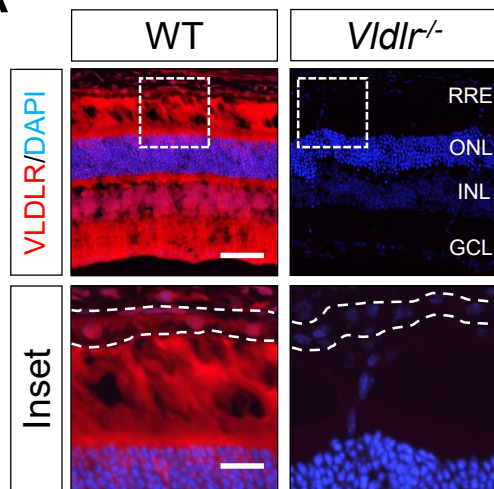
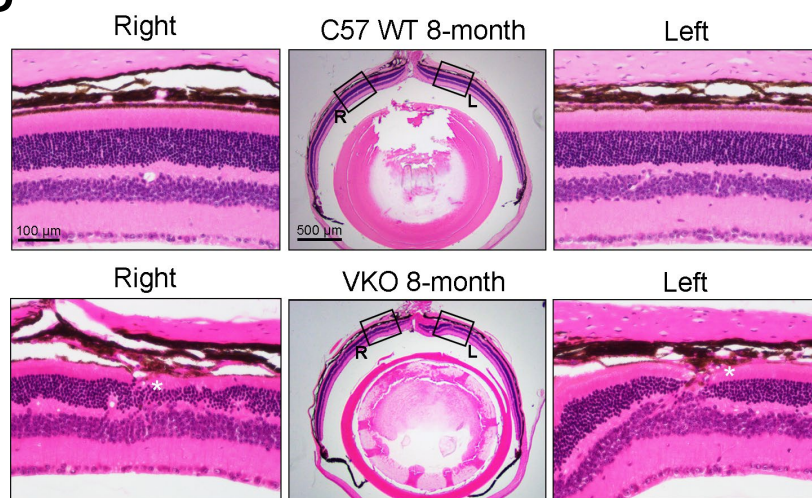
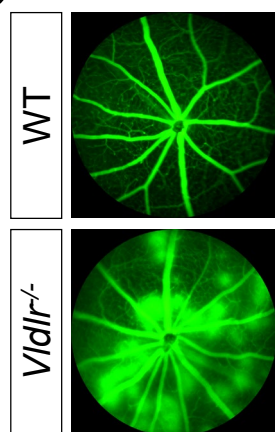
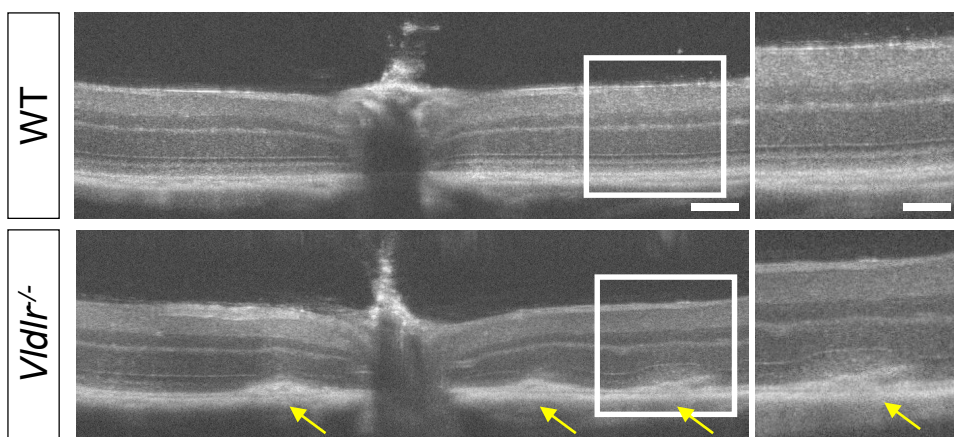
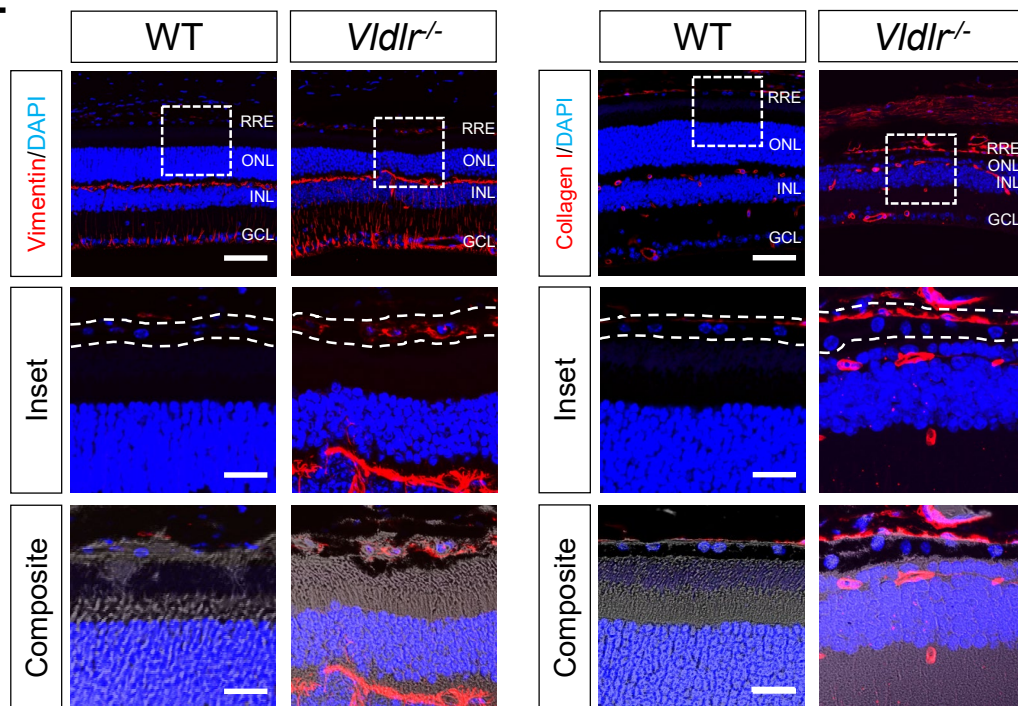
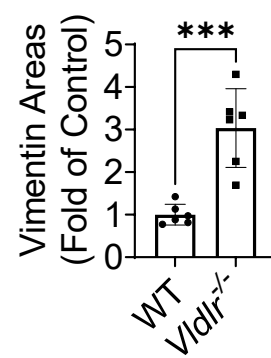
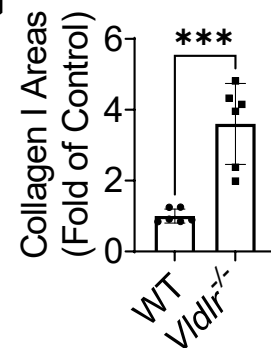
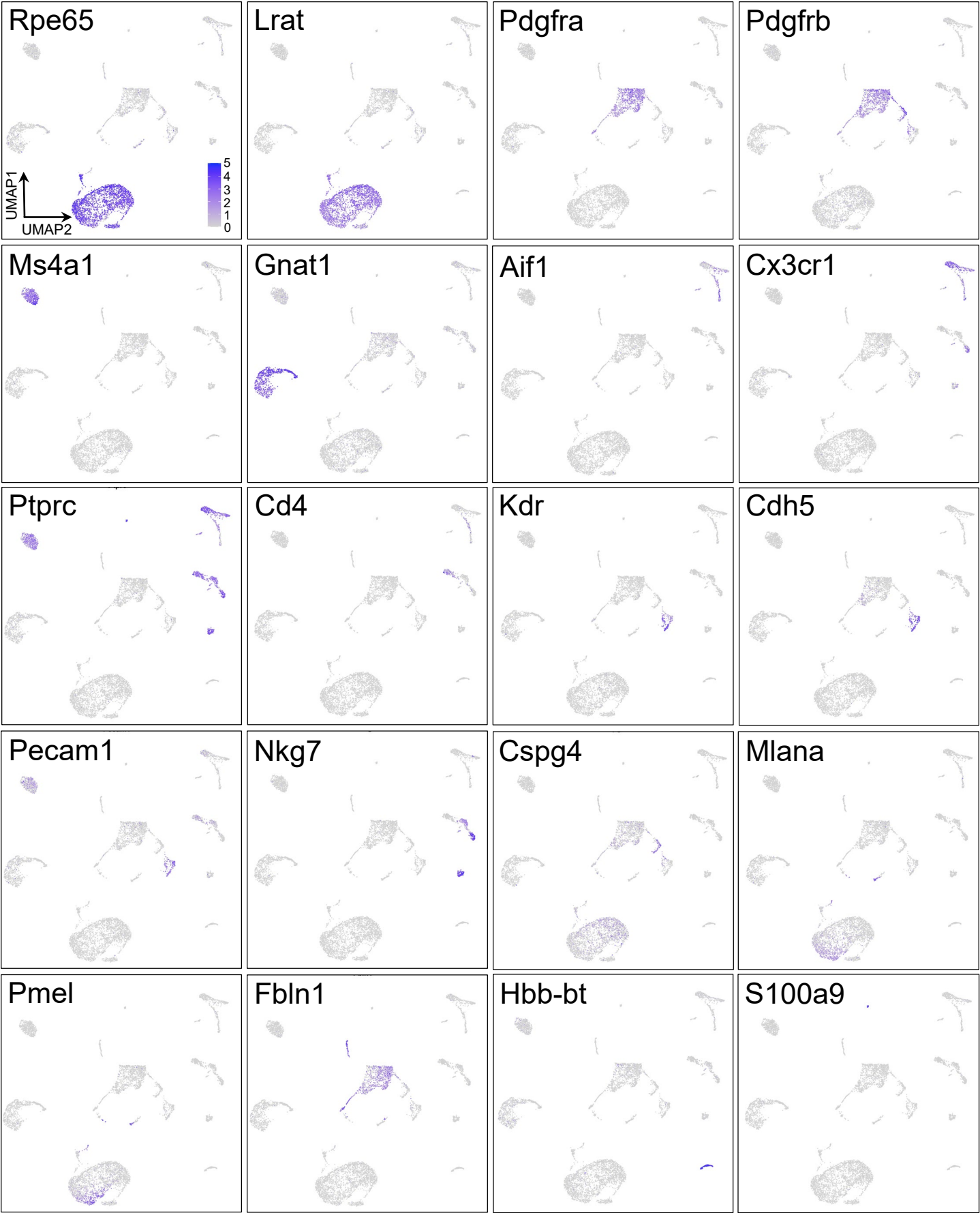


A**B****C****D****E****F****G**

Supplementary Figure 1. Characterization of subretinal neovascularization and fibrosis in *Vldlr*^{-/-} mice.

A: Representative immunostaining of VLDLR ocular cryosection of 1-month-old WT and *Vldlr*^{-/-} mice. Scale bar: 50 μ m. **B:** Hematoxylin and eosin staining on the retinal sections of 8-month-old *Vldlr*^{-/-} and WT mice. The white star indicates the CNV lesion. Scale bar: 100 μ m in the enlarged image and 500 μ m in the whole eye section. **C:** Representative images of fundus fluorescein angiography (FFA) of WT and *Vldlr*^{-/-} mice at the age of 1 month. **D:** Representative images of Optical Coherence Tomography (OCT) of WT and *Vldlr*^{-/-} mice at the age of 3 months. The yellow arrows indicate CNV lesions. Scale bar: 50 μ m. **E:** Representative immunostaining of vimentin and collagen I in ocular cryosection of 3-month-old WT and *Vldlr*^{-/-} mice. Scale bar: 50 μ m. **F, G:** Quantification of vimentin-positive areas (E) and fibronectin-positive areas (F) in (D) (n = 6). GCL: ganglion cell layer, INL: inner nuclear layer, ONL, outer nuclear layer, RPE: retinal pigment epithelium. Data are presented as mean $\pm$ SD. *** P < 0.001.

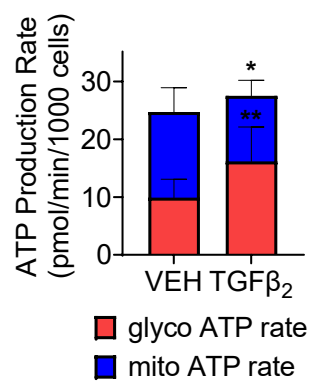
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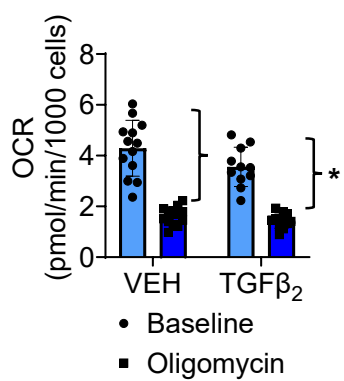
Supplementary Figure 2. UMAP plots of known cell markers across cell clusters.

The degree of blue color indicates the expression level in each cell clusters.

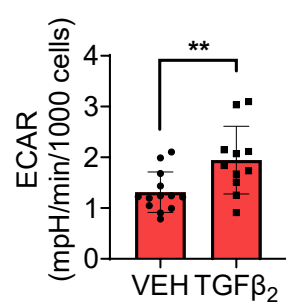
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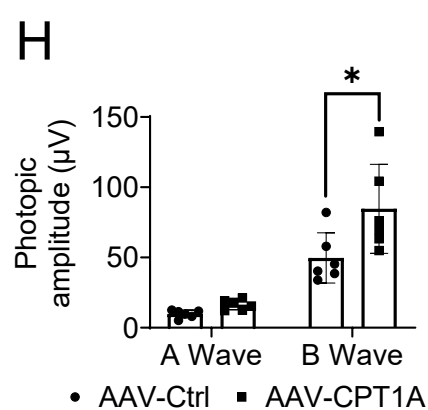
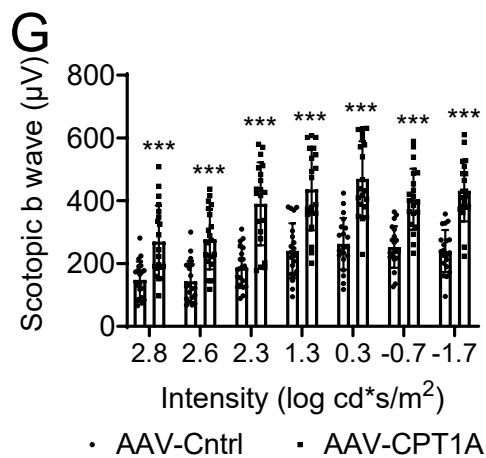
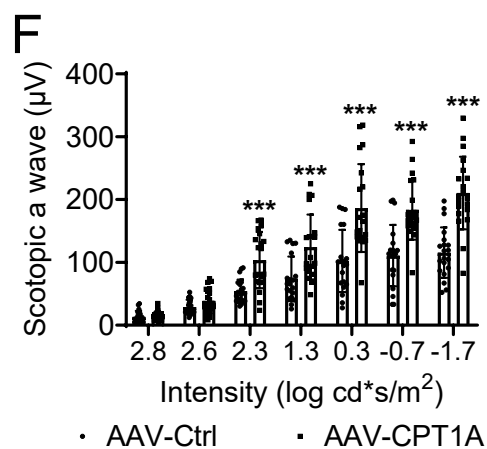
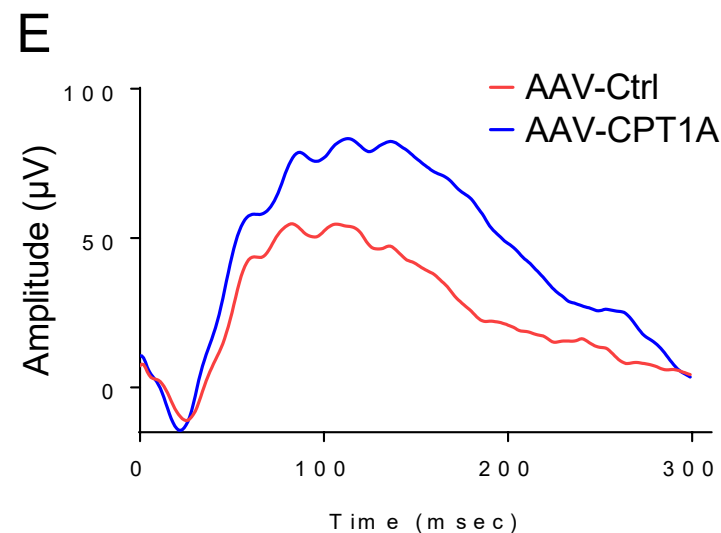
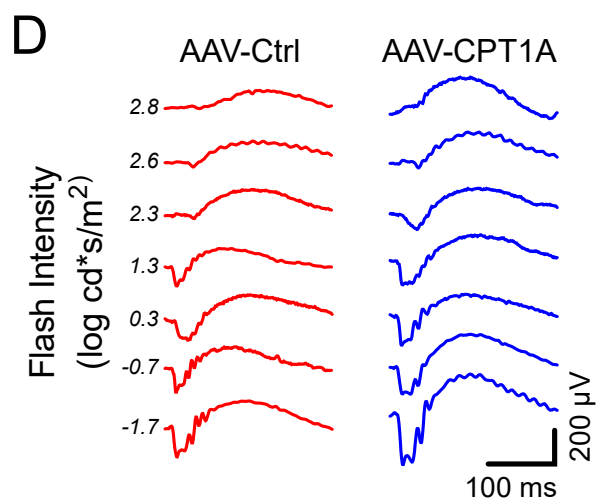
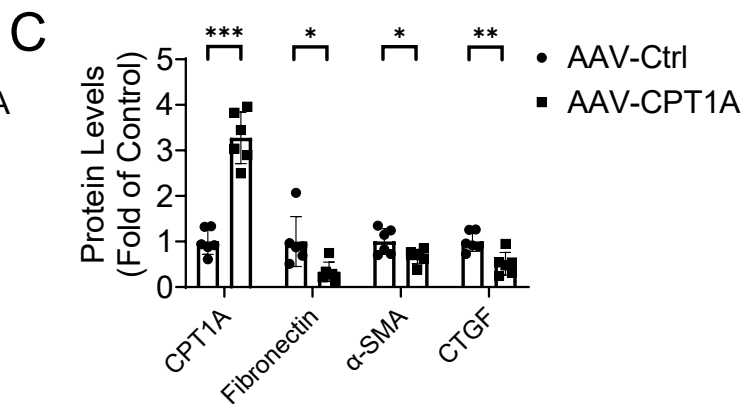
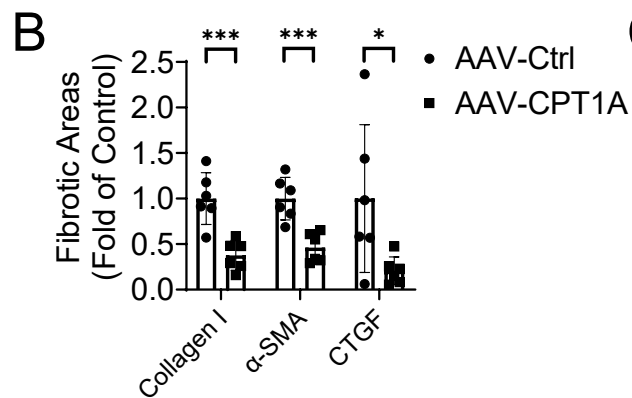
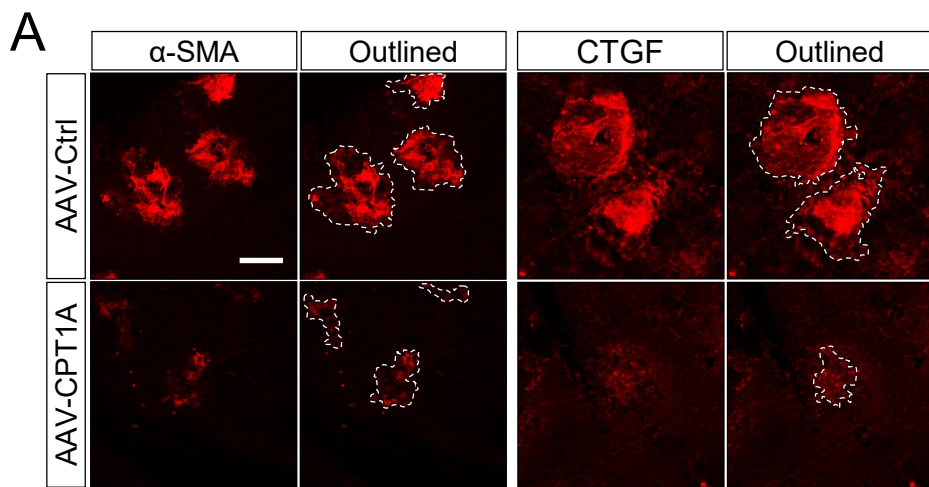


C



Supplementary Figure 3. ATP-rate assay of TGF β -treated RPE cells.

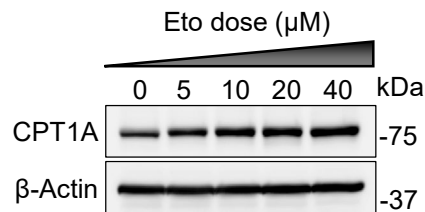
A: ATP production rate in human primary RPE cells treated with 5 ng/ml TGF β_2 or vehicle (VEH) for 24 hr (n = 11-13). The ATP production rate was measured using a Seahorse analyzer. **B:** The actual oxygen consumption rate (OCR) data used for the calculation of ATP production rate (n = 11-13). **C:** The actual extracellular acidification rate (ECAR) data used for the calculation of ATP production rate (n = 11-13). Data are presented as mean $\pm$ SD. * P < 0.05, ** P < 0.01.



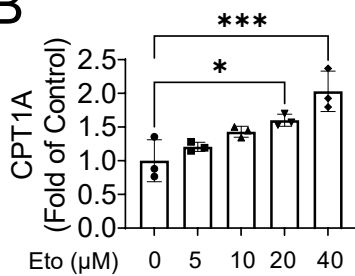
Supplementary Figure 4. Overexpression of CPT1A plays anti-fibrotic and neuroprotective effects.

A-C: Human CPT1A was overexpressed in *Vldlr*^{-/-} mice to investigate the anti-fibrotic effect of CPT1A. One microliter of 2×10^{13} gene copy (GC) / ml of AAV-*Best1-CPT1A* was subretinally injected into the *Vldlr*^{-/-} pups at the age of P14. The contralateral eye was injected with AAV-*GFP* at the same titer. Six weeks after the injection, the eyecups were harvested to measure the fibrosis by flatmounted immunostaining (Figure 6K) and Western blot analysis (Figure 6L). **A:** Representative immunostaining of α -SMA and CTGF in the flatmounted eyecups at 6 weeks post injection. Scale bar: 50 μ m. **B:** Quantification of areas of collagen I (Figure 6K), α -SMA, and CTGF (Supplementary Figure 4A) (n = 6). **C:** The quantification of Western blotting in Figure 6L (n = 6). **D-H:** ERG response in dark-adapted 2-month-old *Vldlr*^{-/-} mice after subretinal injection (AAV-CPT1A or AAV-Control). **D:** Representative scotopic traces in subretinal injected 2-month-old *Vldlr*^{-/-} mice, AAV-control (left) AAV-CPT1A (right). Single-flash ERG was recorded over a range of increasing scotopic light intensities in indicated mice. **E:** Representative photopic traces obtained in subretinally injected 2-month-old *Vldlr*^{-/-} mice with indicated AAV. **F, G:** The quantitative evaluation of scotopic a-wave (F) and b-wave (G) amplitudes in *Vldlr*^{-/-} AAV-control and *Vldlr*^{-/-} AAV-CPT1A mice subretinally injected mice (n = 20 eyes). The X-axis values were log-transformed. **H:** Comparison of photopic a-wave and b-wave amplitudes in 2-month-old *Vldlr*^{-/-} mice after indicated treatments (n = 6). Data are presented as mean $\pm$ SD. * P < 0.05, ** P < 0.01, *** P < 0.001.

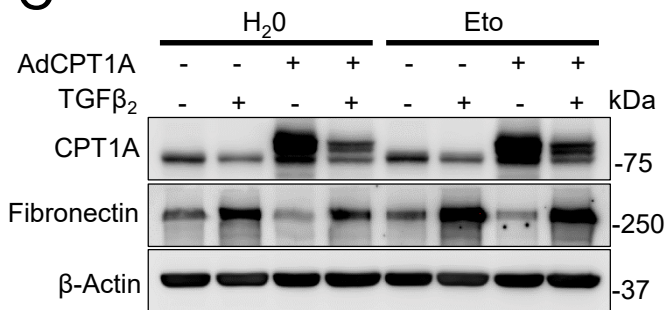
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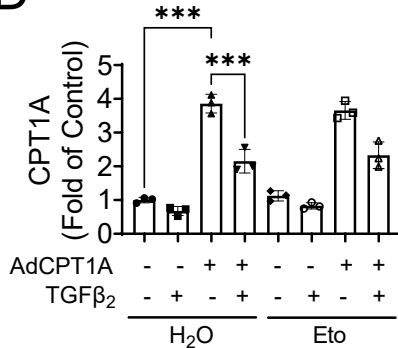
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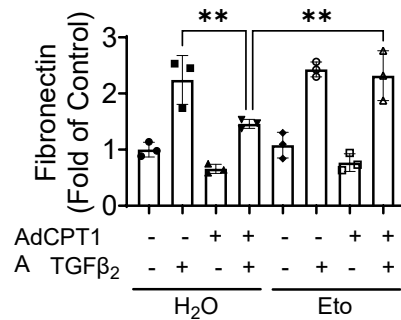
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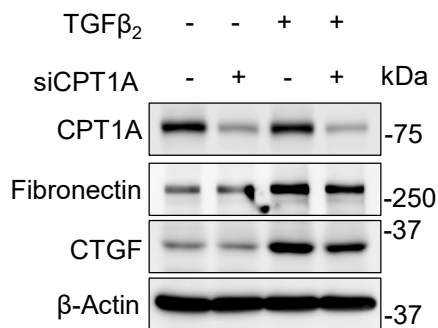
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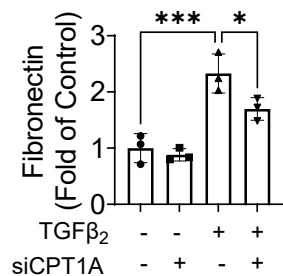
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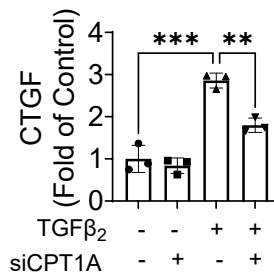
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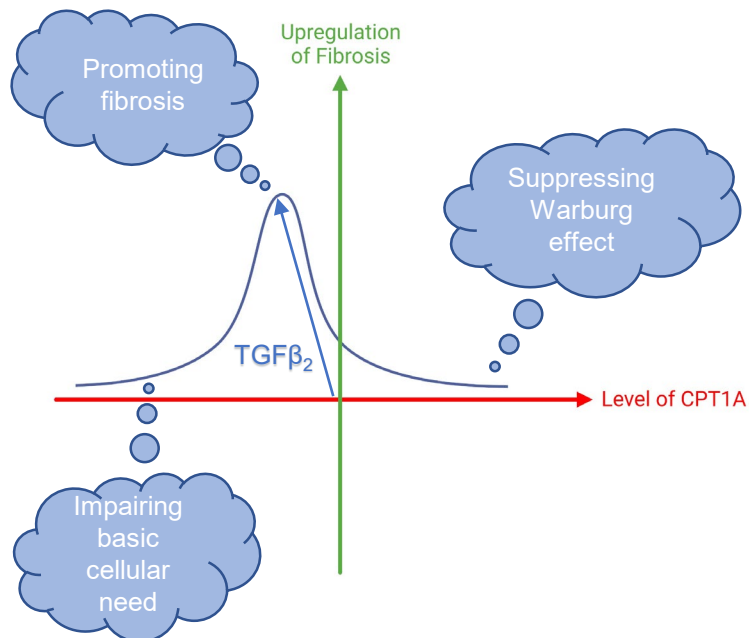
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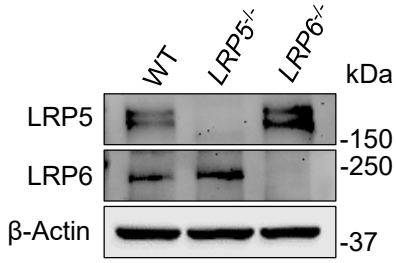
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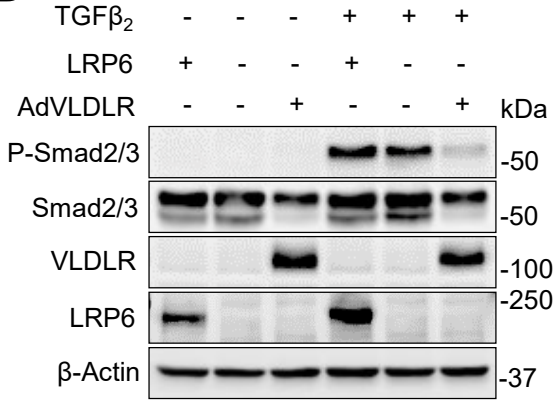
Supplementary Figure 5. CPT1A plays an anti-fibrotic effect through its function of lipid transportation.

A: Representative images of Western blotting of CPT1A in human primary RPE cells treated with indicated Eto dose for 24 hr. **B:** Quantification of CPT1A in A (n = 3). **C-E:** Representative images of Western blotting of CPT1A and fibronectin in human primary RPE cells with indicated treatment. RPE cells were transduced with AdCPT1A or AdRFP (MOI = 50) for 48 hr. Then, RPE cells were treated with 5 ng/ml TGF β_2 with or without Eto for 24 hr. **D, E:** Quantification of CPT1A and fibronectin in C (n = 3). **F-H:** Representative images of Western blotting of CPT1A, fibronectin, and CTGF in human primary RPE cells with indicated treatment. RPE cells were transfected with siCPT1A for 48 hr. Then, RPE cells were treated with 5 ng/ml TGF β_2 for 24 hr. **G, H:** Quantification of fibronectin and CTGF in F (n = 3). Data are presented as mean $\pm$ SD. * P < 0.05, ** P < 0.01, *** P < 0.001. **I.** Correlation of the levels of CPT1A and fibrosis.

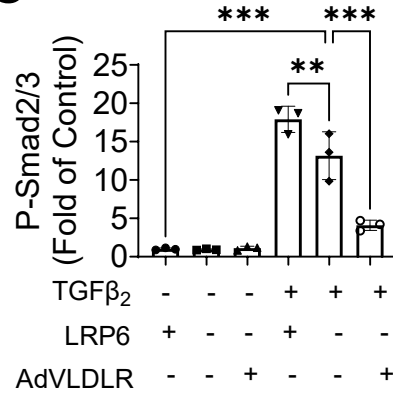
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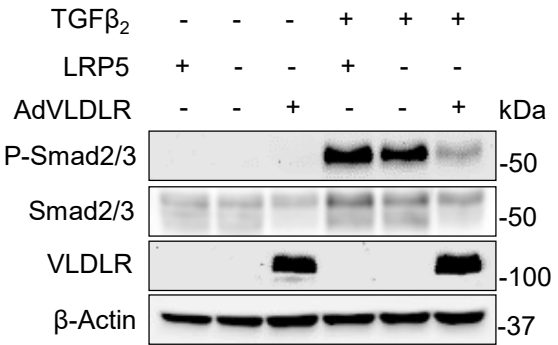
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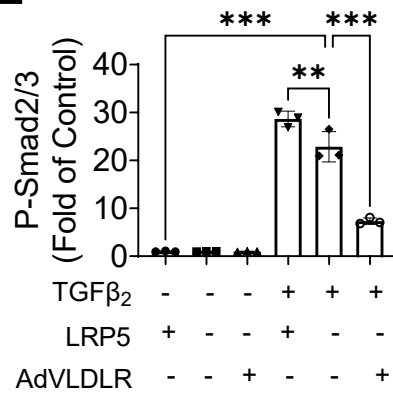
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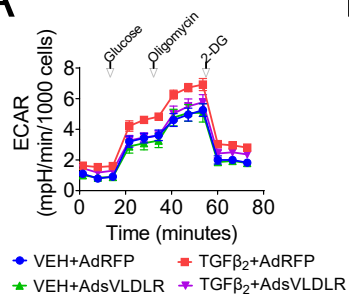
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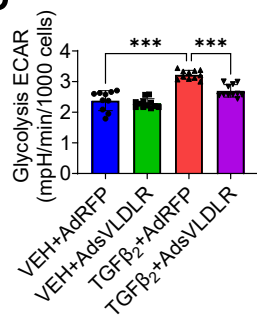
Supplementary Figure 6. VLDLR exerts anti-fibrotic effects in a Wnt coreceptor-independent manner

A: Representative Western blots of LRP5 and LRP6 in WT ARPE-19 cells, ARPE-19 cells with *LRP5* KO, and ARPE-19 cells with *LRP6* KO. **B, C:** Representative images of Western blots in WT ARPE-19 cells and ARPE-19 cells with *LRP5* KO with indicated treatments. Cells were infected with AdVLDLR or AdRFP (MOI = 50) for 24 hr. Then, cells were treated with 5 ng/ml TGF β_2 or vehicle for another 24 hr. **C:** Levels of P-Smad2/3 in (B) were quantified (n = 3). **D, E:** Representative images of Western blots in WT ARPE-19 cells and ARPE-19 cells with *LRP6* KO with indicated treatments. Cells were infected with AdVLDLR or AdRFP (MOI = 50) for 24 hr. Then, cells were treated with 5 ng/ml TGF β_2 or vehicle for another 24 hr. **E:** Levels of P-Smad2/3 in (D) were quantified (n = 3). Data are presented as mean $\pm$ SD. ** P < 0.01, *** P < 0.001.

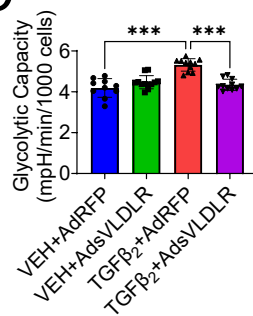
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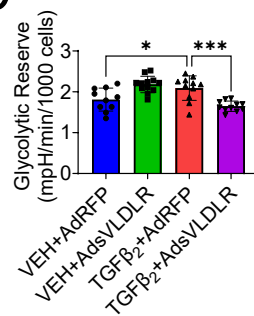
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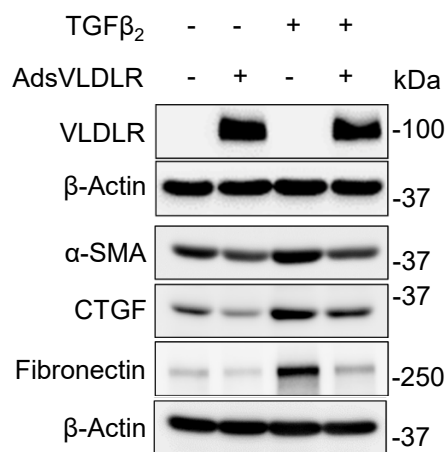
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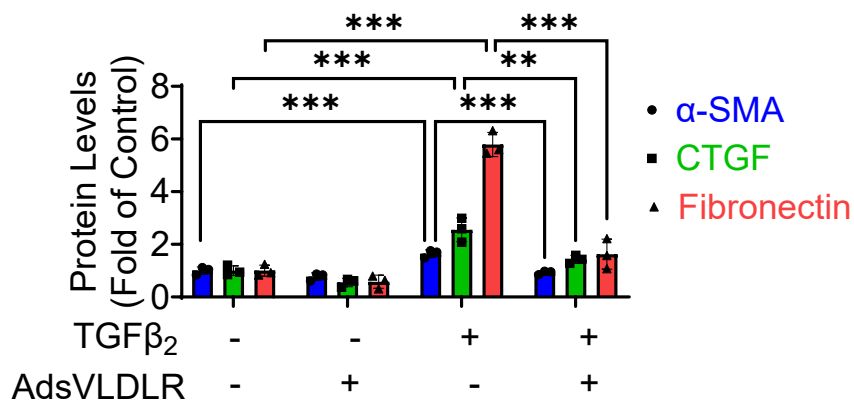
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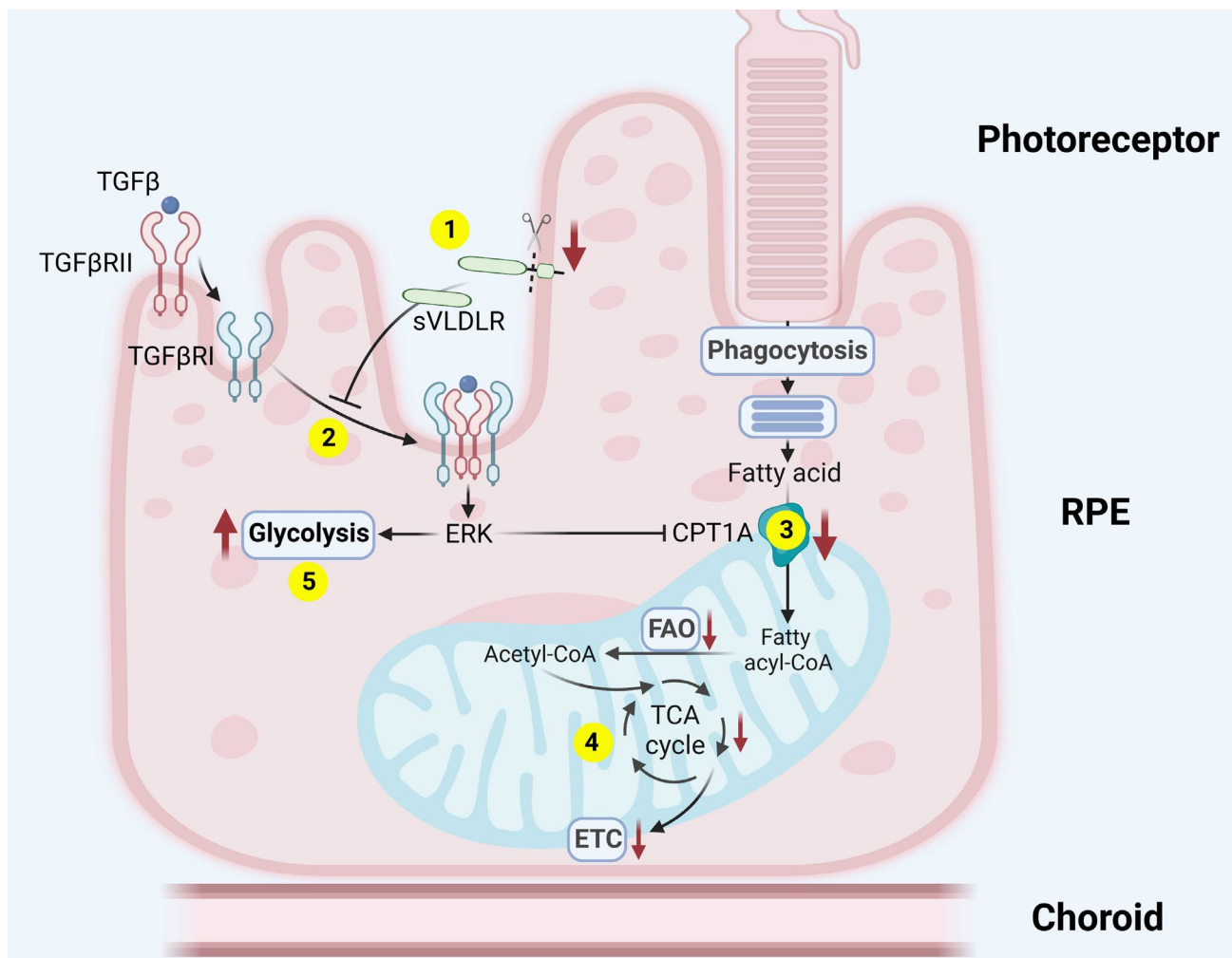


F



Supplementary Figure 7. The soluble ectodomain of VLDLR (sVLDLR) suppresses the TGF β -induced Warburg-like effect and fibrosis

Human primary RPE cells were used for glycolysis stress tests and fibrosis analysis. Cells were infected with AdsVLDLR or AdRFP (MOI = 50) for 24 hr. Then, cells were treated with 5 ng/ml TGF β ₂ or vehicle (VEH) for another 24 hr, and were used for Seahorse assays (A) or Western blot analysis (E). **A:** Glycolysis stress test in human primary RPE cells treated with indicated conditions. Glycolysis (B), glycolytic capacity (C), and glycolytic reserve (D) were compared between groups (n = 10-12). **E:** Representative Western blots of fibrosis markers in human primary RPE cells treated with indicated conditions. **F:** Levels of α -SMA, CTGF, and fibronectin in E were quantified (n = 3). One-way ANOVA analysis was used to compare each group to third group with TGF β ₂ and control virus. Data are presented as mean $\pm$ SD. ** P < 0.01, *** P < 0.001.



Supplementary Figure 8. VLDLR blocks TGF β -induced metabolic reprogramming and fibrosis by interacting with TGF β receptor II in retinal epithelium

In the current study, we found that soluble ectodomain of VLDLR (sVLDLR) blocks TGF β -induced metabolic reprogramming and fibrosis at TGF β receptor level (Number 1 and 2). TGF β_2 induced a Warburg-like effect in an ERK-dependent manner. TGF β_2 suppressed the accessibility of fatty acids (FA) in the mitochondrial matrix by promoting the degradation of carnitine palmitoyltransferase 1A (CPT1A), a crucial enzyme that facilitates FA entrance into mitochondria (Number 3). TGF β_2 induced metabolic reprogramming with the downregulation of mitochondrial metabolism and upregulation of glycolysis, which worsened the health of photoreceptors by reducing the glucose supply from choroidal vessels into the interphotoreceptor matrix (Number 4 and number 5). Our work indicates that VLDLR rebalances metabolic reprogramming and potentially suppresses TGF β_2 -mediated fibrogenesis by interacting with unglycosylated TGF β receptor II and blocking the heterotetramer formation between TGF β receptor I and TGF β receptor II (Number 2). The anti-fibrotic effect of VLDLR was independent of its well-known function in lipid uptake, since the soluble ectodomain of VLDLR (sVLDLR) also exerted an anti-fibrotic effect (Number 1). This study provides insightful clues for treating subretinal fibrosis. FAO: fatty acid β -oxidation, ETC: electron transport chain. Figure was prepared by Biorender.

Figure 1F: α -SMA, CTGF, Fibronectin, VLDLR, β -Actin

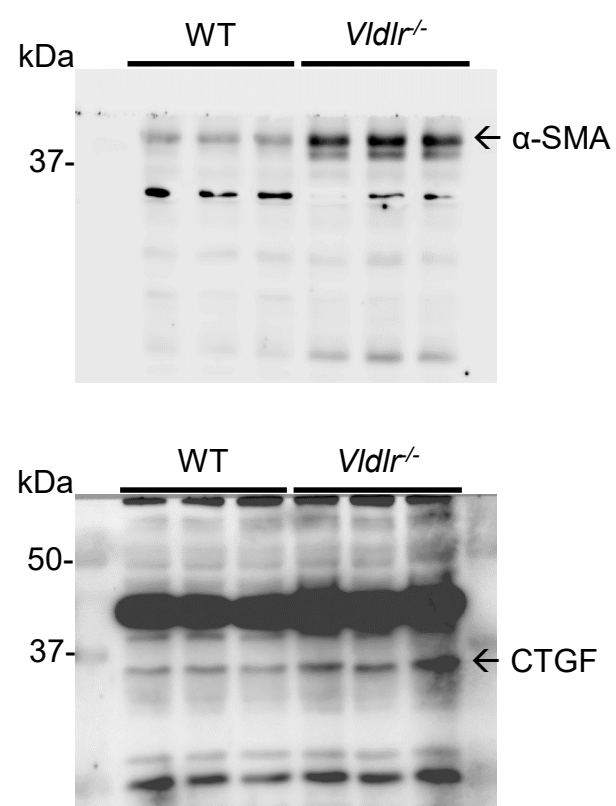


Figure 1F: α -SMA, CTGF, Fibronectin, VLDLR, β -Actin

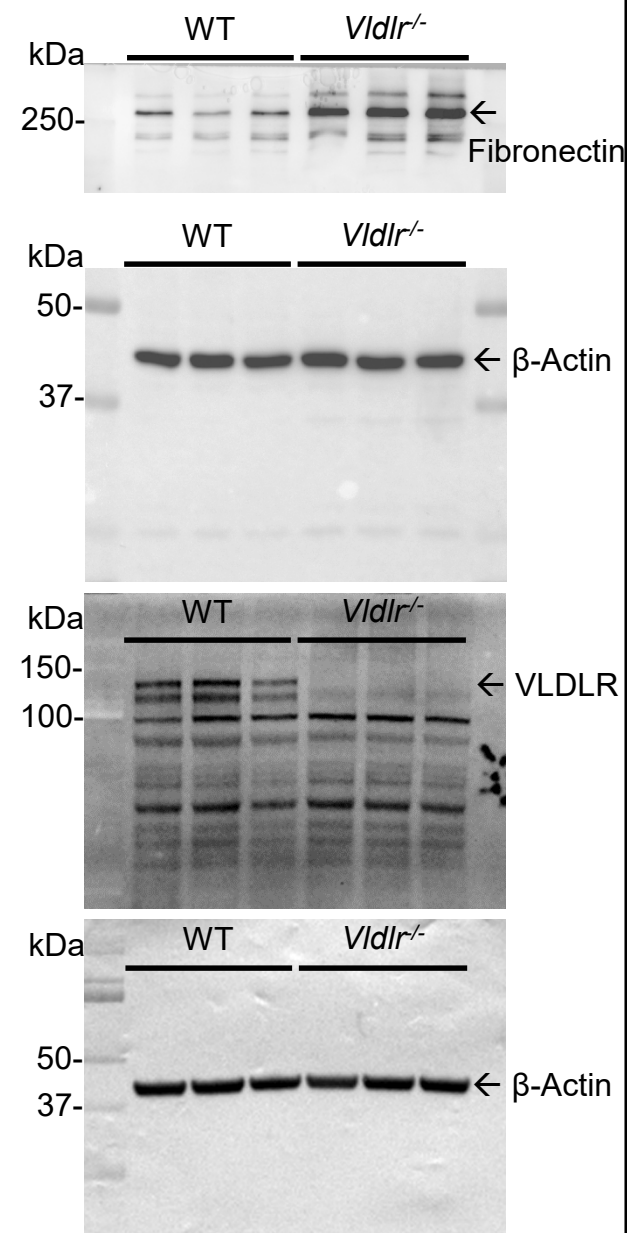


Figure 4M: VLDLR, α -SMA, CTGF, Fibronectin, β -Actin

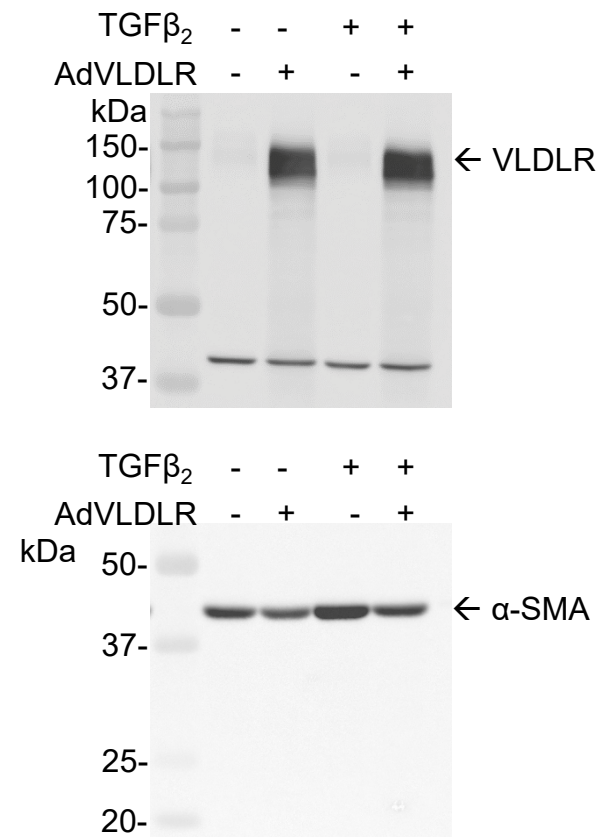


Figure 4M: VLDLR, α -SMA, CTGF, Fibronectin, β -Actin

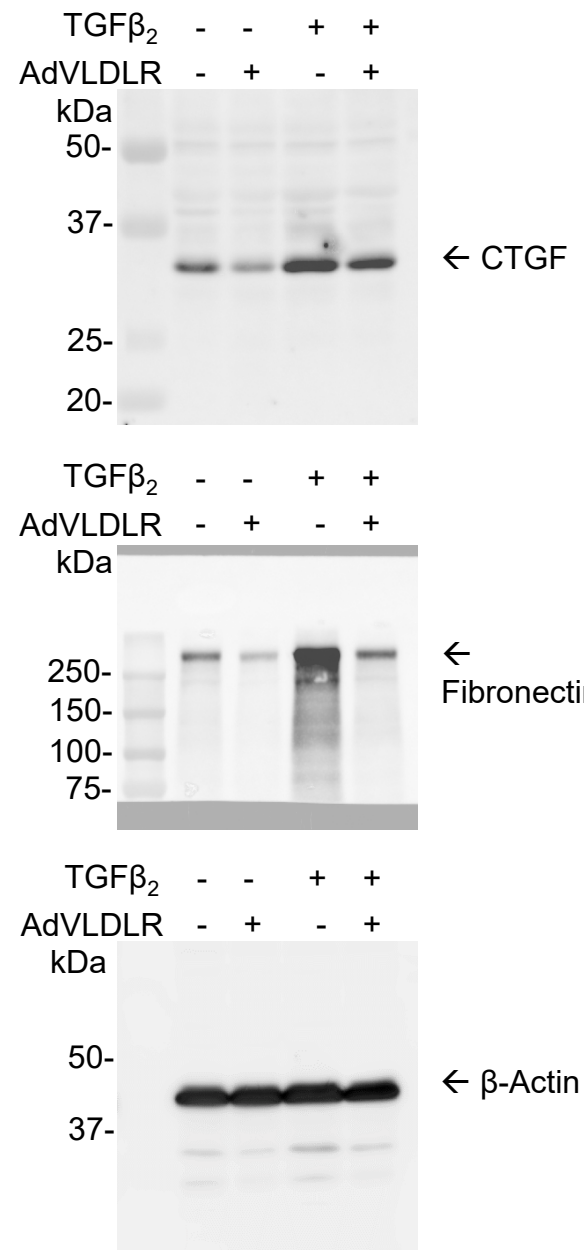


Figure 4O: α -SMA, CTGF, Fibronectin, β -Actin

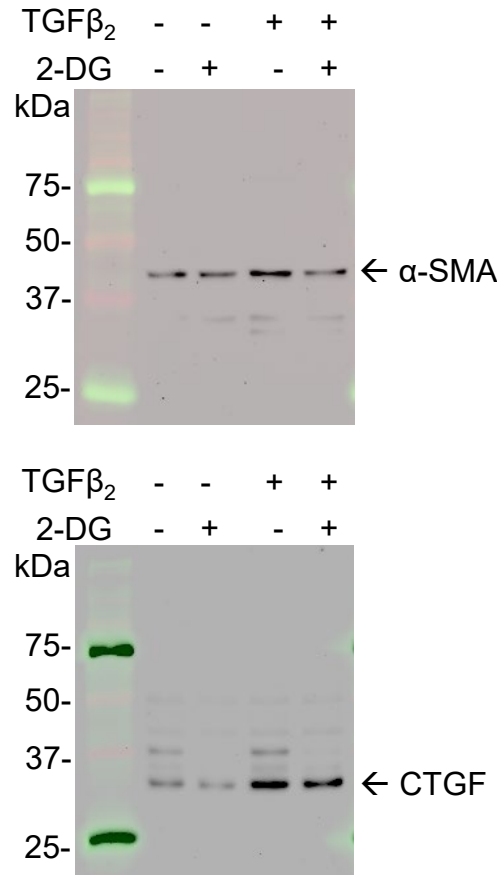


Figure 4O: α -SMA, CTGF, Fibronectin, β -Actin

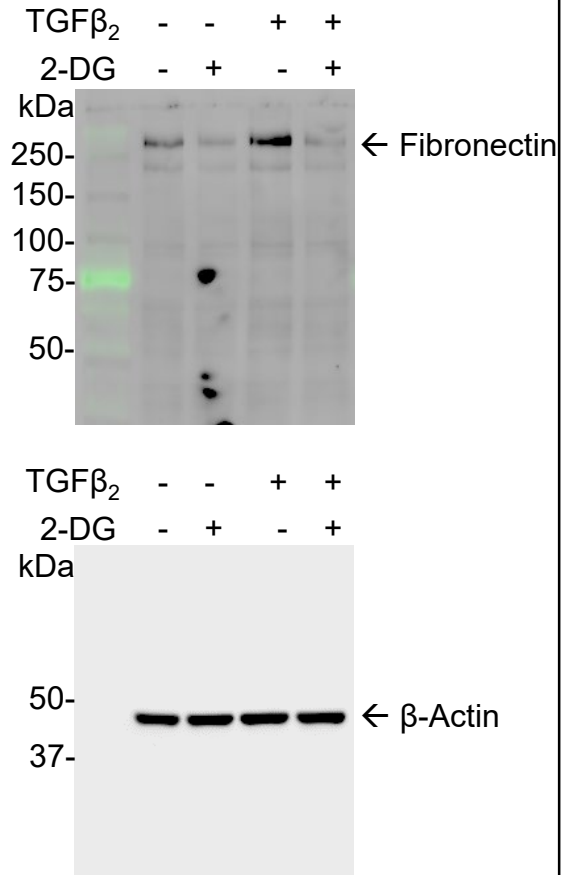


Figure 5C: CPT1A, β -Actin

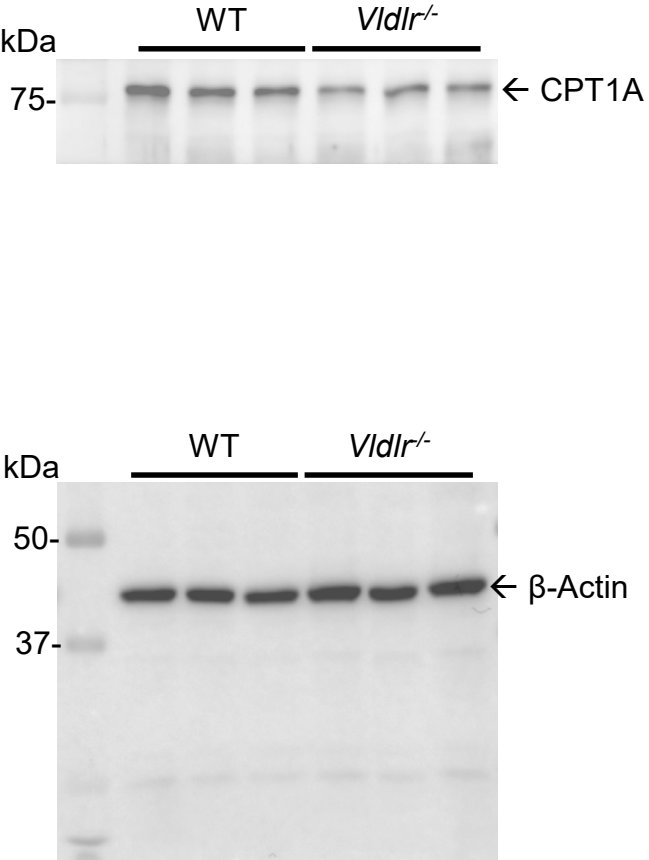


Figure 6I: CPT1A, α -SMA, CTGF, Fibronectin, β -Actin

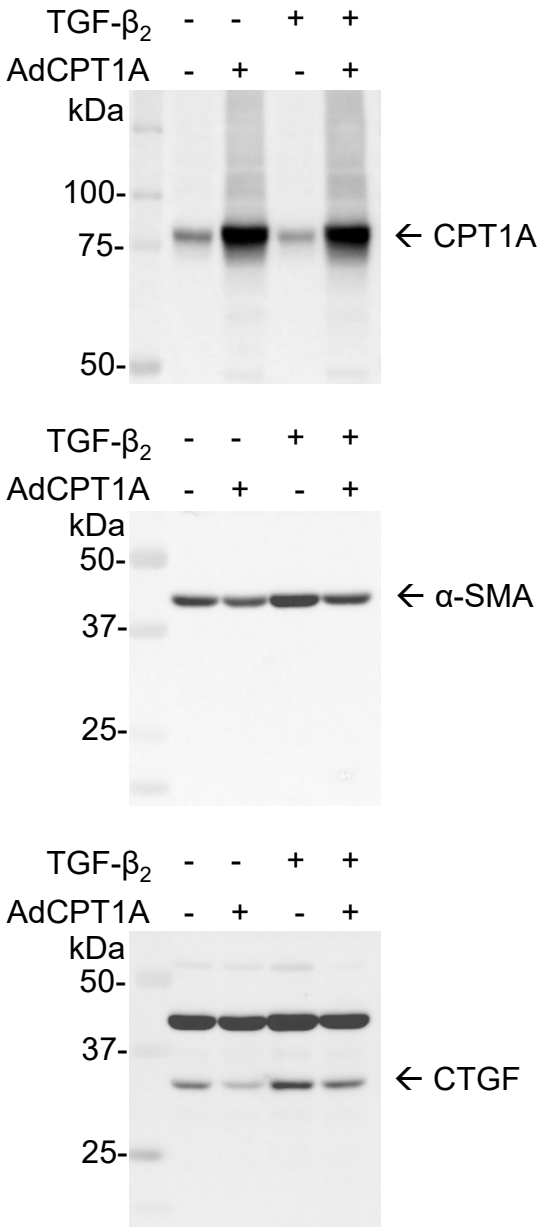


Figure 6I: CPT1A, α -SMA, CTGF, Fibronectin, β -Actin

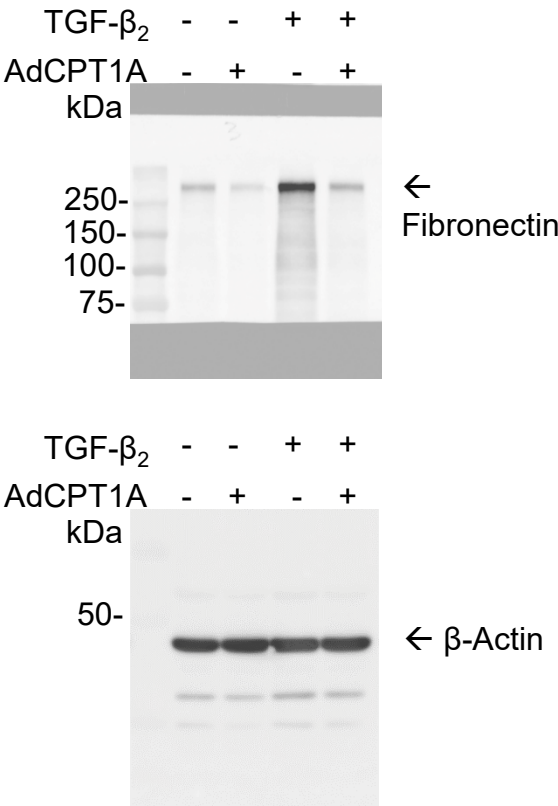


Figure 6L: CPT1A, α -SMA, CTGF, Fibronectin, β -Actin

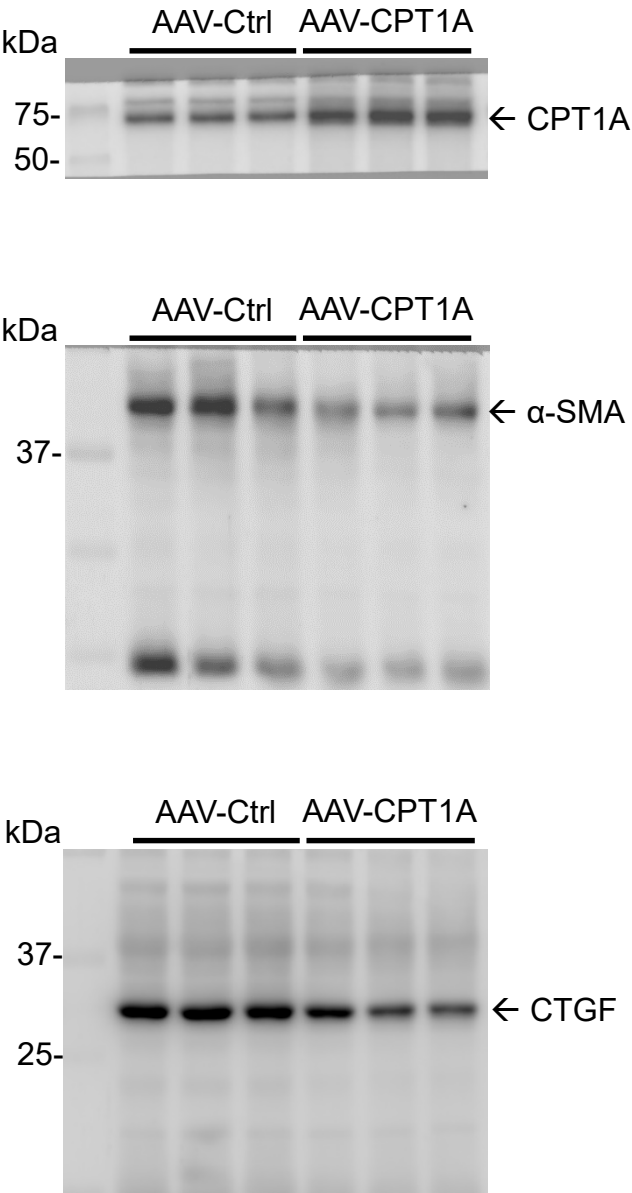


Figure 6L: CPT1A, α -SMA, CTGF, Fibronectin, β -Actin

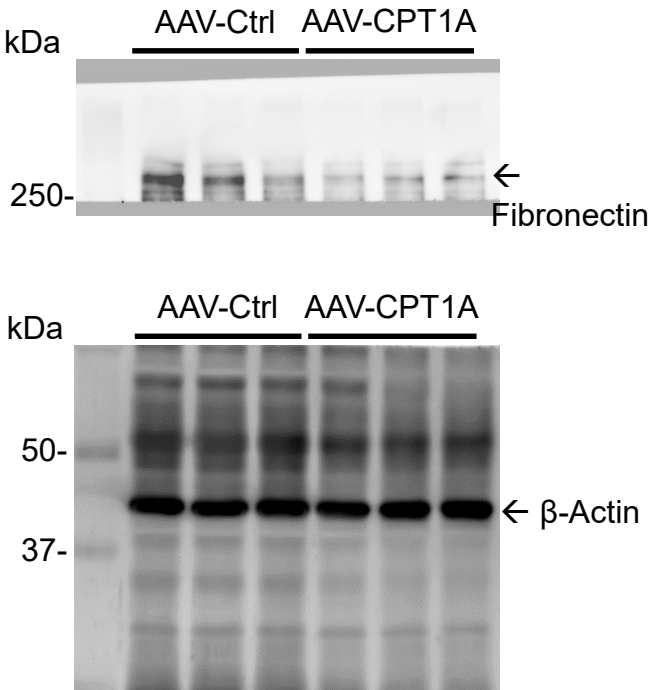
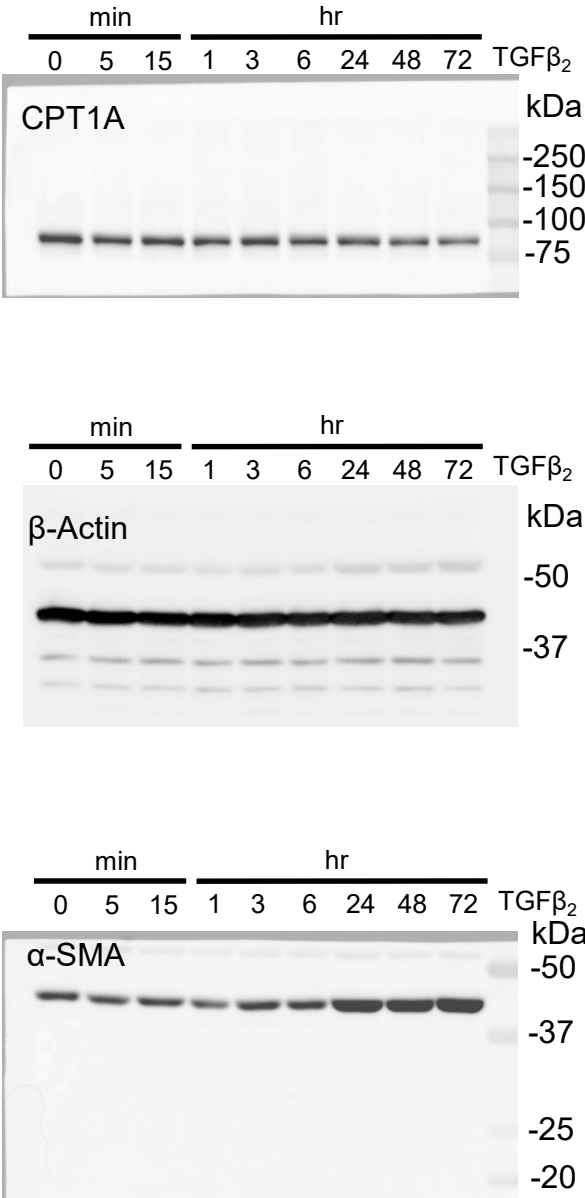
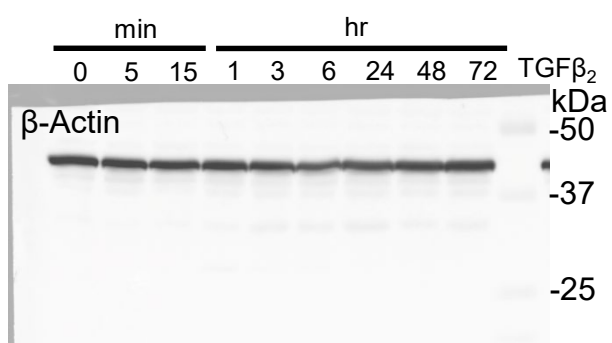
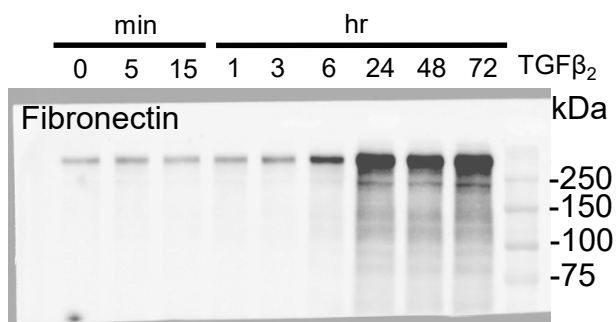


Figure 7A: CPT1A, β -Actin, α -SMA, CTGF, Fibronectin, β -Actin

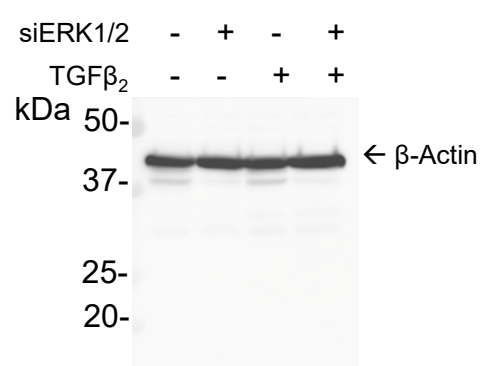
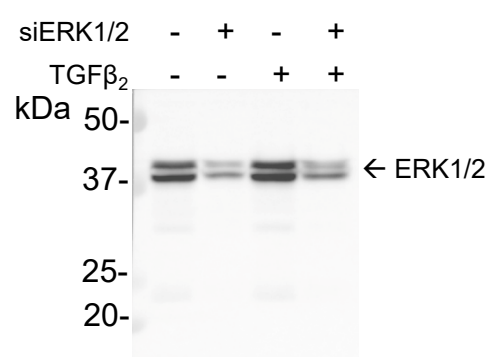


Western blot analysis of CTGF protein levels in HSCs. The blot shows protein bands at approximately 37 kDa (CTGF) and 25 kDa (TGFβ2). Time points are 0, 5, 15 min and 1, 3, 6, 24, 48, 72 hr. An arrow points to the CTGF band at 37 kDa.

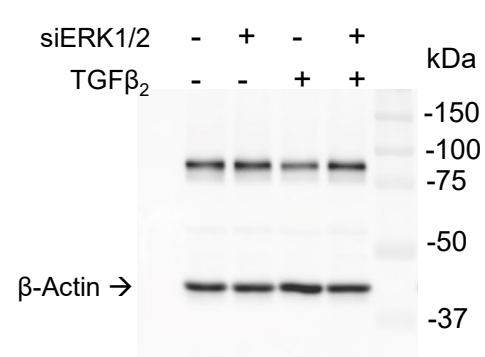


siERK1/2	-	+	-	+
TGFβ ₂	-	-	+	+
kDa	50-			
	37-			
	25-			
	20-			

← P-ERK1/2

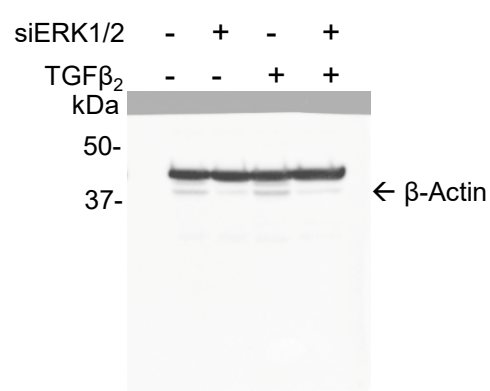
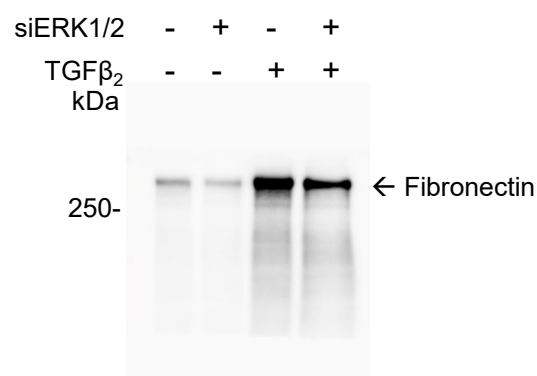


siERK1/2	-	+	-	+	
TGFβ ₂	-	-	+	+	kDa
CPT1A →					

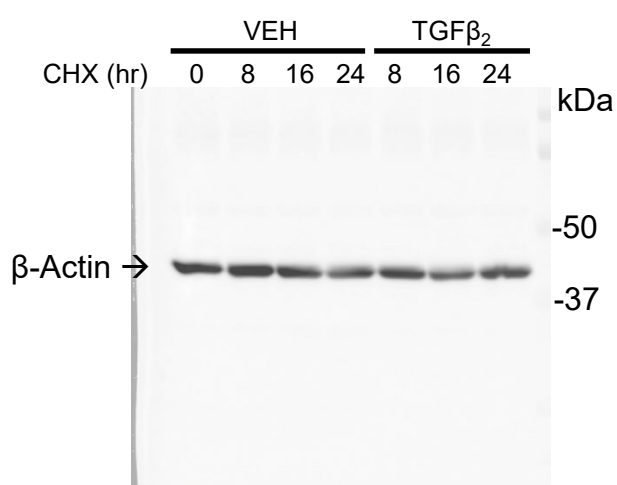


siERK1/2	-	+	-	+
TGFβ ₂	-	-	+	+
kDa				
37-				
25-				

← CTGF

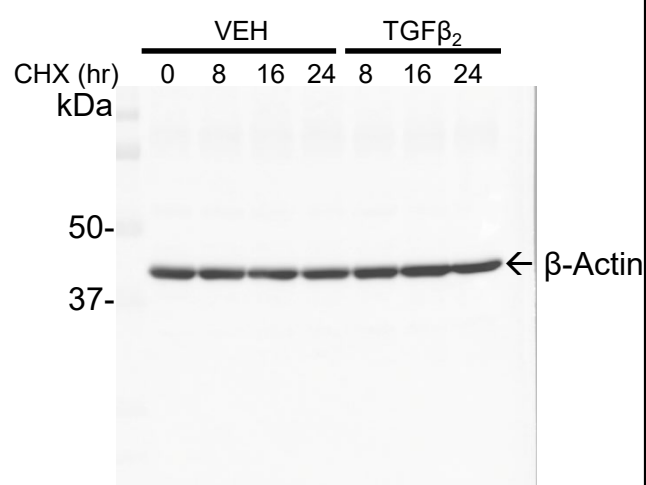


CHX (hr)	VEH				TGFβ ₂				kDa
	0	8	16	24	8	16	24		
CPT1A →	~100	~100	~100	~100	~100	~100	~100	~100	250 150 100 75



CHX (hr)	VEH				TGFβ ₂			
	0	8	16	24	8	16	24	
250-								
150-								
100-								
75-								

← CPT1A



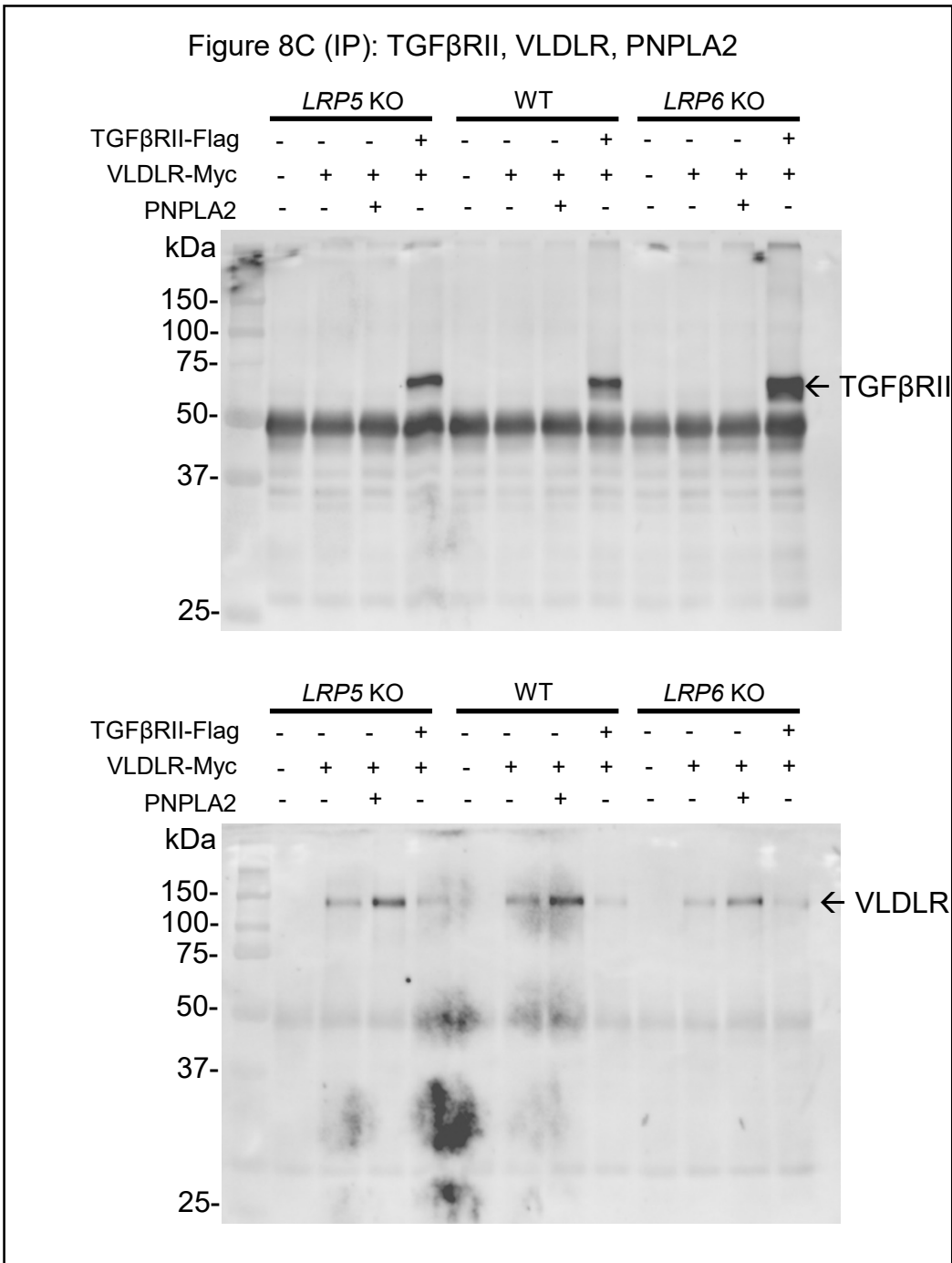
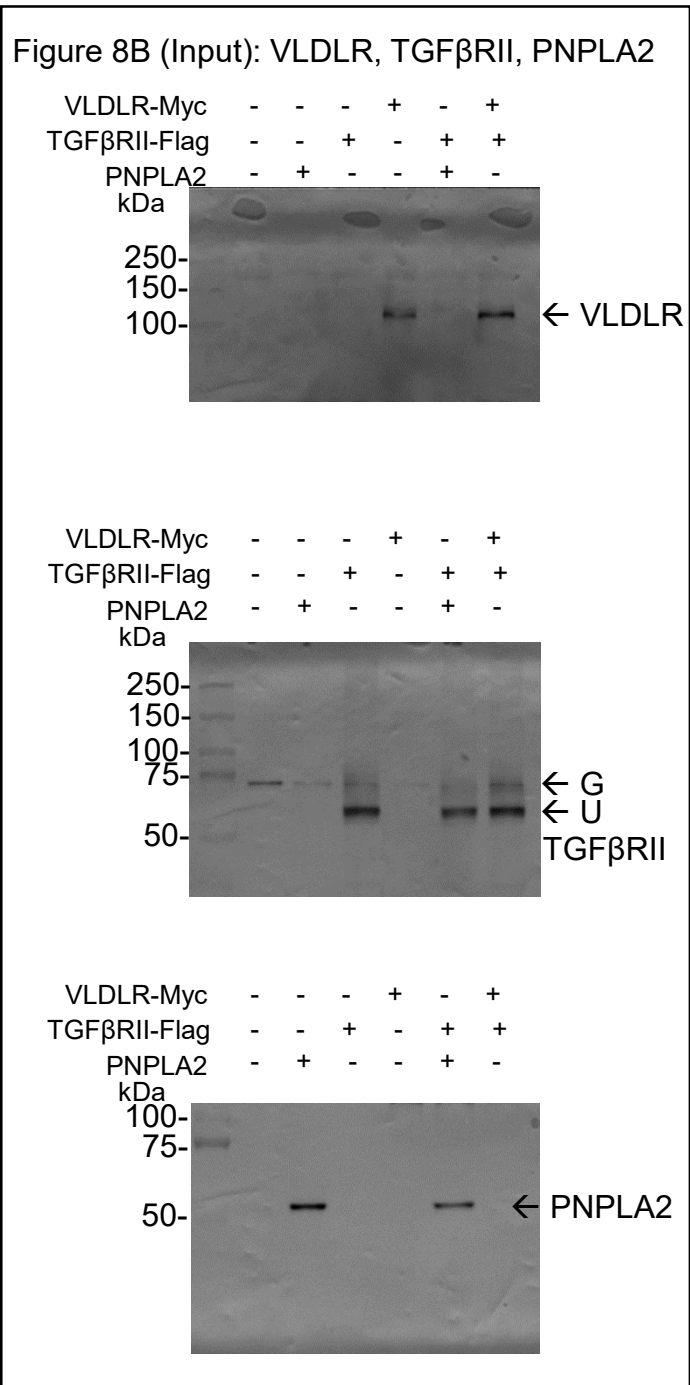
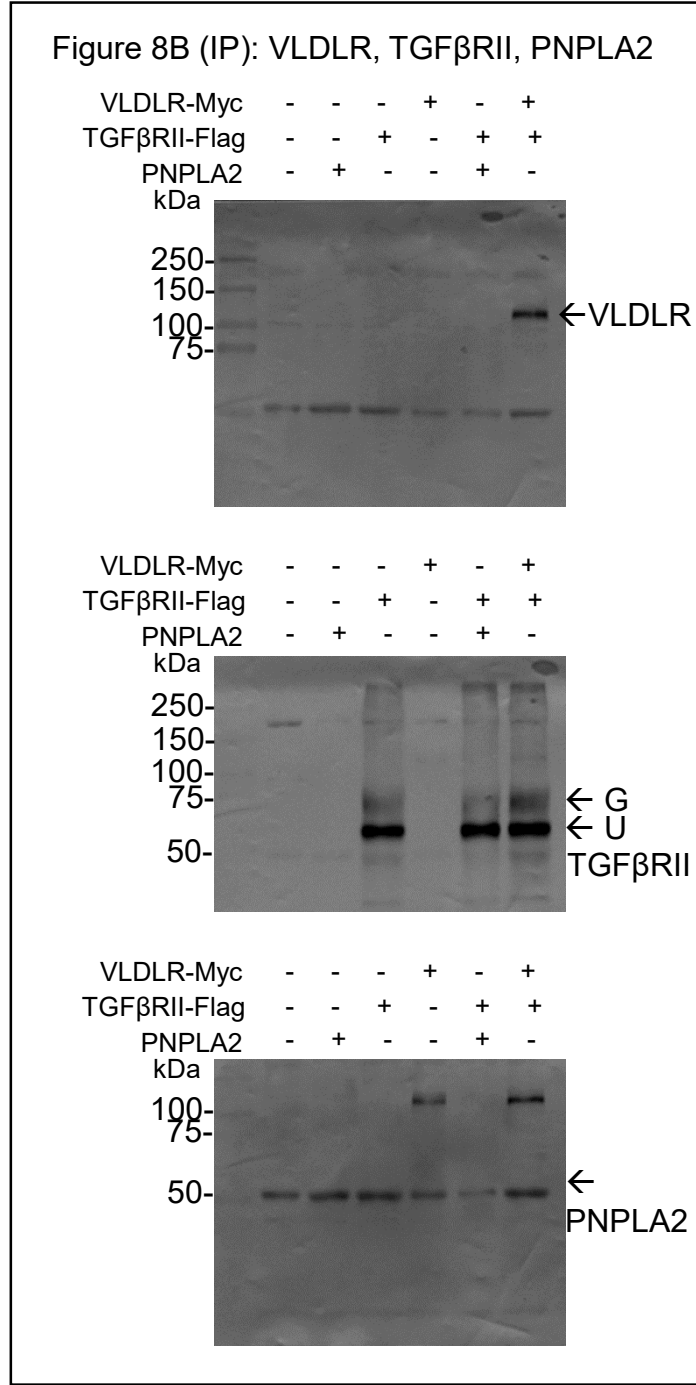
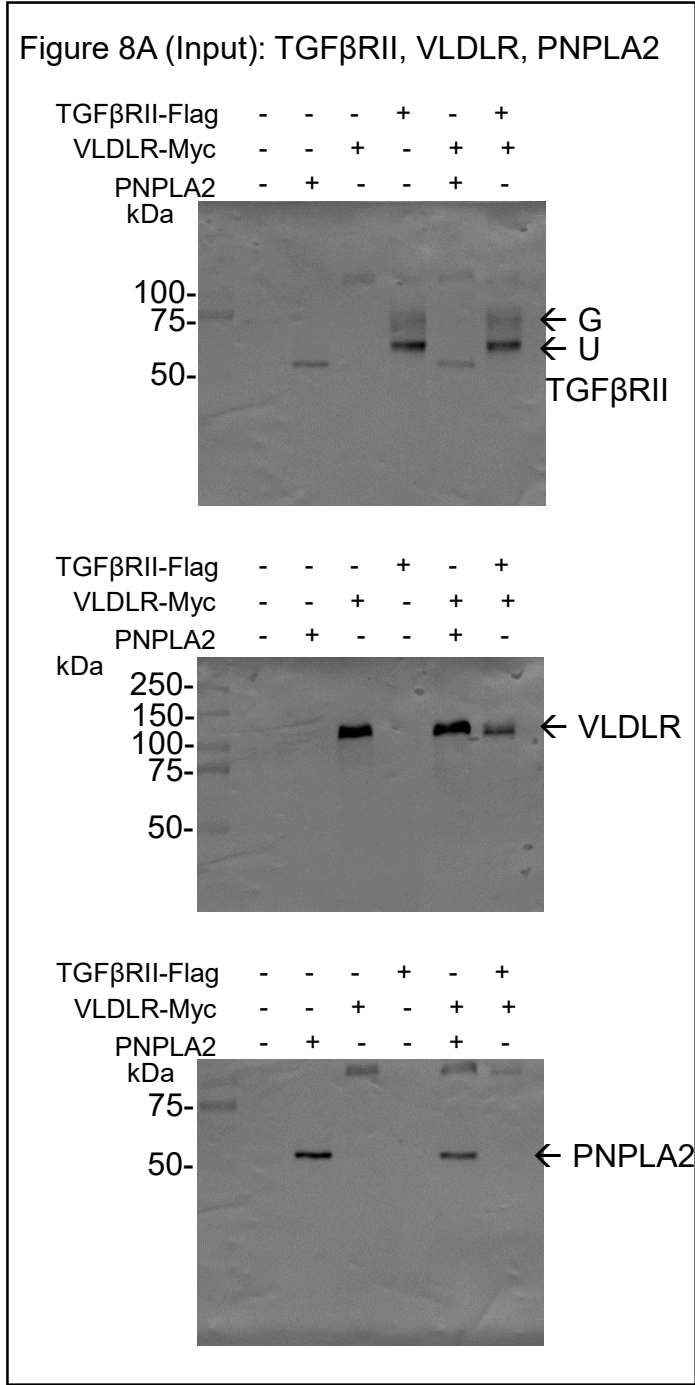
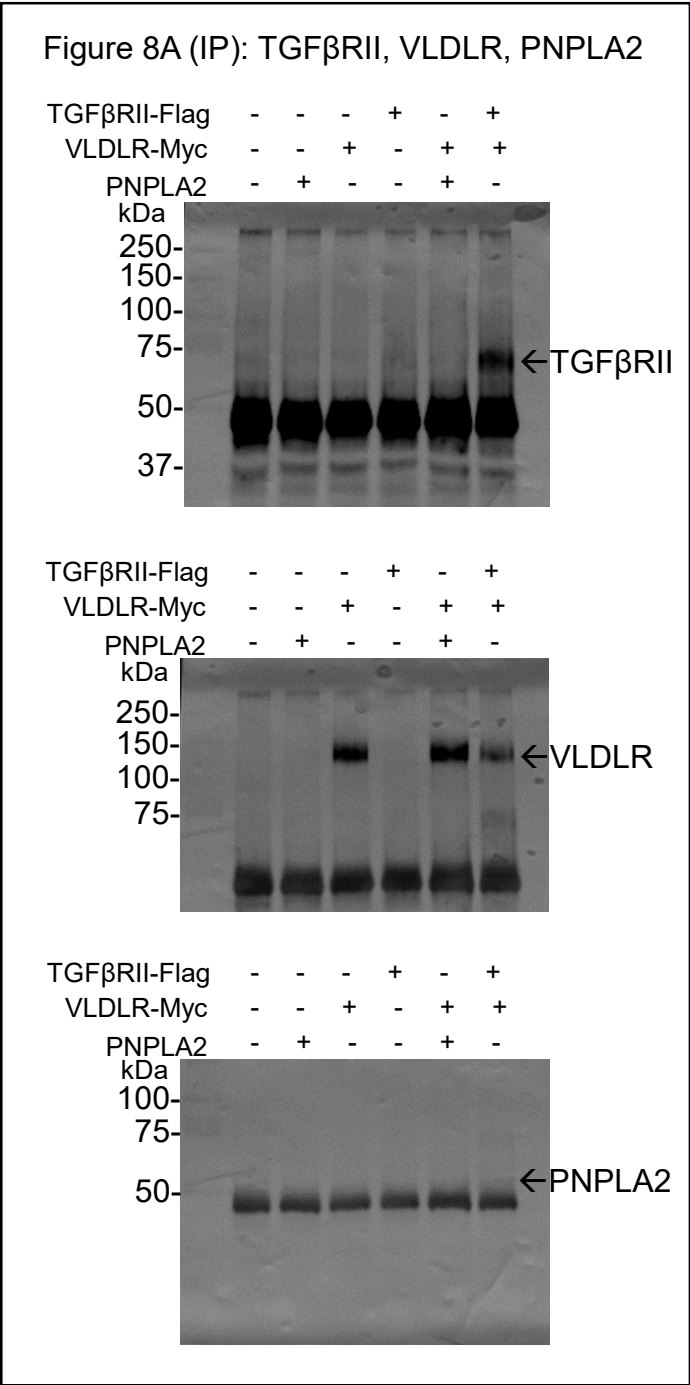


Figure 8C (IP): TGFβRII, VLDLR, PNPLA2

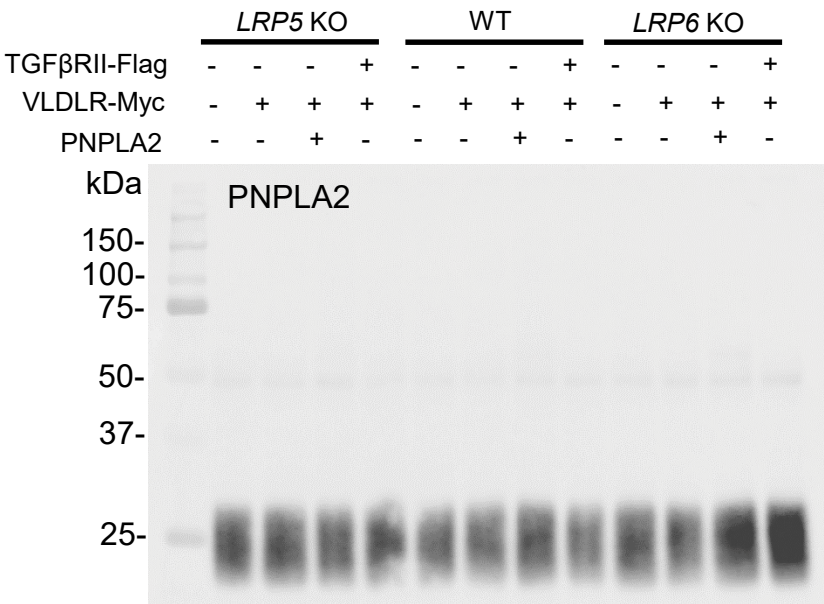


Figure 8C (input): TGFβRII, VLDLR, PNPLA2, GAPDH

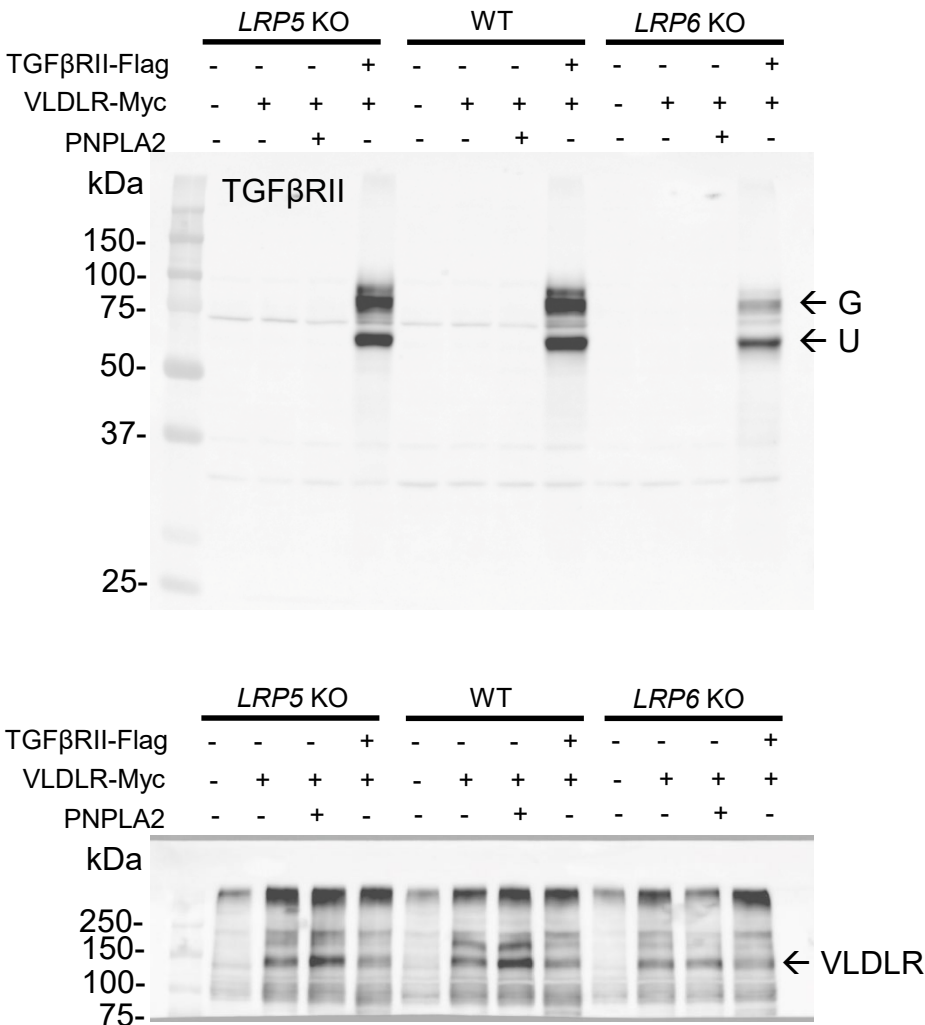


Figure 8C (input): TGFβRII, VLDLR, PNPLA2, GAPDH

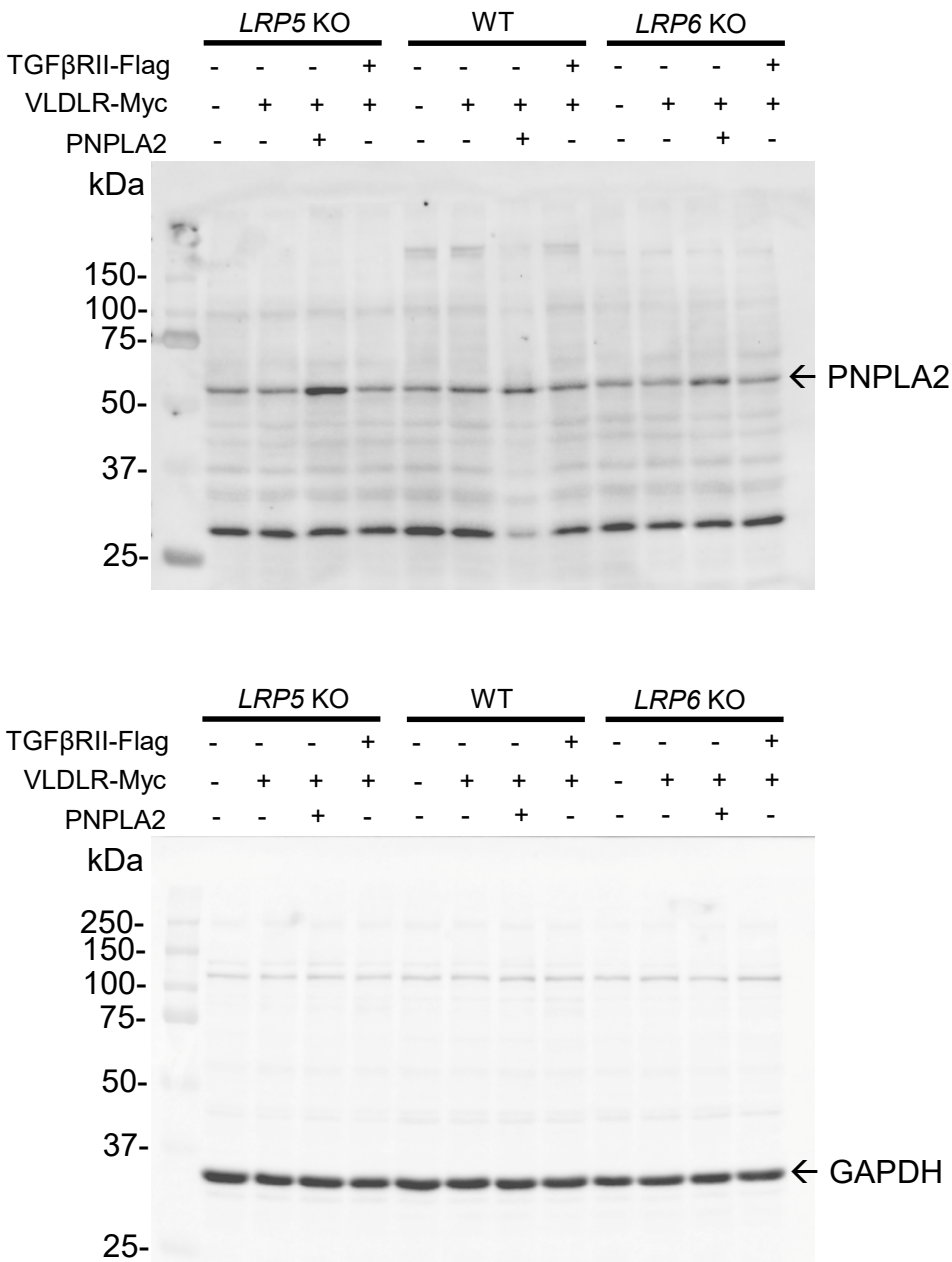


Figure 8D (IP): TGFβRI, TGFβRII, VLDLR

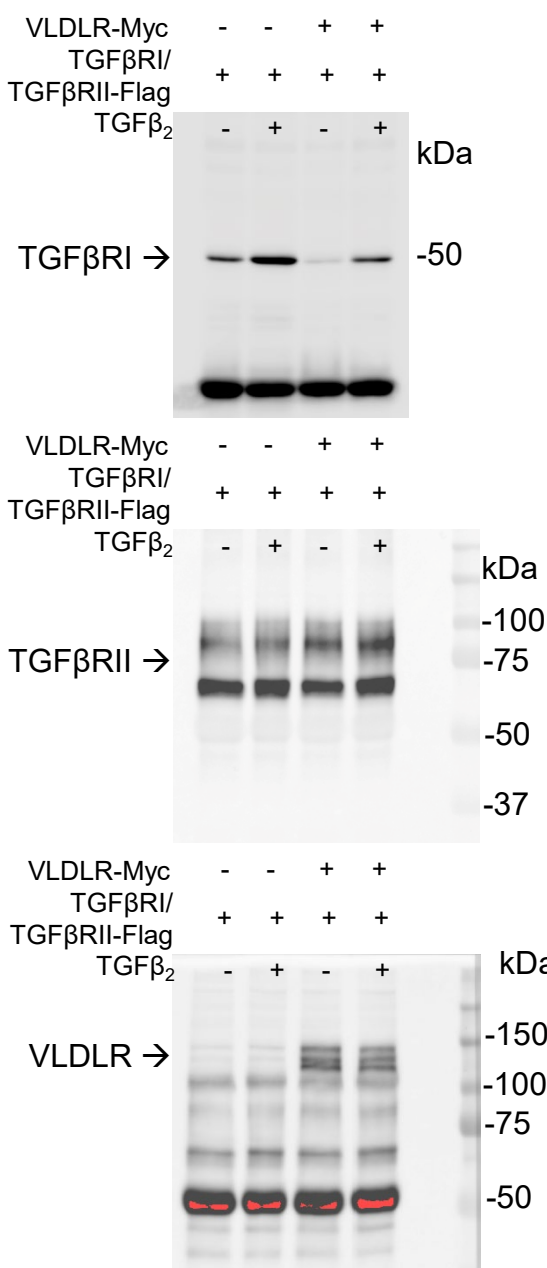


Figure 8D (Input): TGFβRI, TGFβRII, VLDLR

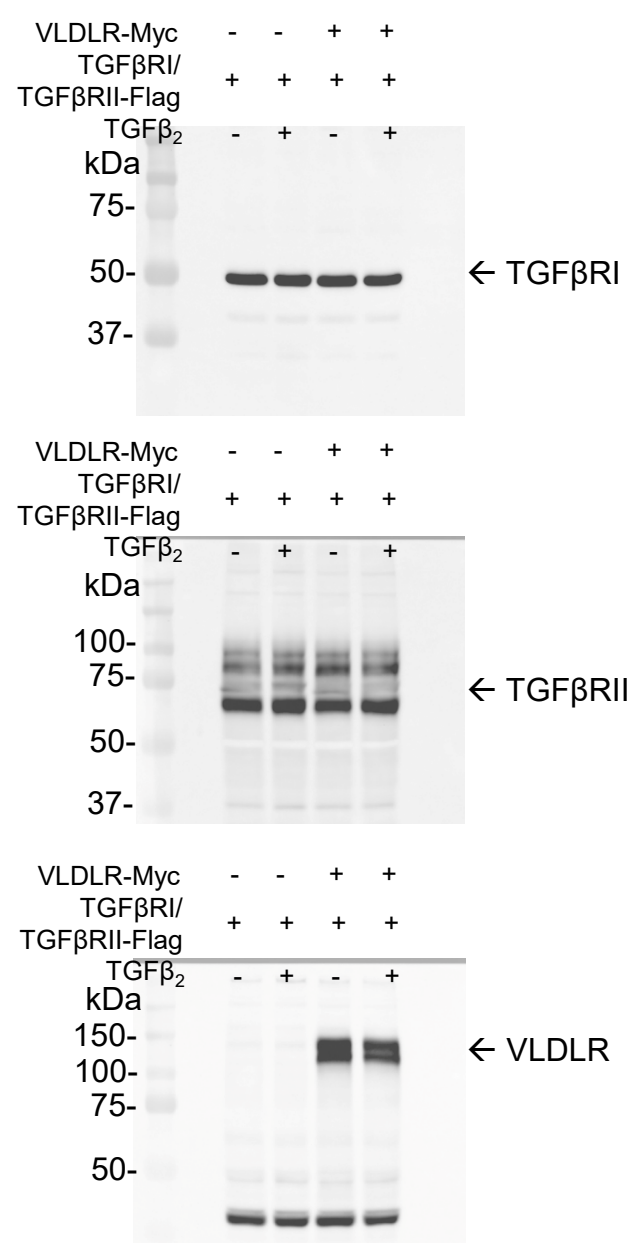


Figure S5A: CPT1A, β-Actin

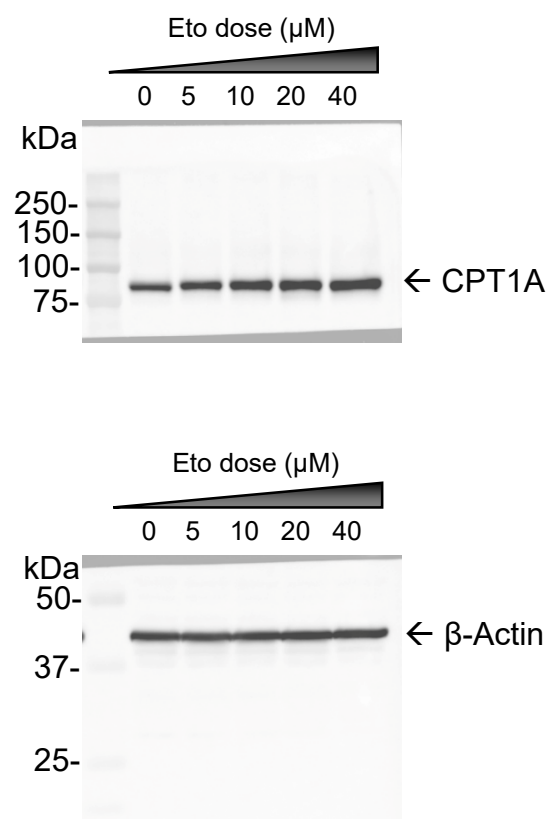


Figure S5C: CPT1A, Fibronectin, β-Actin

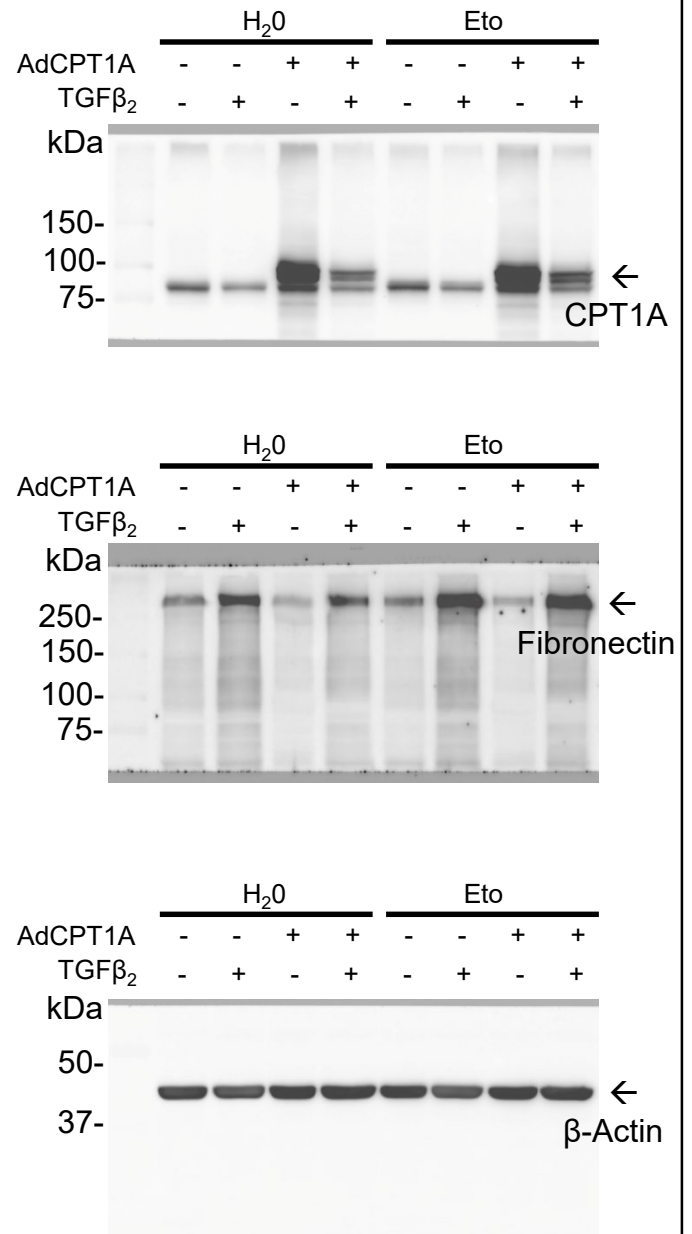


Figure S5F: CPT1A, Fibronectin, CTGF, β-Actin

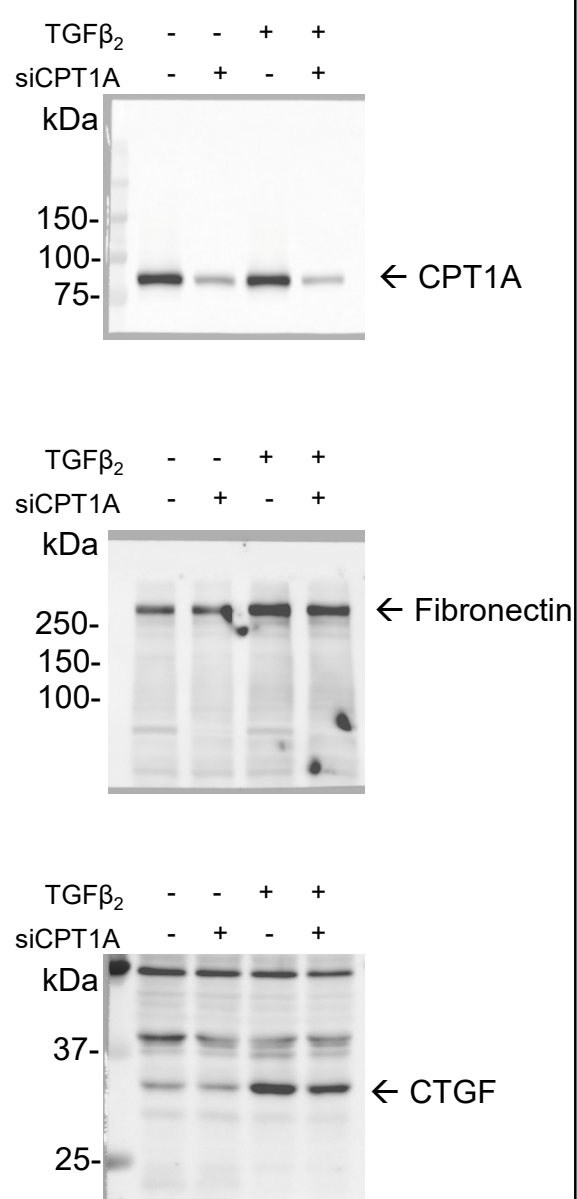


Figure S5C: CPT1A, Fibronectin, CTGF, β-Actin

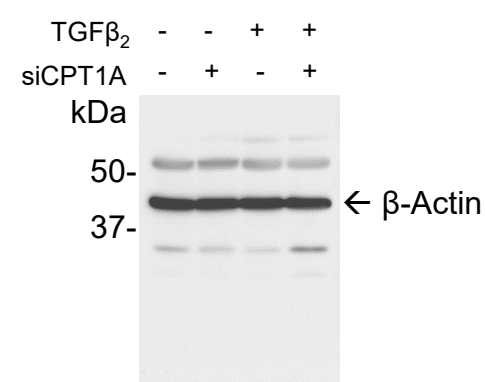
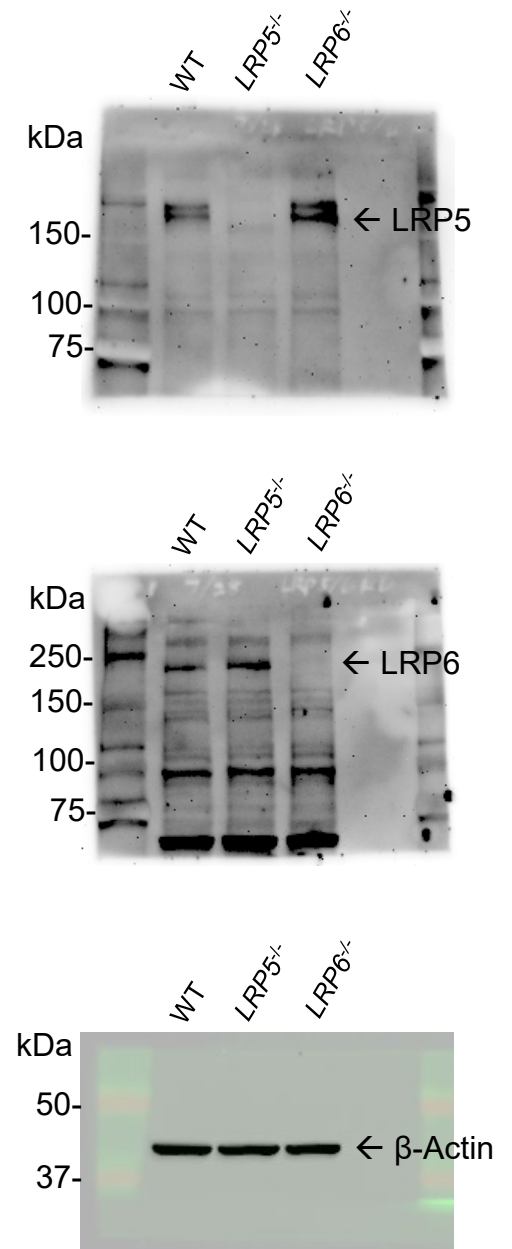
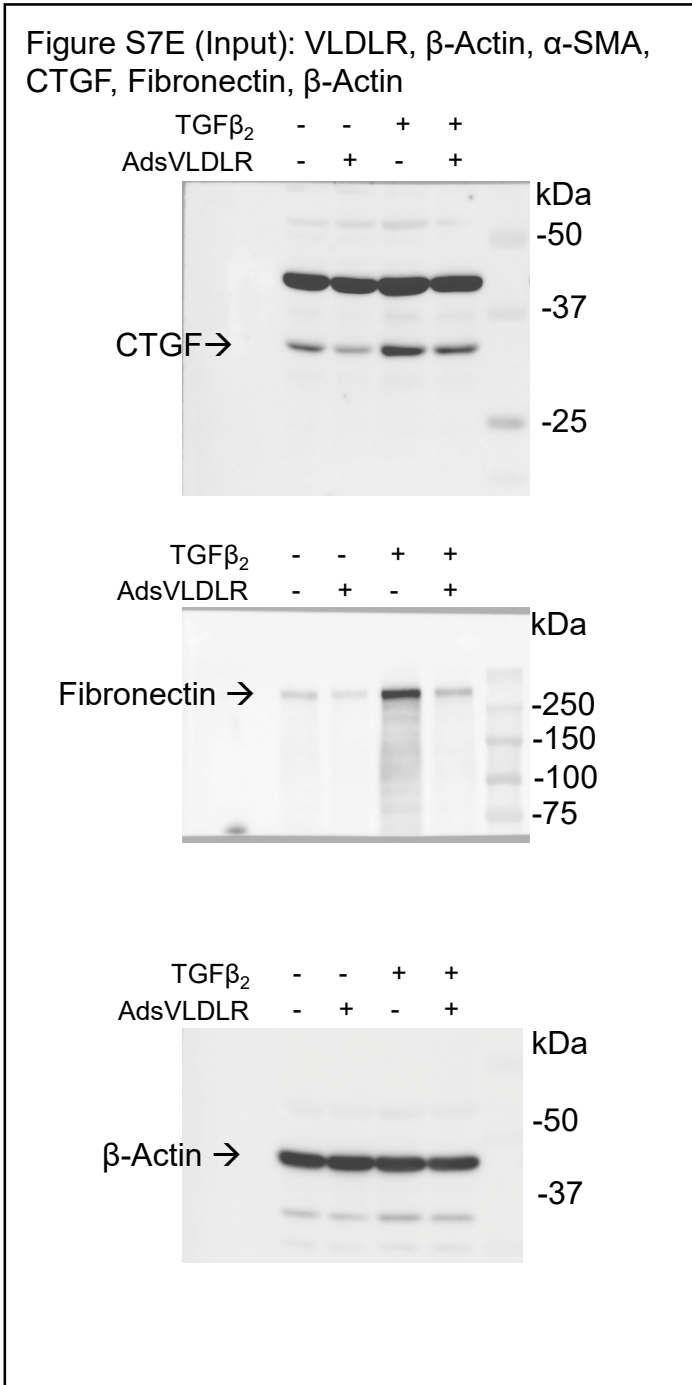
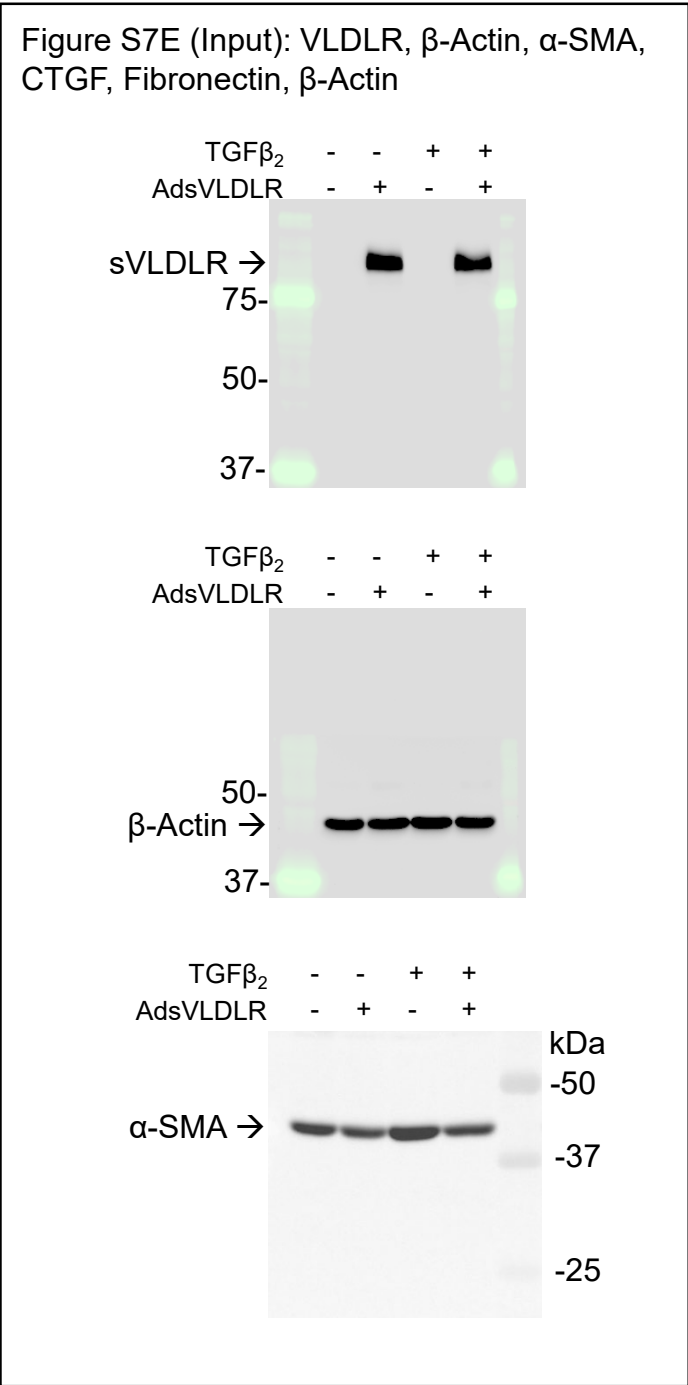
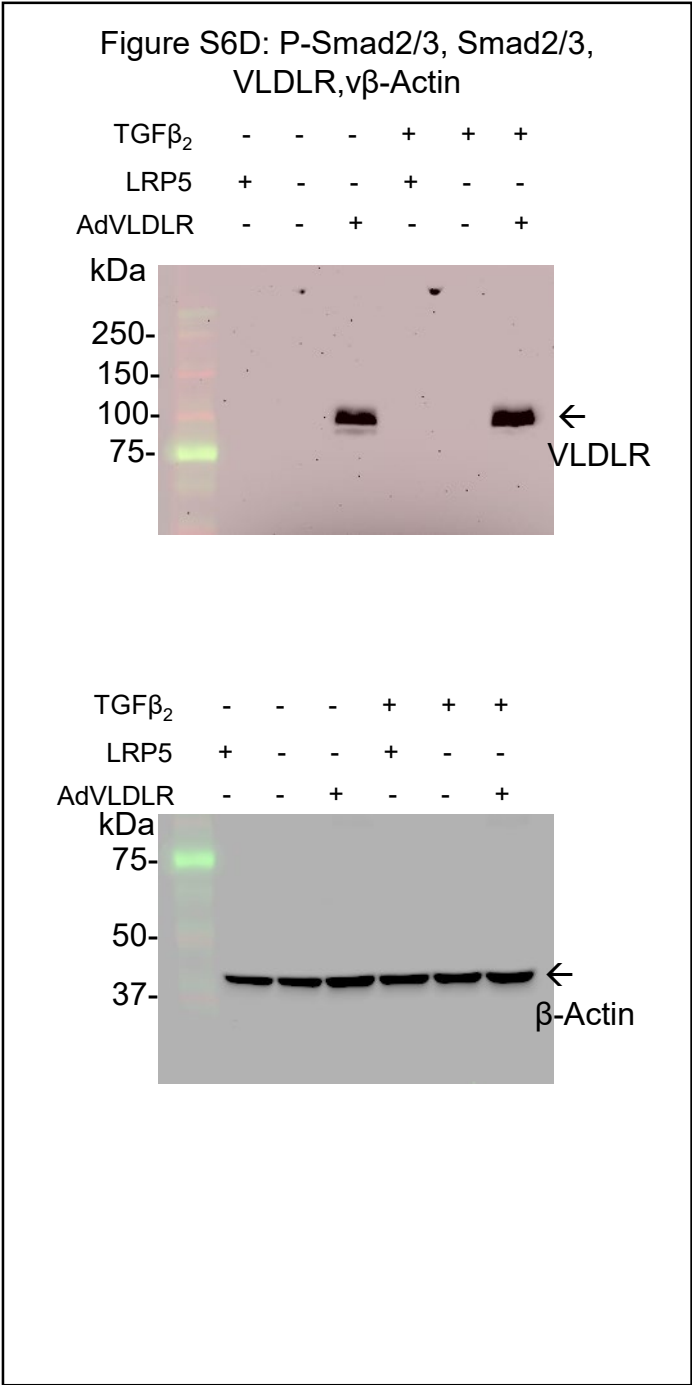
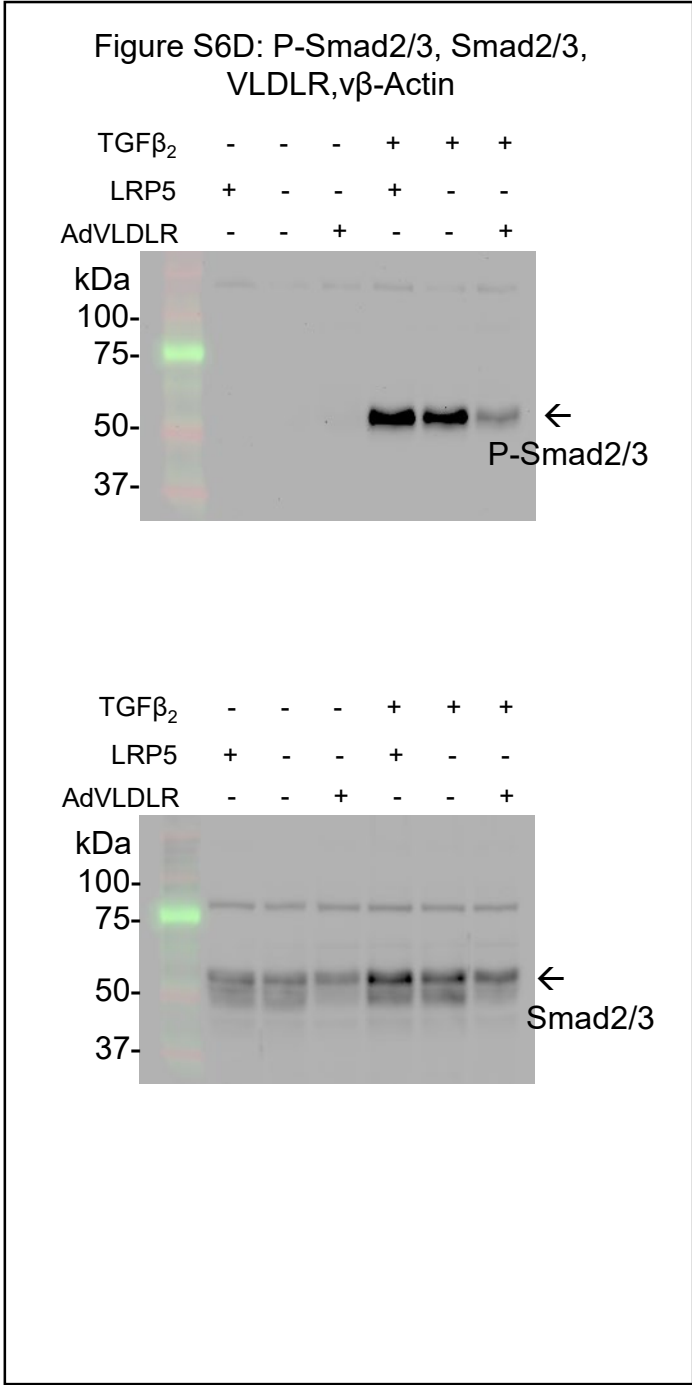
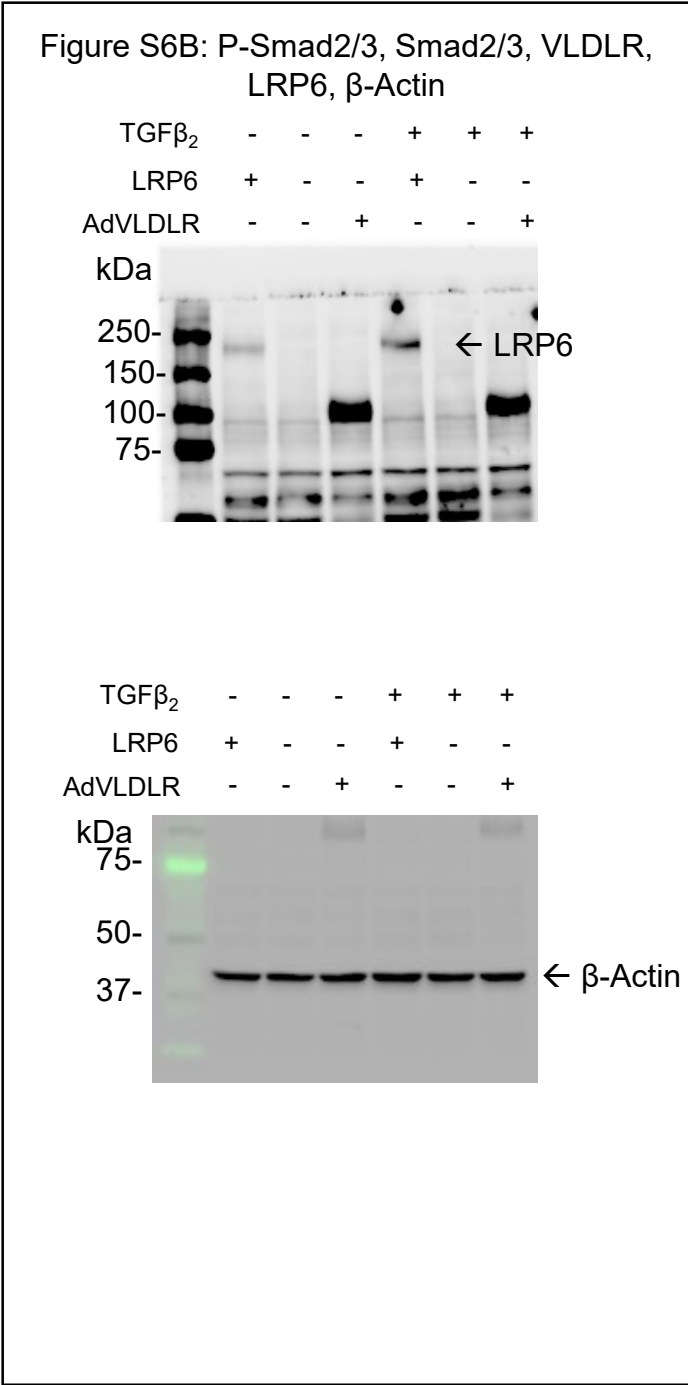
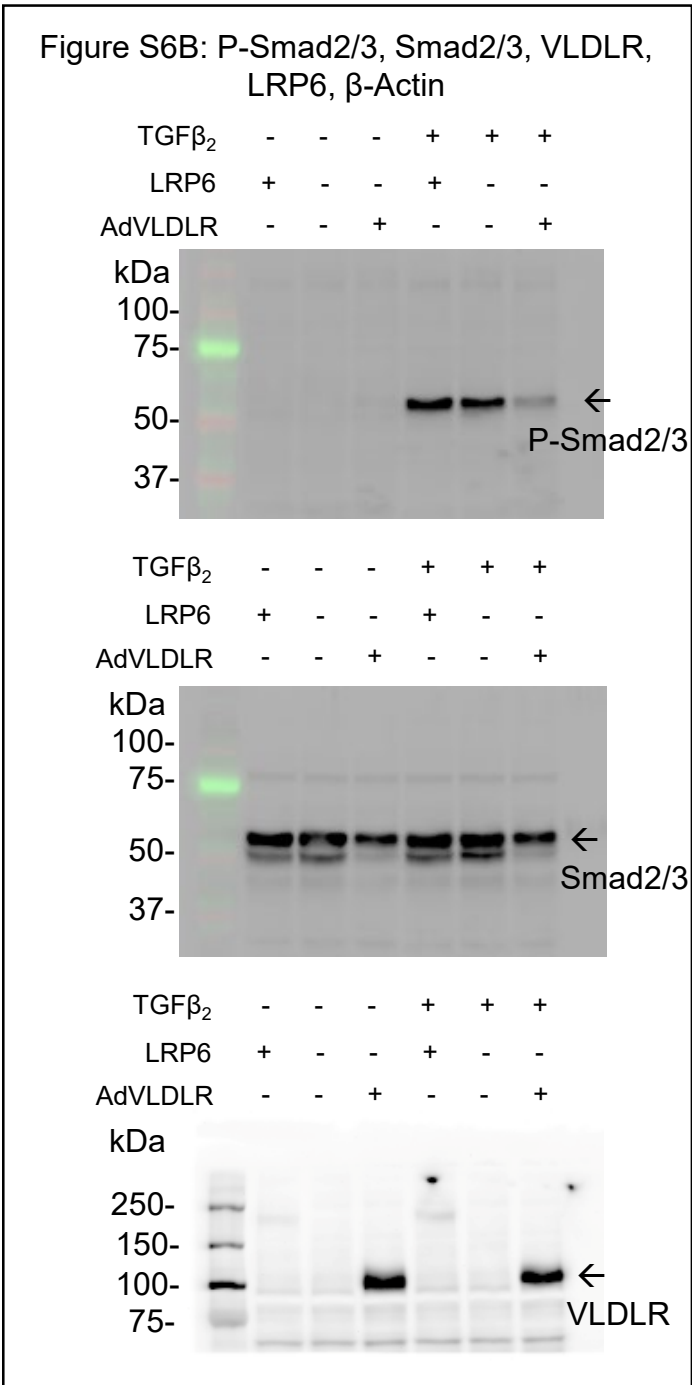


Figure S6A: LRP5, LRP6, β-Actin





Supplementary Figure 9. Uncropped and unedited Western blots of all the indicated figures

Supplementary Table 1. Differential expressed genes in each cluster.
(Genes with avg_log2FC larger or equal to 2.5 were listed)

	p_val	avg_log2FC	pct.1	pct.2	p_val_adj	cluster
Ttr	0	3.22427557	1	0.593	0	0
Ptgds	0	2.91535797	1	0.64	0	0
Rbp1	0	2.71466434	1	0.516	0	0
Mt3	0	2.55525348	0.992	0.308	0	0
Rdh5	0	2.53192969	0.999	0.367	0	0
Lum	0	3.47088789	0.967	0.087	0	1
Mgp	0	3.43952631	0.979	0.203	0	1
Serpine2	0	3.31192313	0.989	0.149	0	1
Igfbp5	0	3.18580021	1	0.433	0	1
Lsamp	0	3.1546578	0.94	0.077	0	1
Cebpd	0	3.1414973	0.907	0.217	0	1
Egr1	0	2.99273885	0.838	0.167	0	1
Cxcl12	0	2.94788494	0.95	0.103	0	1
Igfbp4	0	2.89842637	0.965	0.194	0	1
Cdh11	0	2.86628719	0.959	0.11	0	1
Gsn	0	2.83669728	0.95	0.192	0	1
Edn3	0	2.81880985	0.953	0.108	0	1
Tsc22d1	0	2.73121304	0.938	0.356	0	1
Cped1	0	2.70331709	0.965	0.126	0	1
Akap12	0	2.65118169	0.955	0.173	0	1
Pdgfra	0	2.64165938	0.896	0.066	0	1
Angpt1	0	2.56670969	0.86	0.09	0	1
Mir99ahg	0	2.55314333	0.943	0.186	0	1
Lama2	0	2.53043569	0.86	0.093	0	1
Pgf	0	2.50428915	0.85	0.096	0	1
Jun	4.02E-297	2.89770775	0.838	0.251	1.30E-292	1
Fos	9.76E-250	2.71267581	0.809	0.264	3.15E-245	1
Lars2	2.57E-286	2.50979061	0.993	0.917	8.30E-282	2
Gphn	5.89E-249	2.74984678	0.894	0.492	1.90E-244	2
Igkc	0	6.43867831	0.944	0.076	0	4
Cd79a	0	5.19280736	0.989	0.026	0	4
Cd74	0	4.91458333	0.992	0.176	0	4
Ighm	0	4.75715109	0.991	0.121	0	4
Cd79b	0	4.61059924	0.976	0.034	0	4
Ly6d	0	4.48136344	0.94	0.017	0	4
Iglc2	0	4.47998047	0.919	0.016	0	4

H2-Aa	0	4.22951307	0.942	0.077	0	4
Iglc1	0	4.0303691	0.702	0.01	0	4
H2-Ab1	0	3.87775433	0.959	0.076	0	4
H2-Eb1	0	3.83095568	0.946	0.063	0	4
Iglc3	0	3.80995721	0.923	0.012	0	4
Ms4a1	0	3.66694166	0.938	0.009	0	4
Ighd	0	3.50702011	0.891	0.012	0	4
Cd37	0	3.31931644	0.972	0.121	0	4
Fcmr	0	3.24918843	0.901	0.008	0	4
Ebf11	0	3.13396881	0.987	0.184	0	4
Ltb	0	2.85186234	0.927	0.091	0	4
Ly6e	0	2.79051933	0.989	0.291	0	4
Vpreb3	0	2.78419563	0.719	0.004	0	4
H2-Ob	0	2.76656164	0.901	0.021	0	4
Bank1	0	2.66967584	0.88	0.013	0	4
Cd55	0	2.64096843	0.878	0.04	0	4
H2-DMb2	0	2.59477533	0.882	0.012	0	4
Rp1	0	4.03778332	1	0.081	0	5
Sag	0	3.93892508	1	0.196	0	5
Rho	0	3.89452641	0.995	0.312	0	5
Pdc	0	3.7556852	0.993	0.142	0	5
Gnat1	0	3.74864962	0.991	0.146	0	5
Prph2	0	3.71530989	0.993	0.114	0	5
Cadm2	0	3.54093775	0.805	0.091	0	5
Mir124-2hg	0	3.53451427	0.97	0.064	0	5
Mir124a-1hg	0	3.51591079	0.984	0.053	0	5
Neurod1	0	3.44647727	0.94	0.051	0	5
Gngt1	0	3.43663191	0.988	0.22	0	5
Pde6b	0	3.42684839	0.981	0.073	0	5
Guca1a	0	3.42012139	0.974	0.124	0	5
Pde6a	0	3.37928341	0.981	0.076	0	5
Pde6g	0	3.35058901	0.986	0.154	0	5
Rcvrn	0	3.3426807	0.963	0.107	0	5
Hcn1	0	3.34096241	0.888	0.039	0	5
Nr2e3	0	3.3039255	0.953	0.065	0	5
Cnga1	0	3.29256693	0.963	0.071	0	5
Rbp3	0	3.2787088	0.898	0.07	0	5
Kcnb1	0	3.18369695	0.947	0.117	0	5
Tulp1	0	3.16852287	0.977	0.086	0	5

Rpgrip1	0	3.15679094	0.986	0.235	0	5
Pex5l	0	3.15165262	0.96	0.049	0	5
Guca1b	0	3.13647442	0.97	0.086	0	5
Rtbdn	0	3.11963066	0.942	0.06	0	5
Rs1	0	3.11906095	0.919	0.068	0	5
Nrl	0	3.07179568	0.944	0.068	0	5
Cplx4	0	3.05661677	0.956	0.061	0	5
Dmd	0	3.05178296	0.909	0.193	0	5
Syt1	0	3.00871229	0.898	0.145	0	5
Cngb1	0	2.9295327	0.965	0.096	0	5
Rims2	0	2.92835303	0.893	0.047	0	5
Slc17a7	0	2.87165367	0.926	0.053	0	5
Vax2os	0	2.83203369	0.567	0.052	0	5
Aipl1	0	2.81121597	0.921	0.058	0	5
AI847159	0	2.80720724	0.898	0.044	0	5
11-Mar	0	2.77721702	0.893	0.14	0	5
Fam57b	0	2.76508288	0.923	0.113	0	5
Pdzph1	0	2.7594482	0.802	0.024	0	5
Casz1	0	2.72804268	0.851	0.069	0	5
Reep6	0	2.72257651	0.856	0.052	0	5
Map1b	0	2.7021811	0.912	0.172	0	5
Prom1	0	2.68012363	0.926	0.065	0	5
Grk1	0	2.67816003	0.879	0.039	0	5
Crx	0	2.6689647	0.886	0.044	0	5
Pcdh15	0	2.65588874	0.644	0.022	0	5
Vtn	0	2.58086548	0.886	0.151	0	5
Rdh12	0	2.55984217	0.884	0.078	0	5
Samd11	0	2.55369894	0.858	0.038	0	5
Hk2	0	2.54015435	0.895	0.107	0	5
Sgip1	0	2.51903498	0.858	0.085	0	5
Fam161a	0	2.50129123	0.863	0.09	0	5
Rom1	3.55E-279	3.27051757	0.995	0.4	1.15E-274	5
Pcmtd2	1.07E-269	2.52877761	0.933	0.311	3.46E-265	5
Unc119	2.58E-241	2.81219886	0.974	0.479	8.35E-237	5
Gnb1	1.19E-238	3.26904762	0.995	0.695	3.86E-234	5
Pmel	0	3.85099217	0.858	0.084	0	6
Trpm11	0	2.55247874	0.882	0.103	0	6
Cox8b2	4.84E-221	3.36816067	0.907	0.205	1.56E-216	6
Dct3	1.18E-196	2.88581871	1	0.364	3.81E-192	6
Lyz2	0	5.2041602	0.989	0.171	0	7

Cybb1	0	3.77951016	0.993	0.074	0	7
Lst1	0	3.75365987	0.953	0.063	0	7
Fcer1g	0	3.68042672	0.978	0.101	0	7
Tyrobp	0	3.42163348	0.956	0.105	0	7
Itgal	0	3.20665993	0.891	0.081	0	7
Gngt2	0	3.20144115	0.895	0.11	0	7
Ms4a6c	0	3.08207956	0.942	0.047	0	7
Alox5ap	0	3.07104619	0.931	0.05	0	7
S100a4	0	3.02318348	0.847	0.074	0	7
Ear2	0	3.0149148	0.713	0.006	0	7
Ace	0	2.92494498	0.76	0.031	0	7
Spi11	0	2.91450848	0.949	0.079	0	7
Pou2f21	0	2.90920552	0.927	0.103	0	7
Clec4a3	0	2.89480857	0.924	0.018	0	7
Fyb	0	2.79845555	0.971	0.119	0	7
Lgals3	0	2.78537173	0.931	0.116	0	7
Ifitm6	0	2.7776298	0.855	0.015	0	7
Apoc2	0	2.76562187	0.822	0.011	0	7
Ccl6	0	2.72981414	0.913	0.029	0	7
Mpeg1	0	2.71847104	0.942	0.037	0	7
Itgb2	0	2.65116366	0.942	0.107	0	7
Cx3cr1	0	2.57877619	0.898	0.049	0	7
Adgre4	0	2.54873082	0.844	0.004	0	7
Tnfrsf1b	0	2.51936542	0.909	0.056	0	7
Ctss1	7.83E-304	2.98673388	0.982	0.174	2.53E-299	7
Plac81	1.14E-285	3.8154555	0.88	0.139	3.69E-281	7
Laptm51	3.28E-272	2.61503246	0.996	0.201	1.06E-267	7
Itga41	5.99E-268	2.61195638	0.949	0.173	1.93E-263	7
Ptprc1	2.03E-254	2.56654984	0.996	0.2	6.55E-250	7
Nr4a11	7.51E-246	2.52135973	0.913	0.167	2.42E-241	7
Msrb1	6.17E-234	2.94480255	0.895	0.201	1.99E-229	7
Coro1a1	8.49E-226	2.58561193	0.964	0.223	2.74E-221	7
Cebpb1	2.61E-222	3.72162176	0.978	0.299	8.43E-218	7
Sat11	4.18E-183	2.89589049	0.989	0.384	1.35E-178	7
Ifitm31	5.40E-181	3.02955416	0.949	0.316	1.74E-176	7
Gpx1	1.46E-154	3.10532654	0.949	0.496	4.72E-150	7
Mfap51	0	2.92048378	0.958	0.1	0	8
Fmo11	6.44E-280	2.58366696	0.92	0.115	2.08E-275	8
Igfbp6	1.13E-264	3.32723036	0.91	0.121	3.65E-260	8
Crispld21	2.38E-261	2.66721581	0.939	0.122	7.68E-257	8

Apod1	3.88E-238	3.16954676	0.863	0.106	1.25E-233	8
Edn31	8.90E-224	2.71744156	0.995	0.166	2.87E-219	8
Dcn1	8.46E-207	3.29791665	0.995	0.208	2.73E-202	8
Myoc	3.37E-191	3.18574658	0.401	0.023	1.09E-186	8
Ccn21	8.49E-191	2.99843228	0.943	0.18	2.74E-186	8
S100a62	9.69E-169	2.82468804	0.986	0.251	3.13E-164	8
Igfbp51	1.00E-116	2.6073819	1	0.473	3.24E-112	8
Chil11	1.51E-23	2.70111961	0.453	0.21	4.86E-19	8
Trbc2	0	3.66973983	0.964	0.059	0	9
Ms4a4b	0	3.19057338	0.984	0.076	0	9
Cd3d	0	2.8484363	0.938	0.049	0	9
Il7r	0	2.80806961	0.833	0.033	0	9
Lef1	0	2.78822677	0.953	0.061	0	9
Tcf7	0	2.77262858	0.953	0.044	0	9
Cd3g	0	2.59966715	0.932	0.044	0	9
Ms4a6b1	7.32E-289	2.733834	0.953	0.108	2.36E-284	9
Trbc1	1.02E-288	3.12025074	0.651	0.04	3.29E-284	9
Satb11	7.38E-248	2.56647446	0.958	0.136	2.38E-243	9
Gm12840	1.29E-192	2.80821636	0.578	0.053	4.17E-188	9
Tmsb102	5.15E-107	2.67237542	0.984	0.508	1.66E-102	9
Rpl121	1.24E-102	2.6546888	0.979	0.701	3.99E-98	9
Gm26917	1.89E-12	3.04649333	0.38	0.182	6.11E-08	9
Mir124a-1hg1	7.83E-279	3.95168221	0.904	0.092	2.53E-274	10
Mir124-2hg1	2.12E-195	3.29425662	0.809	0.104	6.84E-191	10
Rp11	1.27E-192	3.20500346	0.865	0.121	4.09E-188	10
Tulp11	1.77E-181	3.12902222	0.848	0.125	5.72E-177	10
Pde6b1	7.63E-171	2.81351165	0.809	0.114	2.46E-166	10
Pde6a1	2.63E-156	2.69049772	0.787	0.117	8.48E-152	10
Cplx41	3.13E-154	2.68988058	0.73	0.102	1.01E-149	10
Samd111	3.65E-152	3.02743852	0.618	0.076	1.18E-147	10
Sag1	3.42E-151	3.20609961	0.972	0.229	1.10E-146	10
Pex5l1	3.31E-145	2.74040042	0.669	0.092	1.07E-140	10
Guca1b1	4.60E-125	2.52634483	0.736	0.127	1.48E-120	10
Rpgrip11	1.02E-114	3.50296711	0.865	0.268	3.29E-110	10
Neurod11	5.06E-113	2.57276558	0.612	0.095	1.63E-108	10
Prom11	7.13E-109	2.67650296	0.618	0.107	2.30E-104	10
Cngb11	1.93E-100	2.58252559	0.674	0.138	6.24E-96	10
Vax2os1	3.06E-86	3.40177935	0.466	0.075	9.88E-82	10

12-Mar	4.75E-81	2.63013013	0.657	0.176	1.53E-76	10
Fam57b1	4.55E-75	2.57435596	0.612	0.153	1.47E-70	10
Hk21	7.53E-72	2.56100843	0.584	0.147	2.43E-67	10
Dmd1	1.28E-67	2.50268448	0.685	0.227	4.12E-63	10
Fam161a1	2.57E-57	2.51631069	0.5	0.13	8.31E-53	10
Flt1	0	4.70706792	0.983	0.037	0	11
Plvap	0	4.34972385	0.865	0.023	0	11
Ptprb	0	4.27900257	0.966	0.007	0	11
Igfbp3	0	4.24735084	0.871	0.038	0	11
Rgcc1	0	3.92948993	0.871	0.059	0	11
Plpp1	0	3.91291942	0.927	0.08	0	11
Kdr	0	3.89577567	0.882	0.016	0	11
Egfl7	0	3.83941557	0.933	0.026	0	11
Cldn5	0	3.55409822	0.876	0.005	0	11
Ctla2a	0	3.53347587	0.888	0.04	0	11
Podxl1	0	3.33295036	0.955	0.051	0	11
Adgrf5	0	3.29446506	0.944	0.018	0	11
Slc9a3r2	0	3.27536062	0.91	0.072	0	11
Cdh51	0	2.95039162	0.921	0.021	0	11
Cyvr1	0	2.93980673	0.927	0.009	0	11
Adgrl4	0	2.91619795	0.882	0.005	0	11
Mmrn2	0	2.85047195	0.91	0.004	0	11
Esam	0	2.79179329	0.927	0.016	0	11
Sox18	0	2.64248533	0.882	0.002	0	11
Tie1	0	2.51145884	0.854	0.022	0	11
Eng2	3.33E-303	3.49150051	0.955	0.103	1.08E-298	11
Tm4sf12	1.58E-244	3.13404654	0.899	0.108	5.09E-240	11
Aqp12	3.84E-236	2.78691608	0.68	0.056	1.24E-231	11
Arl15	3.20E-226	3.29345059	0.865	0.114	1.03E-221	11
Emcn1	3.60E-208	3.11233158	0.955	0.151	1.16E-203	11
Id12	1.19E-187	2.92296662	0.904	0.157	3.83E-183	11
Ptprg	3.10E-182	3.1289442	0.876	0.156	1.00E-177	11
Col4a12	2.90E-176	2.54220819	0.91	0.162	9.37E-172	11
Cd2002	5.41E-164	2.53219969	0.921	0.189	1.75E-159	11
Clic42	1.95E-143	3.15896358	0.91	0.234	6.29E-139	11
Heg12	1.08E-122	2.50892654	0.916	0.286	3.50E-118	11
Six34	1.74E-106	2.86073837	0.831	0.255	5.61E-102	11
Insr2	1.87E-81	2.5011096	0.82	0.299	6.03E-77	11
C1qa	0	5.44330939	0.944	0.022	0	12
C1qb	0	5.36640991	0.963	0.024	0	12

C1qc	0	5.01032484	0.957	0.018	0	12
Mrc1	0	3.66616777	0.584	0.011	0	12
Pf4	0	3.59492549	0.565	0.008	0	12
Ms4a7	0	3.57115802	0.758	0.014	0	12
Trem21	0	3.19568889	0.689	0.022	0	12
Fcrls	0	2.81853941	0.658	0.007	0	12
Aif11	0	2.69054519	0.72	0.031	0	12
Stab11	3.50E-290	2.95601077	0.596	0.028	1.13E-285	12
Fcgr31	1.05E-274	2.60145193	0.745	0.053	3.39E-270	12
Fcer1g1	9.29E-224	3.15104897	0.963	0.117	3.00E-219	12
Mpeg11	2.02E-220	2.55687618	0.708	0.058	6.51E-216	12
Tyrobp1	4.73E-213	3.51017049	0.95	0.121	1.53E-208	12
Wfdc171	2.87E-195	3.11104534	0.615	0.05	9.28E-191	12
Rgs102	7.32E-189	2.85272936	0.77	0.092	2.36E-184	12
Cd681	6.40E-169	2.94760719	0.727	0.091	2.07E-164	12
Lyz21	6.31E-157	3.43735941	0.944	0.187	2.04E-152	12
Ctss2	5.79E-146	3.70382516	0.901	0.191	1.87E-141	12
Dab23	1.42E-109	2.67227415	0.621	0.102	4.59E-105	12
Selenop2	2.25E-81	2.96967677	0.863	0.342	7.27E-77	12
Apoe5	1.64E-76	3.39490389	0.988	0.728	5.29E-72	12
Fth13	3.29E-71	2.69172941	0.981	0.927	1.06E-66	12
Ftl12	1.54E-69	2.79404406	0.994	0.879	4.98E-65	12
Lgmn1	8.65E-68	2.62181339	0.77	0.316	2.79E-63	12
Ctsb4	2.63E-66	3.02863182	0.919	0.675	8.50E-62	12
Maf2	8.42E-55	2.52670827	0.621	0.203	2.72E-50	12
Ctsz3	8.44E-44	2.57411467	0.764	0.471	2.72E-39	12
Fabp51	1.59E-36	2.87310199	0.335	0.078	5.14E-32	12
Nrl2	1.26E-276	3.57171154	0.981	0.104	4.08E-272	13
Reep62	2.75E-267	3.05719405	0.907	0.085	8.87E-263	13
Rbp32	1.08E-264	3.40257715	0.975	0.102	3.47E-260	13
Rs12	2.72E-264	3.2674985	0.975	0.102	8.77E-260	13
Smim401	3.39E-259	3.42048587	0.944	0.107	1.09E-254	13
Rtbdn2	3.97E-243	2.99103644	0.925	0.097	1.28E-238	13
Cnga12	3.72E-239	3.15094537	0.957	0.108	1.20E-234	13
Rcvrn2	3.49E-236	4.09036935	1	0.142	1.13E-231	13
Guca1b2	2.68E-228	3.20194864	0.969	0.123	8.66E-224	13
Slc17a72	3.23E-227	2.62483251	0.882	0.09	1.04E-222	13
Prph22	5.06E-218	3.62409054	1	0.15	1.63E-213	13
Aipl12	5.28E-218	2.62428906	0.876	0.095	1.71E-213	13
Nr2e32	8.83E-215	2.84973989	0.907	0.104	2.85E-210	13

Cplx42	3.54E-214	2.53695015	0.901	0.099	1.14E-209	13
Mgarp1	5.28E-212	3.07061541	0.907	0.122	1.70E-207	13
Tulp12	4.57E-211	2.84631193	0.963	0.124	1.47E-206	13
Guca1a2	3.50E-206	3.63348058	0.994	0.159	1.13E-201	13
Cngb12	1.30E-198	2.76074137	0.95	0.132	4.20E-194	13
Pde6b2	1.80E-196	2.57528189	0.919	0.113	5.80E-192	13
Pdc2	1.77E-193	3.78080257	1	0.177	5.71E-189	13
Pde6g2	1.96E-193	4.33060245	0.994	0.189	6.34E-189	13
Pde6a2	5.32E-193	2.70171606	0.913	0.116	1.72E-188	13
Gnat12	9.43E-193	3.94225449	0.994	0.181	3.04E-188	13
Vtn2	6.91E-169	3.21954029	0.938	0.18	2.23E-164	13
Fam57b2	3.17E-167	2.54980435	0.913	0.147	1.02E-162	13
Gngt12	8.20E-162	4.53539249	0.994	0.252	2.65E-157	13
Kcnb12	1.06E-157	2.60296971	0.907	0.153	3.42E-153	13
Sag2	7.24E-147	3.18007623	1	0.23	2.34E-142	13
Rho2	2.61E-133	4.2565633	0.994	0.34	8.41E-129	13
Rom12	5.19E-119	3.71082211	1	0.425	1.68E-114	13
Stx32	2.31E-112	2.52628656	0.876	0.241	7.47E-108	13
Prcd3	1.78E-106	2.63810714	0.938	0.341	5.74E-102	13
Unc1192	7.67E-106	3.3125723	0.988	0.499	2.47E-101	13
Atp1a32	1.34E-101	2.62075194	0.863	0.261	4.34E-97	13
Tma72	2.50E-100	3.61995967	0.994	0.737	8.07E-96	13
Gnb12	5.65E-94	3.34048109	0.994	0.708	1.82E-89	13
Gapdh2	5.36E-89	2.66323084	0.988	0.816	1.73E-84	13
Hmgn12	5.95E-86	2.6948445	0.969	0.635	1.92E-81	13
Igfbp52	4.36E-69	2.79710273	0.941	0.479	1.41E-64	14
Igfbp42	2.10E-60	2.94440572	0.757	0.26	6.79E-56	14
Egr12	1.27E-59	3.01989751	0.691	0.224	4.10E-55	14
Ccn22	3.55E-55	2.88787799	0.651	0.194	1.15E-50	14
Cd8b1	0	3.02554817	0.763	0.024	0	15
Cd3d1	0	2.84143077	0.914	0.057	0	15
Cd3g1	0	2.70985012	0.921	0.051	0	15
Il7r1	0	2.60273	0.856	0.039	0	15
Trbc21	1.65E-289	3.10910684	0.928	0.067	5.34E-285	15
Ms4a4b1	7.15E-212	2.63670789	0.892	0.086	2.31E-207	15
Trbc11	5.69E-145	2.56589556	0.554	0.047	1.84E-140	15
Tmsb103	5.59E-75	2.68950039	0.978	0.512	1.80E-70	15
Rgs52	0	5.36976522	0.957	0.071	0	16
Myh11	0	4.67973884	0.681	0.01	0	16
Notch32	0	3.29828342	0.891	0.062	0	16

Ccn3	0	2.67026012	0.536	0.014	0	16
Ctnna3	0	2.57499449	0.442	0.006	0	16
Aspn1	0	2.55629678	0.848	0.035	0	16
Tagln	5.44E-270	4.80181679	0.543	0.021	1.76E-265	16
Myl93	4.00E-187	3.94137957	0.819	0.095	1.29E-182	16
Dgkb	1.33E-176	2.59538663	0.667	0.061	4.28E-172	16
Pde3a2	5.36E-159	3.13733252	0.819	0.116	1.73E-154	16
Sparcl12	1.02E-153	3.26190013	0.804	0.107	3.29E-149	16
Nrxn1	5.11E-141	2.66676092	0.391	0.023	1.65E-136	16
Tpm22	2.08E-140	4.15038295	0.761	0.11	6.71E-136	16
Gpc64	2.70E-132	3.27982825	0.913	0.186	8.71E-128	16
Rcan21	8.11E-132	2.59753035	0.616	0.07	2.62E-127	16
Mylk4	3.31E-124	2.97301626	0.877	0.175	1.07E-119	16
Dlc12	3.51E-120	2.5283677	0.841	0.157	1.13E-115	16
Prkg14	2.57E-117	3.08617125	0.819	0.15	8.30E-113	16
Rbpms3	1.62E-112	2.73207213	0.884	0.211	5.24E-108	16
Pdgfrb3	1.47E-102	2.66667468	0.855	0.185	4.73E-98	16
Filip1l3	1.08E-93	3.02007642	0.826	0.215	3.48E-89	16
Tpm12	1.11E-89	3.53729889	0.841	0.25	3.58E-85	16
Igfbp73	3.52E-74	2.56775526	0.971	0.526	1.14E-69	16
Plcl11	1.10E-69	2.73547001	0.616	0.13	3.55E-65	16
Pde4d4	5.66E-69	2.56834286	0.775	0.222	1.83E-64	16
Spp13	3.22E-55	3.83626648	0.449	0.084	1.04E-50	16
Crip16	3.68E-54	2.59954973	0.87	0.37	1.19E-49	16
Acta2	2.72E-40	4.79362181	0.558	0.189	8.77E-36	16
S100b1	1.34E-64	4.5051487	0.462	0.07	4.33E-60	18
Ednrb1	9.85E-49	2.61849434	0.274	0.03	3.18E-44	18
Mlana2	2.72E-17	3.3469601	0.359	0.133	8.77E-13	18
Pmel1	2.25E-11	2.80485374	0.291	0.115	7.27E-07	18
Dct4	6.28E-11	2.90039266	0.53	0.389	2.03E-06	18
Tyrp13	3.14E-07	3.11235747	0.393	0.273	0.0101455	18
Kidins220	0.00056701	2.59978054	0.154	0.356	1	18
Optc	0	3.00628688	0.526	0.006	0	19
Crhbp	0	2.74665014	0.578	0.004	0	19
Nlgn1	0	2.55693371	0.629	0.017	0	19
Kcna1	1.60E-306	2.74158917	0.259	0.001	5.18E-302	19
Penk	2.77E-256	3.88007699	0.638	0.029	8.95E-252	19
Ppp1r1a	1.11E-177	2.56564601	0.672	0.052	3.59E-173	19
Gpx31	2.11E-153	5.02283927	0.698	0.07	6.80E-149	19
Atp1a23	9.03E-138	3.73253167	0.862	0.128	2.92E-133	19

Csmd1	1.28E-123	3.4143113	0.25	0.008	4.12E-119	19
Ank32	4.24E-108	2.53868479	0.802	0.141	1.37E-103	19
Col23a11	1.50E-102	2.67395169	0.69	0.098	4.83E-98	19
Podxl21	3.52E-85	2.72354927	0.69	0.132	1.14E-80	19
Frmpd41	4.33E-81	2.65015279	0.56	0.082	1.40E-76	19
Sned11	2.93E-79	2.98498453	0.655	0.124	9.45E-75	19
Fam129a4	6.90E-76	2.56087947	0.759	0.18	2.23E-71	19
Fbln12	4.39E-69	3.20956872	0.664	0.147	1.42E-64	19
Pkp43	1.26E-66	2.51160945	0.681	0.158	4.08E-62	19
Dkk34	5.50E-62	3.3771926	0.698	0.189	1.78E-57	19
Nudt41	2.03E-58	2.81196714	0.802	0.285	6.56E-54	19
Plp1	5.15E-46	2.67981164	0.267	0.03	1.66E-41	19
Cdh19	7.40E-39	2.86102231	0.302	0.045	2.39E-34	19
Sfrp2	0	3.79634901	0.602	0.01	0	20
H19	8.53E-307	2.94351861	0.454	0.008	2.75E-302	20
Col6a31	6.79E-299	2.71348917	0.806	0.038	2.19E-294	20
Myoc1	1.24E-277	3.75753486	0.657	0.025	4.01E-273	20
Aspn2	7.82E-269	3.1222249	0.778	0.039	2.52E-264	20
Mmp3	2.23E-267	3.08472374	0.361	0.005	7.19E-263	20
Col12a11	4.03E-263	3.20101511	0.694	0.032	1.30E-258	20
Fn12	3.07E-251	2.78570512	0.769	0.042	9.92E-247	20
Clec3b	4.31E-247	3.13045161	0.519	0.017	1.39E-242	20
Fndc11	2.59E-217	2.60940854	0.806	0.056	8.35E-213	20
Angptl7	1.44E-211	2.83147308	0.315	0.006	4.66E-207	20
Itih51	1.68E-208	2.53251148	0.704	0.043	5.43E-204	20
Itgbl12	6.93E-168	2.55768781	0.769	0.066	2.24E-163	20
Meg35	2.08E-166	3.31473537	0.852	0.087	6.72E-162	20
Serpinf12	8.86E-155	4.22616779	0.963	0.14	2.86E-150	20
Mmp22	1.23E-151	3.09560423	0.88	0.108	3.96E-147	20
Aebp12	1.75E-151	2.502252	0.824	0.092	5.65E-147	20
Igfbp61	7.17E-151	3.90221891	0.935	0.133	2.31E-146	20
Apod2	1.53E-146	3.51437122	0.907	0.118	4.93E-142	20
Pi161	4.63E-146	4.55681284	0.639	0.055	1.50E-141	20
Nbl13	2.09E-139	2.51341645	0.87	0.109	6.75E-135	20
Serping13	4.81E-136	3.24159441	0.972	0.162	1.55E-131	20
Col1a13	2.36E-135	5.37858178	1	0.188	7.61E-131	20
Col14a13	1.63E-132	2.77650775	0.824	0.105	5.25E-128	20
Col1a23	1.94E-130	5.05023658	1	0.206	6.26E-126	20
Fbln13	5.16E-127	2.80915436	0.926	0.143	1.67E-122	20
Gas14	3.35E-126	3.31307823	0.917	0.146	1.08E-121	20

Cd343	3.86E-121	2.7258098	0.759	0.095	1.25E-116	20
Dcn3	2.75E-117	4.47762541	0.991	0.221	8.89E-113	20
Col3a14	1.81E-111	3.93854549	0.954	0.185	5.86E-107	20
Ecrq42	3.63E-105	3.79629284	0.593	0.066	1.17E-100	20
Mfap52	1.77E-102	2.8255851	0.769	0.116	5.71E-98	20
Bgn5	6.61E-94	3.08599619	0.907	0.196	2.13E-89	20
Ogn4	1.96E-92	3.25896249	0.963	0.269	6.34E-88	20
Mfap43	2.56E-89	2.64201319	0.639	0.087	8.26E-85	20
Gsn3	1.77E-82	3.77673615	0.944	0.257	5.73E-78	20
Fstl15	1.55E-74	3.20747248	0.926	0.287	4.99E-70	20
Cdkn1c3	6.11E-74	2.50057192	0.824	0.193	1.97E-69	20
Fmod1	1.49E-71	3.28207277	0.472	0.061	4.82E-67	20
Sparc5	1.85E-69	4.21163759	0.991	0.547	5.97E-65	20
Ly6a5	5.92E-46	2.59328259	0.574	0.137	1.91E-41	20
Chil12	3.98E-05	2.79623816	0.343	0.216	1	20
Gzma	0	5.98983725	0.962	0.04	0	21
Nkg71	0	4.58699903	0.981	0.047	0	21
Prf1	0	3.62468682	0.943	0.02	0	21
Klre1	0	3.58437706	0.991	0.012	0	21
Klrd11	0	3.51082043	0.972	0.047	0	21
Ncr1	0	3.39103732	0.943	0.002	0	21
Klrb1c	0	3.36363036	0.981	0.004	0	21
Klrk1	0	3.35788648	0.981	0.019	0	21
Klra4	0	3.26596729	0.396	0.001	0	21
Gzmb	0	3.15789581	0.811	0.015	0	21
Klra9	0	3.11459704	0.481	0.004	0	21
Klra8	0	3.0145106	0.519	0.001	0	21
Il2rb1	0	2.92162239	0.972	0.026	0	21
Ctsw1	0	2.75385487	0.943	0.039	0	21
Klra7	0	2.67769437	0.575	0.002	0	21
Cma1	0	2.60369557	0.726	0.003	0	21
Sytl3	8.76E-270	2.61893353	0.925	0.062	2.83E-265	21
Txk2	2.18E-242	2.66546149	0.934	0.07	7.03E-238	21
Ccl4	4.01E-230	3.48306304	0.642	0.03	1.29E-225	21
Ms4a4b2	4.65E-207	3.05341481	0.981	0.088	1.50E-202	21
Ccl5	1.32E-202	5.05628244	0.991	0.105	4.25E-198	21
AW1120101	1.74E-202	5.03078329	0.981	0.108	5.62E-198	21
Fcer1g2	1.02E-165	3.16956971	1	0.123	3.28E-161	21
Tyrobp2	1.89E-162	3.22559409	1	0.127	6.11E-158	21
Hcst2	1.37E-150	2.53669643	0.934	0.121	4.41E-146	21

Irf83	1.19E-126	2.70918171	0.877	0.127	3.84E-122	21
Ptprc4	5.40E-105	2.64612782	0.991	0.221	1.74E-100	21
Ugcg2	5.45E-95	2.50833481	0.972	0.269	1.76E-90	21
H2afz3	8.17E-70	2.90656667	0.991	0.522	2.64E-65	21
Lgals16	1.14E-64	2.62996728	0.962	0.415	3.68E-60	21
Nkg72	0	4.22911607	0.99	0.048	0	22
Cd8b11	0	3.28359355	0.843	0.027	0	22
Gzmb1	0	3.06669888	0.745	0.017	0	22
Cd3e2	0	2.92142712	0.98	0.053	0	22
Ly6c23	4.18E-303	3.36518652	0.853	0.04	1.35E-298	22
Klrd12	1.34E-298	2.93870833	0.922	0.048	4.32E-294	22
Cd3g2	4.63E-298	2.86266571	0.98	0.055	1.49E-293	22
Cd3d2	5.83E-281	2.86837782	0.99	0.06	1.88E-276	22
Trac2	2.38E-278	2.68773397	0.961	0.059	7.69E-274	22
Lck3	9.46E-268	2.56810932	0.99	0.068	3.05E-263	22
Trbc23	1.01E-242	3.37329964	0.98	0.071	3.26E-238	22
Ms4a4b3	1.54E-220	3.60040772	1	0.089	4.98E-216	22
Hopx4	2.64E-215	2.55539782	0.961	0.085	8.52E-211	22
Gzma1	7.04E-206	4.16680797	0.725	0.044	2.27E-201	22
Ccl51	1.55E-203	5.9985148	1	0.105	5.01E-199	22
AW1120102	1.14E-180	2.92532449	0.98	0.108	3.68E-176	22
Hcst3	1.72E-178	3.32579867	0.99	0.121	5.57E-174	22
H2-Q74	2.98E-156	3.44566208	0.99	0.144	9.63E-152	22
Rac25	5.86E-113	2.86246348	0.99	0.211	1.89E-108	22
Cd526	9.13E-96	2.97079011	0.99	0.244	2.95E-91	22
H2-K16	1.37E-70	2.71808133	1	0.47	4.42E-66	22
Lgals17	2.23E-67	3.04204563	0.98	0.415	7.21E-63	22
Alas2	0	3.7262676	0.979	0.006	0	23
Snca1	0	2.75658147	0.959	0.012	0	23
Ube2l6	5.76E-274	2.5414345	0.938	0.057	1.86E-269	23
Hbb-bt	9.66E-244	9.10168627	1	0.081	3.12E-239	23
Hba-a2	1.74E-137	9.75584999	1	0.174	5.62E-133	23
Hba-a1	3.72E-130	9.98417389	1	0.187	1.20E-125	23
Bpgm2	1.26E-92	2.94418456	0.897	0.193	4.06E-88	23
Hbb-bs	1.51E-78	10.0506462	1	0.421	4.88E-74	23
Mkrm13	1.93E-67	2.50137868	0.948	0.336	6.24E-63	23
Ankfn11	6.06E-188	3.75439723	0.988	0.09	1.96E-183	24
Fhit	2.20E-163	2.81869663	0.988	0.103	7.10E-159	24
Dlg22	8.45E-151	2.92811182	0.976	0.105	2.73E-146	24
Ptprt3	1.91E-134	2.91808759	0.988	0.135	6.16E-130	24

Naaladl23	2.02E-119	2.73106181	0.951	0.135	6.51E-115	24
Zfp385b3	2.07E-100	2.99201781	0.988	0.19	6.68E-96	24
Lrmda3	5.62E-99	3.15801854	0.988	0.195	1.81E-94	24
Gabrb34	7.61E-94	3.33169759	0.988	0.217	2.46E-89	24
Pde1c2	4.86E-93	3.54070083	0.988	0.22	1.57E-88	24
Dlgap14	1.78E-92	2.79555168	0.988	0.212	5.75E-88	24
Magi24	3.08E-91	3.26965812	0.988	0.215	9.95E-87	24
Otx2os13	4.03E-91	3.8979337	0.988	0.23	1.30E-86	24
Tshr5	1.81E-76	2.63293626	1	0.261	5.85E-72	24
Rora6	2.77E-65	3.77646414	0.988	0.397	8.94E-61	24
Trpm36	1.17E-63	3.98127419	0.988	0.421	3.76E-59	24
Cd209a	0	2.65748797	0.569	0.003	0	25
H2-DMb13	2.23E-79	2.65971437	0.785	0.106	7.19E-75	25
S100a42	1.39E-74	2.82264003	0.769	0.1	4.49E-70	25
H2-Eb12	1.55E-70	3.96048848	0.815	0.127	5.00E-66	25
H2-Aa2	5.93E-62	3.68773194	0.8	0.14	1.91E-57	25
H2-Ab12	1.32E-60	3.93616049	0.785	0.141	4.27E-56	25
Cd742	3.40E-45	3.43806055	0.877	0.236	1.10E-40	25
Crip110	5.46E-44	2.90220567	0.985	0.374	1.76E-39	25
Tmsb4x7	2.84E-37	2.58155991	1	0.705	9.16E-33	25
Hist1h2ap	5.68E-22	3.66340476	0.354	0.062	1.83E-17	25
S100a9	0	9.34131052	0.963	0.01	0	26
S100a8	0	8.9753976	0.963	0.006	0	26
Retnlg	0	6.49672246	0.889	0.002	0	26
Slpi	0	4.7080499	0.926	0.01	0	26
Il1r2	0	4.58701404	0.815	0.006	0	26
Cxcr2	0	3.94007565	0.926	0.006	0	26
Mmp9	0	3.4496995	0.852	0.001	0	26
Cstdc4	0	3.14382114	0.296	0	0	26
Wfdc211	4.70E-247	3.60349463	0.704	0.009	1.52E-242	26
Mmp8	6.20E-240	2.98035119	0.556	0.005	2.00E-235	26
Ccr11	2.80E-227	3.44088373	0.889	0.017	9.04E-223	26
Hdc	2.26E-198	4.11011068	0.815	0.017	7.28E-194	26
Trem1	2.78E-195	2.6551517	0.667	0.011	8.97E-191	26
Clec4d1	6.36E-195	3.1467965	0.852	0.019	2.05E-190	26
Csf3r1	1.95E-160	4.70103919	0.963	0.032	6.30E-156	26
Cd300lf1	3.11E-157	2.70117191	0.778	0.02	1.00E-152	26
Adam8	3.55E-155	2.64518949	0.667	0.014	1.15E-150	26
Lrg11	9.29E-149	2.7607627	0.667	0.015	3.00E-144	26
Arg2	2.45E-141	2.75872468	0.704	0.018	7.90E-137	26

Sirpb1b1	3.08E-137	2.79657087	0.815	0.026	9.95E-133	26
Il1b1	4.98E-133	5.68182905	0.889	0.032	1.61E-128	26
Nlrp31	4.87E-121	2.59622776	0.704	0.022	1.57E-116	26
Hp1	1.35E-115	3.88777615	0.815	0.031	4.37E-111	26
Lcn2	4.24E-96	3.36530045	0.444	0.01	1.37E-91	26
Clec4e1	2.01E-94	2.53838557	0.593	0.02	6.49E-90	26
Trem31	1.65E-87	2.97314432	0.63	0.024	5.32E-83	26
Jaml3	4.37E-85	2.64322056	0.704	0.032	1.41E-80	26
Lilr4b2	1.93E-83	2.87162099	0.704	0.032	6.23E-79	26
Gda3	9.58E-83	3.72368085	0.889	0.056	3.09E-78	26
Lilrb4a3	3.46E-74	2.82724562	0.852	0.055	1.12E-69	26
Ccl63	3.62E-72	3.80136888	0.889	0.063	1.17E-67	26
Cd300ld1	9.91E-69	2.65432106	0.704	0.04	3.20E-64	26
Cxcl2	4.85E-67	3.70233212	0.333	0.008	1.57E-62	26
Alox5ap3	1.44E-64	3.13782517	0.963	0.083	4.65E-60	26
Nfam13	1.10E-63	2.62652337	0.815	0.06	3.55E-59	26
Pglyrp14	1.28E-47	2.85519029	0.852	0.089	4.14E-43	26
H2-Q102	2.08E-45	2.557621	0.593	0.044	6.71E-41	26
Ncf25	2.26E-44	2.95243771	0.889	0.111	7.29E-40	26
Lst13	4.47E-41	2.53925457	0.852	0.097	1.44E-36	26
Tyrobp4	6.08E-41	3.41700956	0.963	0.137	1.96E-36	26
Gcnt23	3.24E-40	3.18231055	0.815	0.102	1.05E-35	26
Mxd12	1.08E-39	3.32229974	0.889	0.13	3.50E-35	26
Fgl25	3.90E-39	2.73090222	0.704	0.073	1.26E-34	26
Lmn13	1.02E-36	2.99227915	0.778	0.101	3.28E-32	26
Socs34	2.68E-33	2.92040427	0.852	0.138	8.65E-29	26
Samsn15	1.99E-32	2.84598179	0.778	0.112	6.43E-28	26
Plek5	5.38E-32	2.8807748	0.852	0.14	1.74E-27	26
Selplg6	2.58E-31	2.5523474	0.889	0.154	8.34E-27	26
Msr11	1.43E-30	4.21093466	0.963	0.227	4.61E-26	26
Lcp18	2.31E-29	3.16405695	0.926	0.208	7.45E-25	26
Ptprc7	2.72E-29	3.03837663	1	0.23	8.79E-25	26
Srgn8	5.28E-29	4.21346842	1	0.284	1.70E-24	26
Lyst4	9.93E-29	2.98168128	0.889	0.19	3.20E-24	26
Syk5	6.28E-28	2.52459028	0.778	0.13	2.03E-23	26
Fxyd58	8.24E-28	3.22895602	0.963	0.241	2.66E-23	26
Pygl2	1.18E-27	2.71171546	0.778	0.139	3.80E-23	26
Ripor25	3.04E-27	2.95486345	0.852	0.162	9.82E-23	26
Wfdc173	5.88E-27	2.63844334	0.556	0.062	1.90E-22	26
Mir142hg6	1.14E-24	2.82966121	0.593	0.082	3.70E-20	26

Stk17b8	2.56E-24	2.8567771	0.963	0.269	8.26E-20	26
Dusp19	2.74E-23	3.70033913	0.926	0.291	8.86E-19	26
Arhgap158	7.96E-23	3.16510324	0.815	0.184	2.57E-18	26
Anxa17	8.05E-22	2.6248317	0.815	0.184	2.60E-17	26
Zfp368	9.49E-22	2.90373042	0.963	0.32	3.06E-17	26
Litaf4	2.17E-21	2.59914779	0.778	0.187	7.01E-17	26
Tnfaip23	9.81E-21	2.86167288	0.741	0.168	3.17E-16	26
S100a1110	1.29E-20	4.21634798	0.926	0.363	4.17E-16	26
Antxr23	1.47E-20	2.52602352	0.593	0.099	4.76E-16	26
S100a69	2.67E-20	3.1569468	0.926	0.272	8.63E-16	26
Fos6	8.41E-20	2.75888157	0.963	0.316	2.72E-15	26
Tpd523	1.00E-19	2.78168699	0.963	0.412	3.23E-15	26
Dennd4a6	2.44E-19	3.49752069	0.778	0.212	7.89E-15	26
Mcl18	4.75E-19	3.26430543	0.963	0.456	1.53E-14	26
Kdm7a4	5.79E-19	2.53419274	0.852	0.268	1.87E-14	26
Pag13	1.51E-18	2.59197487	0.667	0.147	4.87E-14	26
Cd445	1.52E-18	2.83242974	0.852	0.283	4.90E-14	26
Ifitm13	2.05E-18	3.06836762	0.593	0.104	6.61E-14	26
Fbxl53	2.47E-18	2.78769277	0.852	0.287	7.96E-14	26
Cebpb3	8.08E-17	2.71589209	0.889	0.325	2.61E-12	26
Cers63	2.09E-16	2.8713402	0.593	0.127	6.75E-12	26
Neat113	3.66E-15	3.22460085	0.815	0.326	1.18E-10	26
Btg28	5.15E-15	2.62504638	0.926	0.394	1.66E-10	26
Iqgap16	1.45E-14	2.51512699	0.889	0.482	4.69E-10	26
Picalm7	4.85E-14	2.58433161	0.852	0.413	1.57E-09	26
Sorl14	5.94E-14	2.50756989	0.852	0.391	1.92E-09	26
Junb10	2.20E-13	2.54525997	0.926	0.439	7.12E-09	26
Txn110	5.02E-13	2.671276	0.852	0.505	1.62E-08	26
Tmcc14	1.59E-11	2.54993849	0.704	0.268	5.12E-07	26
Ier35	0.00081948	2.61424913	0.407	0.199	1	26

Supplementary Table 2. Biological pathway downregulated in RPE of *Vldlr* KO.

ID	Description	pvalue	p.adjust	Count
GO:0009060	aerobic respiration	6.66E-15	1.60E-11	17
GO:0045333	cellular respiration	4.30E-14	5.18E-11	18
GO:0015980	energy derivation by oxidation of organic compounds	8.93E-14	7.17E-11	20
GO:0019646	aerobic electron transport chain	3.48E-12	1.93E-09	10
GO:0006091	generation of precursor metabolites and energy	4.01E-12	1.93E-09	21
GO:0006119	oxidative phosphorylation	8.43E-12	3.38E-09	13
GO:0042775	mitochondrial ATP synthesis coupled electron transport	3.44E-11	1.18E-08	10
GO:0042773	ATP synthesis coupled electron transport	4.58E-11	1.38E-08	10
GO:0009152	purine ribonucleotide biosynthetic process	6.02E-11	1.61E-08	14
GO:0009260	ribonucleotide biosynthetic process	1.31E-10	3.14E-08	14
GO:0006164	purine nucleotide biosynthetic process	1.78E-10	3.89E-08	14
GO:0046390	ribose phosphate biosynthetic process	2.26E-10	4.54E-08	14
GO:0072522	purine-containing compound biosynthetic process	2.87E-10	5.31E-08	14
GO:0009206	purine ribonucleoside triphosphate biosynthetic process	3.09E-10	5.31E-08	11
GO:0009145	purine nucleoside triphosphate biosynthetic process	3.39E-10	5.44E-08	11
GO:0009201	ribonucleoside triphosphate biosynthetic process	4.86E-10	7.31E-08	11
GO:0022904	respiratory electron transport chain	7.31E-10	1.04E-07	10
GO:0015986	proton motive force-driven ATP synthesis	7.85E-10	1.05E-07	9
GO:0009142	nucleoside triphosphate biosynthetic process	1.13E-09	1.43E-07	11
GO:0006754	ATP biosynthetic process	1.95E-09	2.35E-07	10
GO:0022900	electron transport chain	2.14E-09	2.46E-07	10
GO:0009165	nucleotide biosynthetic process	2.29E-09	2.51E-07	14
GO:1901293	nucleoside phosphate biosynthetic process	2.92E-09	3.06E-07	14
GO:0009150	purine ribonucleotide metabolic process	3.08E-09	3.09E-07	17
GO:0009259	ribonucleotide metabolic process	6.10E-09	5.88E-07	17
GO:0006163	purine nucleotide metabolic process	6.97E-09	6.45E-07	17
GO:0019693	ribose phosphate metabolic process	8.75E-09	7.81E-07	17
GO:0072521	purine-containing compound metabolic process	2.03E-08	1.75E-06	17
GO:0009205	purine ribonucleoside triphosphate metabolic process	1.03E-07	8.54E-06	12
GO:0009144	purine nucleoside triphosphate metabolic process	1.33E-07	1.03E-05	12
GO:0009199	ribonucleoside triphosphate metabolic process	1.33E-07	1.03E-05	12
GO:0032543	mitochondrial translation	2.03E-07	1.53E-05	9
GO:0042776	proton motive force-driven mitochondrial ATP synthesis	2.21E-07	1.61E-05	7
GO:0009141	nucleoside triphosphate metabolic process	2.75E-07	1.95E-05	12
GO:0002181	cytoplasmic translation	5.11E-07	3.51E-05	9
GO:0006635	fatty acid beta-oxidation	7.81E-07	5.22E-05	7
GO:0006122	mitochondrial electron transport, ubiquinol to cytochrome c	1.18E-06	7.66E-05	4
GO:0140053	mitochondrial gene expression	1.35E-06	8.58E-05	9
GO:0072329	monocarboxylic acid catabolic process	2.01E-06	0.000124	8
GO:0046034	ATP metabolic process	2.26E-06	0.000136	10

GO:0016042	lipid catabolic process	2.40E-06	0.000141	12
GO:0044242	cellular lipid catabolic process	2.65E-06	0.000152	10
GO:0009062	fatty acid catabolic process	5.11E-06	0.000286	7
GO:0090150	establishment of protein localization to membrane	8.18E-06	0.000448	10
GO:0019395	fatty acid oxidation	1.25E-05	0.00067	7
GO:0034440	lipid oxidation	1.92E-05	0.001005	7
GO:0044282	small molecule catabolic process	1.99E-05	0.001019	11
GO:0016032	viral process	2.26E-05	0.001136	11
GO:0006120	mitochondrial electron transport, NADH to ubiquinone	3.61E-05	0.001741	4
GO:0034341	response to interferon-gamma	3.62E-05	0.001741	7
GO:0045069	regulation of viral genome replication	3.73E-05	0.001762	6
GO:0019058	viral life cycle	5.63E-05	0.002606	9
GO:0006099	tricarboxylic acid cycle	6.09E-05	0.002766	4
GO:0006790	sulfur compound metabolic process	7.31E-05	0.003259	10
GO:0006801	superoxide metabolic process	8.20E-05	0.003591	5
GO:0006605	protein targeting	0.000102	0.004369	9
GO:0030258	lipid modification	0.000105	0.004415	8
GO:0046395	carboxylic acid catabolic process	0.000122	0.005064	8
GO:0016054	organic acid catabolic process	0.00013	0.005289	8
GO:0050792	regulation of viral process	0.000154	0.006177	7
GO:0098760	response to interleukin-7	0.000172	0.006661	3
GO:0098761	cellular response to interleukin-7	0.000172	0.006661	3
GO:0019079	viral genome replication	0.000212	0.008113	6
GO:0071786	endoplasmic reticulum tubular network organization	0.000242	0.009108	3
GO:0006914	autophagy	0.000266	0.009502	11
GO:0061919	process utilizing autophagic mechanism	0.000266	0.009502	11
GO:0072348	sulfur compound transport	0.000268	0.009502	4
GO:0072599	establishment of protein localization to endoplasmic reticulum	0.000268	0.009502	4
GO:0050821	protein stabilization	0.00028	0.009778	7
GO:0044403	biological process involved in symbiotic interaction	0.000426	0.014665	8
GO:2000378	negative regulation of reactive oxygen species metabolic process	0.000454	0.015313	4
GO:0019221	cytokine-mediated signaling pathway	0.000458	0.015313	10
GO:1903900	regulation of viral life cycle	0.000474	0.015627	6
GO:0072594	establishment of protein localization to organelle	0.00052	0.016931	10
GO:0045071	negative regulation of viral genome replication	0.000556	0.017858	4
GO:0015711	organic anion transport	0.000565	0.017896	9
GO:2000377	regulation of reactive oxygen species metabolic process	0.000664	0.020769	6
GO:0006576	cellular biogenic amine metabolic process	0.000712	0.021692	5
GO:0007006	mitochondrial membrane organization	0.000712	0.021692	5
GO:0061077	chaperone-mediated protein folding	0.000808	0.024325	4
GO:0006457	protein folding	0.000855	0.025424	6
GO:0035455	response to interferon-alpha	0.00106	0.030397	3

GO:0045454	cell redox homeostasis	0.00106	0.030397	3
GO:1901798	positive regulation of signal transduction by p53 class mediator	0.00106	0.030397	3
GO:0015800	acidic amino acid transport	0.001131	0.031682	4
GO:1905710	positive regulation of membrane permeability	0.001131	0.031682	4
GO:0072593	reactive oxygen species metabolic process	0.00115	0.031735	7
GO:0072337	modified amino acid transport	0.001164	0.031735	3
GO:0036293	response to decreased oxygen levels	0.001178	0.031735	7
GO:0044106	cellular amine metabolic process	0.001186	0.031735	5
GO:0009636	response to toxic substance	0.00123	0.032558	5
GO:0016236	macroautophagy	0.001263	0.033046	7
GO:0006612	protein targeting to membrane	0.001323	0.033893	5
GO:0042274	ribosomal small subunit biogenesis	0.001323	0.033893	4
GO:0090322	regulation of superoxide metabolic process	0.001392	0.034905	3
GO:1903901	negative regulation of viral life cycle	0.001392	0.034905	3
GO:0006979	response to oxidative stress	0.001442	0.035404	9
GO:0070972	protein localization to endoplasmic reticulum	0.001463	0.035404	4
GO:0009308	amine metabolic process	0.00147	0.035404	5
GO:0044000	movement in host	0.00147	0.035404	5
GO:0006084	acetyl-CoA metabolic process	0.001515	0.036115	3
GO:0006900	vesicle budding from membrane	0.001536	0.036266	4
GO:0006749	glutathione metabolic process	0.001943	0.045416	4
GO:0098656	anion transmembrane transport	0.002124	0.049176	6
GO:1990542	mitochondrial transmembrane transport	0.002219	0.049786	4
GO:1901029	negative regulation of mitochondrial outer membrane permeabilization involved in apoptotic signaling pathway	0.002221	0.049786	2
GO:1903332	regulation of protein folding	0.002221	0.049786	2
GO:0042398	cellular modified amino acid biosynthetic process	0.002233	0.049786	3

Supplementary Table 3. List of siRNA target sequences.

Gene Target	siRNA Target Sequence
CPT1A	SMARTpool Target 1: CCGCAAUUCUUCUGGCAAA SMARTpool Target 2: GACGUUAGAUGAAACUGAA SMARTpool Target 3: CGACAUCAAUCCGAACAUU SMARTpool Target 4: GGACAGCUACGCCAAAUCU
ERK1/MAPK3	SMARTpool Target 1: GACCGGAUGUUAACCUUUA SMARTpool Target 2: CCUGCGACCUUAAGAUUUG SMARTpool Target 3: CCAAUAAACGGAUCACAGU SMARTpool Target 4: AGACUGACCUGUACAAGUU
ERK2/MAPK1	SMARTpool Target 1: UCGAGUAGCUAUCAAGAAA SMARTpool Target 2: CACCAACCAUCGAGCAAAU SMARTpool Target 3: GGUGUGCUCUGCUUAUGAU SMARTpool Target 4: ACACCAACCUCUCGUACAU

Supplementary Table 4. List of antibodies used in this study.

Antibodies	Host	Dilution	Company	Catalog No.
a-SMA	Mouse	1:500 for Western blot, 1:200 for immunostaining	Santa Cruz	sc-32251
CTGF	Mouse	1:200	Santa Cruz	sc-365970
Fibronectin	Mouse	1:200	Santa Cruz	sc-271098
VLDLR	Goat	1:500	R&D	AF2258
VLDLR	Mouse	1:500	Homemade ¹	
CPT1A	Mouse	1:1000 for Western blot, 1:100 for immunostaining	Abcam	ab128568
Collagen I	Rabbit	1:100	Abcam	ab34710
P-ERK1/2	Rabbit	1:1000	Cell Signaling	4695
ERK1/2	Rabbit	1:1000	Cell Signaling	4370
PNPLA2	Rabbit	1:1000	Cell Signaling	2138
TGF β Receptor I	Rabbit	1:1000	Abcam	ab31013
TGF β Receptor II	Rabbit	1:1000	Abcam	ab186838
LRP5	Rabbit	1:1000	Cell Signaling	5731
LRP6	Mouse	1:1000	Homemade ²	
P-Smad2/3	Rabbit	1:500	Cell Signaling	8828
Smad2/3	Rabbit	1:500	Santa Cruz	sc-8832
β -Actin	Mouse	1:2000	Santa Cruz	sc-47778
GAPDH	Mouse	1:5000	Novus Biologicals	NB300-221
Anti-mouse IgG	Horse	1:3000	Vector Laboratories	PI-2000
Anti-rabbit IgG	Goat	1:3000	Vector Laboratories	PI-1000
Anti-goat IgG	Donkey	1:3000	Vector Laboratories	PI-9500
Anti-mouse IgG (Alexa Fluor 594)	Donkey	1:250	Jackson ImmunoResearch Laboratories Inc.	715-585-150
Anti-mouse IgG (Alexa Fluor 488)	Donkey	1:250	Jackson ImmunoResearch Laboratories Inc.	715-545-150
Anti-rabbit IgG (Alexa Fluor 594)	Donkey	1:250	Jackson ImmunoResearch Laboratories Inc.	715-585-152

Reference

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