00000204961	PCDHA9	1.636561174	3.17E-06	7.79E-05
ENSG00000123892	RAB38	-1.878537426	3.24E-06	7.93E-05
ENSG00000271738	RP11-137H2.6	1.835817717	3.30E-06	8.04E-05
ENSG00000142233	NTN5	1.787489299	3.79E-06	9.11E-05
ENSG00000158246	FAM46B	-1.568842653	3.85E-06	9.23E-05

ENSG00000074370	ATP2A3	-1.993221746	3.86E-06	9.26E-05
ENSG00000232878	DPYD-AS1	-1.687176785	3.90E-06	9.34E-05
ENSG00000159713	TPPP3	1.902756654	3.92E-06	9.35E-05
ENSG00000161267	BDH1	-1.576577423	4.28E-06	0.000101799
ENSG00000243137	PSG4	1.554913944	5.39E-06	0.0001246
ENSG00000213123	TCTEX1D2	1.544570733	6.30E-06	0.000143467
ENSG00000204970	PCDHA1	1.54434584	6.70E-06	0.000151562
ENSG00000103023	PRSS54	1.517113586	6.88E-06	0.000155146
ENSG00000154760	SLFN13	-1.593331501	7.36E-06	0.000164229
ENSG00000161133	USP41	1.702109331	7.68E-06	0.000170894
ENSG00000092758	COL9A3	-1.562760527	8.13E-06	0.000180153
ENSG00000236404	RP11-125B21.2	-1.796916292	8.14E-06	0.000180153
ENSG00000116183	PAPPA2	-1.610528511	8.41E-06	0.000185302
ENSG00000115919	KYNU	1.56233135	9.16E-06	0.000200186
ENSG00000259175	RP11-379K22.2	-1.845228476	9.37E-06	0.000204324
ENSG00000196233	LCOR	1.63573508	9.50E-06	0.000206531
ENSG00000135549	PKIB	1.539918402	9.64E-06	0.000209138
ENSG00000253661	ZFHX4-AS1	-1.641344628	9.87E-06	0.000212341
ENSG00000138829	FBN2	-1.71766899	1.01E-05	0.000216051
ENSG00000188783	PRELP	-1.599691136	1.01E-05	0.000216405
ENSG00000103489	XYLT1	-1.542611947	1.07E-05	0.000227323
ENSG00000234638	AC053503.6	-1.819074615	1.13E-05	0.000237492
ENSG00000273090	RP11-78I14.1	-1.810137727	1.24E-05	0.000256069
ENSG00000162755	KLHDC9	1.616356262	1.26E-05	0.000258336
ENSG00000146197	SCUBE3	-1.500309747	1.34E-05	0.000271917
ENSG00000176438	SYNE3	-1.636930688	1.36E-05	0.000274621
ENSG00000204850	AC011484.1	-1.523175369	1.39E-05	0.000279585
ENSG00000198208	RPS6KL1	1.542055693	1.83E-05	0.000354709
ENSG00000248383	PCDHAC1	1.550876682	2.01E-05	0.000387481
ENSG00000229056	AC020571.3	1.741974678	2.16E-05	0.000411718
ENSG00000211772	TRBC2	-1.586096595	2.31E-05	0.000436145
ENSG00000212864	RNF208	-1.695845428	2.41E-05	0.000453166
ENSG00000250337	LINC01021	1.578230118	2.75E-05	0.000508336
ENSG00000122367	LDB3	-1.541596167	2.75E-05	0.000508979
ENSG00000260793	RP5-882C2.2	1.639000375	2.78E-05	0.000512474
ENSG00000272114	RP1-261G23.7	-1.715734907	3.54E-05	0.000634391
ENSG00000124116	WFDC3	1.988045171	3.81E-05	0.000676413
ENSG00000269019	AC005932.1	1.519545219	4.67E-05	0.000801024
ENSG00000136895	GARNL3	-1.622328682	4.72E-05	0.000807529
ENSG00000147465	STAR	1.514247527	5.12E-05	0.000863331
ENSG00000139187	KLRG1	1.590695323	6.67E-05	0.001072177
ENSG00000112936	C7	1.523423861	6.76E-05	0.001083843
ENSG00000173267	SNCG	1.530333117	9.46E-05	0.001441859
ENSG00000158352	SHROOM4	-1.64116841	0.000111711	0.00165455
ENSG00000254902	ANO1-AS1	-1.619152964	0.00011274	0.001668244
ENSG00000027075	PRKCH	1.533692551	0.000113942	0.001682684

ENSG00000107611	CUBN	1.564800528	0.000121908	0.001785708
ENSG00000256238	RP11-473N11.2	-1.500623034	0.000127681	0.001856662
ENSG00000267791	CTD-2659N19.2	1.596620559	0.000535327	0.006094605
ENSG00000248898	CTD-2288O8.1	-1.542571814	0.000537089	0.00610471
ENSG00000258186	SLC7A5P2	-1.641829285	0.000570386	0.006419257
ENSG00000177076	ACER2	1.570580665	0.000684439	0.007440835
ENSG00000113396	SLC27A6	-1.58727984	0.001090913	0.010868999
ENSG00000196566	RP11-57C13.3	-1.700404097	0.001566133	0.014559846

SUPPLEMENTAL TABLE 2: Summary of Ingenuity pathway analysis (IPA) for affected canonical pathways and enriched genes in synectin knockdown hepatic stellate cells (HSC) compared to wild type HSC without PDGF-beta treatment.

INGENUITY®
PATHWAY ANALYSIS

Analysis Name: Control shRNA vs synectin shRNA- 2015-12-10 02:33 PM
Analysis Creation Date: 2015-12-10
Build version: 400896M
Content version: 24718999 (Release Date: 2015-09-14)

Analysis Settings

Reference set: Ingenuity Knowledge Base (Genes Only)

Relationship to include: Direct and Indirect

Includes Endogenous Chemicals

Optional Analyses: My Pathways My List

Filter Summary:

Consider only molecules and/or relationships where

(species = Human) AND

(confidence = Experimentally Observed)

Top Canonical Pathways

Name	p-value	Overlap
Molecular Mechanisms of Cancer	1.70E-06	18.7 % 67/359
Hepatic Fibrosis / Hepatic Stellate Cell Activation	8.50E-06	21.5 % 39/181
Paxillin Signaling	5.31E-05	24.5 % 24/98
Superpathway of Inositol Phosphate Compounds	8.78E-05	19.9 % 37/186
Leukocyte Extravasation Signaling	8.92E-05	19.7 % 38/193

Top Upstream Regulators

Upstream Regulators

Upstream Regulator	p-value of overlap	Predicted Activation
IFNA2	4.61E-17	Activated
IFNL1	4.68E-17	Activated
IL1RN	6.78E-17	Inhibited
PRL	2.22E-16	Activated
TNF	1.15E-13	

Causal Networks

Name	p-value of overlap	Predicted Activation
AR	5.92E-29	Inhibited
LDL	4.12E-28	
ADRB2	1.12E-27	
TNKS2	5.74E-27	
TNKS	5.74E-27	

Top Diseases and Bio Functions

Diseases and Disorders

Name	p-value	#Molecules
Cancer	5.93E-03 - 1.93E-13	1725
Organismal Injury and Abnormalities	5.93E-03 - 1.93E-13	1740
Reproductive System Disease	4.51E-03 - 1.93E-13	875
Gastrointestinal Disease	5.93E-03 - 1.25E-09	1222
Hereditary Disorder	2.96E-03 - 8.75E-07	195

Molecular and Cellular Functions

Name	p-value	#Molecules
Cellular Movement	5.87E-03 - 1.45E-19	312
Cellular Growth and Proliferation	5.87E-03 - 6.31E-12	475
Cell Morphology	3.46E-03 - 3.14E-08	202
Cellular Development	5.77E-03 - 3.32E-08	403
Cell Death and Survival	6.27E-03 - 5.15E-08	439

Physiological System Development and Function

Name	p-value	#Molecules
Cardiovascular System Development and Function	6.27E-03 - 5.83E-11	151
Organismal Development	5.87E-03 - 1.19E-09	114
Tissue Development	5.87E-03 - 9.75E-08	231
Nervous System Development and Function	5.22E-03 - 5.97E-07	33
Embryonic Development	5.87E-03 - 8.33E-05	73

Top Tox Functions

Assays: Clinical Chemistry and Hematology

Name	p-value	#Molecules
Increased Levels of Alkaline Phosphatase	4.77E-02 - 4.77E-02	6
Decreased Levels of Albumin	1.04E-01 - 1.04E-01	1
Increased Levels of ALT	1.04E-01 - 1.04E-01	1
Increased Levels of AST	1.04E-01 - 1.04E-01	1
Increased Levels of Albumin	2.82E-01 - 1.04E-01	2

Cardiotoxicity

Name	p-value	#Molecules
Pulmonary Hypertension	1.04E-01 - 1.65E-03	11
Cardiac Hypertrophy	2.35E-01 - 4.13E-02	6
Cardiac Arrythmia	1.00E00 - 5.67E-02	20
Cardiac Stenosis	3.21E-01 - 5.90E-02	5
Congenital Heart Anomaly	4.00E-01 - 7.78E-02	12

Hepatotoxicity

Name	p-value	#Molecules
Liver Hyperplasia/Hyperproliferation	4.24E-01 - 8.81E-06	717
Hepatocellular Carcinoma	3.78E-01 - 3.12E-05	698
Liver Cirrhosis	3.52E-01 - 4.00E-03	24
Liver Proliferation	2.81E-01 - 2.96E-02	5
Liver Necrosis/Cell Death	2.00E-01 - 9.37E-02	5

Nephrotoxicity

Name	p-value	#Molecules
Renal Necrosis/Cell Death	3.57E-01 - 2.64E-04	52
Renal Inflammation	1.00E00 - 1.09E-02	10

Renal Nephritis	1.00E00 - 1.09E-02	10
Glomerular Injury	4.24E-01 - 4.26E-02	7
Renal Hydronephrosis	5.07E-02 - 5.07E-02	7

Top Regulator Effect Networks

ID	Regulators	Diseases & Functions	Consistency Score
1	FGF2,FOS,LGALS3,TMSB4,TPM3	adhesion of connective tissue cells (+9 more)	25.938
2	BMP7,ERK1/2,FGF2,FOS,PPARD,SP3,SP4,TRIB3	adhesion of endothelial cell lines (+11 more)	24.82
3	A2M,APP,BTK,CCND1,CETP,CNOT7,EIF2AK2,GAPDH,GSK3B (+21 more)	apoptosis of breast cell lines (+9 more)	23.947
4	BRD4,CD24,FGF2,FOXM1,GAPDH,Gsk3,LGALS3,MYCN,NEDD9 (+6 more)	adhesion of connective tissue cells (+15 more)	23.905
5	BTK,FGF2,FOXM1,GAPDH,IFNA1/IFNA13,IFNA2,IFNB1 (+8 more)	apoptosis of breast cancer cell lines (+14 more)	22.659

Top Networks

ID	Associated Network Functions	Score
1	Cellular Assembly and Organization, DNA Replication, Recombination, and Repair, Cell Cycle	33
2	Infectious Diseases, Cellular Growth and Proliferation, Antigen Presentation	30
3	Cell Death and Survival, Cellular Function and Maintenance, Embryonic Development	28
4	Drug Metabolism, Lipid Metabolism, Small Molecule Biochemistry	28
5	Cancer, Organismal Injury and Abnormalities, Reproductive System Disease	24

Top Tox Lists

Name	p-value	Overlap
Cardiac Hypertrophy	3.86E-07	18.8 % 74/394
Renal Necrosis/Cell Death	3.01E-06	17.2 % 84/489
Liver Proliferation	4.26E-05	19.5 % 43/221

Liver Necrosis/Cell Death	4.60E-05	18.5 %	50/271
Increases Renal Damage	9.07E-05	26.0 %	20/77

Top Analysis-Ready Molecules

SUPPLEMENTAL TABLE 3: The summary of Ingenuity pathway analysis (IPA) for affected canonical pathways and enriched genes in synectin knockdown hepatic stellate cells (HSCs) compared to wild type HSCs with PDGF-beta treatment.

Analysis Name: ctl PDGF vs shSyn PDGF LogFC1.4-2016-12-13 11:15 AM
Analysis Creation Date: 2016-12-13
Build version: 400896M
Content version: 28820210 (Release Date: 2016-09-24)

Analysis Settings

Reference set: Ingenuity Knowledge Base (Genes Only)

Relationship to include: Direct and Indirect

Includes Endogenous Chemicals

Optional Analyses:

Filter Summary:

Consider only molecules and/or relationships where

(species = Human) AND

(confidence = Experimentally Observed)

Top Canonical Pathways

Name	p-value	Overlap	
Hepatic Fibrosis / Hepatic Stellate Cell Activation	8.18E-07	9.4 %	17/181
Aryl Hydrocarbon Receptor Signaling	5.84E-05	8.9 %	12/135
Role of IL-17A in Psoriasis	1.57E-04	30.8 %	4/13
Role of IL-17F in Allergic Inflammatory Airway Diseases	2.98E-04	14.6 %	6/41
Role of Tissue Factor in Cancer	3.77E-04	8.4 %	10/119

Top Upstream Regulators

Upstream Regulators

Upstream Regulator	p-value of overlap	Predicted Activation
IFNG	5.22E-16	
TNF	1.36E-13	Inhibited
TLR7	1.27E-11	
TREM1	1.36E-11	
IL1RN	2.01E-11	Inhibited

Causal Networks

Name	p-value of overlap	Predicted Activation
CCL5	5.78E-19	
PTGER3	1.28E-18	Inhibited
TREM1	6.94E-18	Inhibited
XBP1	9.88E-18	
IL1A	1.33E-17	

Top Diseases and Bio Functions

Diseases and Disorders

Name	p-value	#Molecules
Dermatological Diseases and Conditions	3.46E-04 - 4.23E-10	223
Organismal Injury and Abnormalities	4.88E-03 - 4.23E-10	410
Endocrine System Disorders	4.28E-03 - 3.85E-09	104
Gastrointestinal Disease	4.28E-03 - 3.85E-09	355
Metabolic Disease	2.98E-03 - 3.85E-09	63

Molecular and Cellular Functions

Name	p-value	#Molecules
Cellular Development	4.87E-03 - 1.02E-08	117
Cellular Growth and Proliferation	4.36E-03 - 1.02E-08	136
Cell Death and Survival	4.64E-03 - 2.82E-08	116
DNA Replication, Recombination, and Repair	2.98E-03 - 9.09E-08	22
Cellular Movement	4.45E-03 - 1.75E-07	82

Physiological System Development and Function

Name	p-value	#Molecules
Cardiovascular System Development and Function	4.45E-03 - 2.24E-09	51
Organismal Development	4.28E-03 - 2.24E-09	54
Organ Development	1.51E-03 - 6.93E-09	39
Skeletal and Muscular System Development and Function	2.98E-03 - 6.93E-09	43
Tissue Development	4.28E-03 - 6.93E-09	84

Top Tox Functions

Assays: Clinical Chemistry and Hematology

Name	p-value	#Molecules
Increased Levels of Alkaline Phosphatase	2.03E-02 - 2.03E-02	3
Decreased Levels of Albumin	6.64E-02 - 2.26E-02	1
Increased Levels of Albumin	6.64E-02 - 6.64E-02	1
Increased Levels of LDH	1.48E-01 - 1.48E-01	1

Cardiotoxicity

Name	p-value	#Molecules
Cardiac Dysfunction	8.09E-02 - 4.88E-03	3
Cardiac Necrosis/Cell Death	4.42E-02 - 6.18E-03	3
Pulmonary Hypertension	3.53E-01 - 2.15E-02	5
Cardiac Arrythmia	4.49E-01 - 2.26E-02	10
Cardiac Arteriopathy	1.67E-01 - 2.26E-02	13

Hepatotoxicity

Name	p-value	#Molecules
Liver Proliferation	2.90E-02 - 1.14E-03	4
Liver Cirrhosis	1.80E-02 - 1.61E-03	12
Hepatocellular Carcinoma	3.96E-01 - 3.48E-03	33
Liver Hyperplasia/Hyperproliferation	3.96E-01 - 3.48E-03	168
Liver Inflammation/Hepatitis	3.05E-01 - 5.64E-03	8

Nephrotoxicity

Name	p-value	#Molecules
Kidney Failure	3.82E-01 - 2.55E-03	9
Renal Inflammation	1.00E00 - 2.98E-03	7
Renal Nephritis	1.00E00 - 2.98E-03	7

Renal Proliferation	2.62E-01 - 5.18E-03	8
Renal Necrosis/Cell Death	4.35E-01 - 7.74E-03	15

Top Regulator Effect Networks

ID	Regulators	Diseases & Functions	Consistency Score
1	AHR,ATG7,CD40,CD40LG,COL18A1,CSF2,ECSIT,FOS,IKBKE (+7 more)	activation of cells,angiogenesis (+15 more)	54.667
2	CD40,CD40LG,IL17A,IL1A,IL1B,Jnk (+3 more)	activation of cells (+11 more)	40.621
3	AHR,Akt,ATG7,CD40,COL18A1,CSF2,ECSIT,F7,FOS,FOXM1 (+15 more)	activation of cells (+14 more)	32.767
4	COL18A1,CSF2,F7,IKBKE,IL17A,IL1A (+5 more)	cell viability,chemotaxis (+4 more)	30.426
5	COL18A1,CSF2,ERK1/2,F7,IL17A,IL1A (+3 more)	chemotaxis,colony formation,generation of cells (+3 more)	24.396

Top Networks

ID	Associated Network Functions	Score
1	Cell-To-Cell Signaling and Interaction, Hematological System Development and Function, Immune Cell Trafficking	34
2	Immunological Disease, Dermatological Diseases and Conditions, Organismal Injury and Abnormalities	28
3	Cell Morphology, Hematological System Development and Function, Hematopoiesis	28
4	Cell Death and Survival, Skeletal and Muscular Disorders, Cell-To-Cell Signaling and Interaction	24
5	Hematological System Development and Function, Organismal Development, Cellular Movement	24

Top Tox Lists

Name	p-value	Overlap	
Cardiac Hypertrophy	3.70E-10	7.8 %	34/435
Cardiac Fibrosis	1.54E-08	10.4 %	20/192
Increases Glomerular Injury	4.59E-07	14.1 %	12/85

Liver Necrosis/Cell Death	2.23E-06	7.4 % 21/284
Liver Proliferation	3.50E-06	8.1 % 18/223

Top Analysis-Ready Molecules

Exp Log Ratio up-regulated

Molecules	Exp. Value	Exp. Chart
HIST1H2BG	↑ 4.577	
RNU6-1	↑ 4.326	
MT1G	↑ 4.182	
HIST1H3D	↑ 3.605	
MT1F	↑ 3.304	
RSAD2	↑ 2.933	
LRRIQ1	↑ 2.844	
BMF	↑ 2.691	
CUBN	↑ 2.611	
HIST1H3H	↑ 2.595	

Exp Log Ratio down-regulated

Molecules	Exp. Value	Exp. Chart
INSIG1	↓ -3.900	
LAMP3	↓ -3.820	
SERPINE1	↓ -3.815	
SLC6A9	↓ -3.797	
TNNT2	↓ -3.757	
DAP	↓ -3.447	
CEMIP	↓ -3.433	
LIMS1	↓ -3.331	
GPR1	↓ -3.283	
LMOD1	↓ -3.257	