

Supplemental Table 1: Major resource table

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
Human/Mouse/Rat Activin A beta A subunit Antibody	R&D	Cat#AF338; RRID: AB_355307
Human/Mouse Follistatin Antibody	R&D	Cat#AF669; RRID: AB_2247223
Anti-Gpnmab antibody	R&D	Cat#AF2330; RRID: AB_2112934
Anti-Smad2 antibody	Cell Signaling Technology	Cat#5339; RRID: AB_10626777
Anti-Smad3 antibody	Cell Signaling Technology	Cat# 9513, RRID: AB_2286450
Phospho Smad2 (Ser465/467) (138D4) Rabbit mAb	Cell Signaling Technology	Cat# 3108, RRID: AB_490941
Recombinant Anti-Smad3 (phospho S423 + S425) antibody	Abcam	Cat# ab52903, RRID: AB_882596
Mouse CD36/SR-B3 Antibody	R&D	Cat# AF2519, RRID: AB_222876
Human/Mouse/Rat FABP5/E-FABP Antibody	R&D	Cat# AF1476, RRID: AB_2293656
Akt (pan) (C67E7) Rabbit mAb	Cell Signaling Technology	Cat# 4691, RRID: AB_915783
Phospho-Akt (Ser473) (D9E) XP® Rabbit mAb	Cell Signaling Technology	Cat# 4060, RRID: AB_2315049
Phospho-S6 Ribosomal Protein (Ser235/236) Antibody	Cell Signaling Technology	Cat# 2211, RRID: AB_331679
S6 Ribosomal Protein (54D2) Mouse mAb	Cell Signaling Technology	Cat# 2317, RRID: AB_2238583
Phospho-GSK-3β (Ser9) Antibody	Cell Signaling Technology	Cat# 9336, RRID: AB_331405
GSK-3β (27C10) Rabbit mAb	Cell Signaling Technology	Cat# 9315, RRID: AB_490890
Phospho-NF-κB p65 (Ser536) (93H1) Rabbit mAb	Cell Signaling Technology	Cat# 3033, RRID: AB_331284
Anti-NF-κB P65 antibody	Abcam	Cat# ab16502, RRID: AB_443394
Phospho-p44/42 MAPK (Erk1/2) (Thr202/Tyr204)	Cell Signaling Technology	Cat# 4370, RRID: AB_2315112
p44/42 MAPK (Erk1/2) (L34F12) Mouse mAb	Cell Signaling Technology	Cat# 4696, RRID: AB_390780
Acetyl CoA Carboxylase (C83B10) Rabbit mAb (ACC)	Cell Signaling Technology	Cat# 3676S, RRID: AB_2219397
Fatty Acid Synthase Mouse antibody (FASN)	BD Biosciences	Cat# 610962, RRID: AB_398275
p21 (F-5)	Santa Cruz	Cat# sc-6246, RRID: AB_628073
FITC anti-CD45	BioLegend	Cat# 103108, RRID: AB_312973
PE anti-mouse CD45.2	BioLegend	Cat# 109807, RRID: AB_313444
PerCP-Cy5.5 anti-mouse Ly-6C	BioLegend	Cat# 128011, RRID: AB_1659242
APC-Cy7 anti-mouse Ly-6G	BioLegend	Cat# 127623, RRID: AB_10645331
PE-Cy7 anti-F4/80	BioLegend	Cat# 123113, RRID: AB_893490
APC anti-F4/80	BioLegend	Cat# 123115, RRID: AB_893493
APC anti-MHCII	Thermo Fisher Scientific	Cat# 17-5321-81, RRID: AB_469454
BV510 anti-CD11b	BioLegend	Cat# 101245, RRID: AB_2561390
PE-Cy7 anti-CD11b	BioLegend	Cat# 101215, RRID: AB_312798
FITC anti-Trem2	Thermo Fisher Scientific	Cat# MA5-28223, RRID: AB_2745193
PE anti-CD9	BioLegend	Cat# 124805, RRID: AB_1279327
PerCP/Cyanine5.5 anti-mouse CD11c	BioLegend	Cat# 117327, RRID: AB_2129642

Alexa Fluro 488 Rabbit-anti-Rat	Thermo Fisher Scientific	Cat# A-21210, RRID: AB_2535796
Alexa Fluro 568 Rabbit-anti-goat	Thermo Fisher Scientific	Cat# A-11079, RRID: AB_2534123
Alexa Fluro 647 Rabbit-anti-mouse	Thermo Fisher Scientific	Cat# A-21239, RRID: AB_2535808
Bacterial and virus strains		
NEB Stable Competent <i>E. coli</i>	New England Biolabs	C3040H
NEB®5-alpha Competent <i>E. coli</i>	New England Biolabs	C2987H
Biological samples		
None		
Chemicals, peptides, and recombinant proteins		
Formalin solution	Sigma-Aldrich	HT501128-4L
20% Paraformaldehyde (formaldehyde) aqueous solution	Fisher Scientific	50-980-492
OptiPrep™ Density Gradient Medium	Sigma-Aldrich	D1556-250ML
cOmplete™ EDTA-free Protease Inhibitor Cocktail, mini-Tablets	Sigma-Aldrich	11836170001
Halt™ Protease and Phosphatase Inhibitor Cocktail	Thermo Fisher Scientific	78444
Fetal Bovine Serum	Thermo Fisher Scientific	10437-028
Mini-PROTEAN® TGX™ Precast Protein Gels, 4-20%, 15-Well, 15 µL	Bio-Rad	4561096
Turbonuclease	Fisher Scientific	NC0298896
Hematoxylin Solution, Harris Modified	Sigma-Aldrich	HHS16-500ML
TRIzol® Reagent	Thermo Fisher Scientific	15596-018
RIPA/SDS buffer	Thermo Fisher Scientific	#89900
Molecular Probes FluoroPure DAPI	Thermo Fisher Scientific	D21490
Hyaluronidase from bovine testes	Sigma-Aldrich	H3506-100MG
Collagenase, Type 1	Worthington Biochemical	LS004196
Collagenase, Type 4	Worthington Biochemical	LS004188
Deoxyribonuclease I bovine	Sigma-Aldrich	D5319-500UG
D- (+)-Glucose monohydrate	Sigma-Aldrich	49159-1KG
D- (-)-Fructose,BioXtra	Sigma-Aldrich	F2543-1KG
D- (+)-Glucose,Hybri-Max™, powder, BioReagent, suitable for hybridoma	Sigma-Aldrich	G5146-1KG
Sucrose, for molecular biology, ≥99.5% (GC)	Sigma-Aldrich	S0389-5KG
Insulin solution human	Sigma-Aldrich	I9278-5ML
Xylenes	Sigma-Aldrich	534056-4L
RIPA Lysis and Extraction Buffer	Sigma-Aldrich	89901
RBC Lysis Buffer (10X) 100 ml	BioLegend	420301
Cholesterol-Water Soluble	Sigma-Aldrich	C4951
Palmitic acid	Sigma-Aldrich	P0500
Oleic acid	Sigma-Aldrich	O1383

Oxidized Low Density Lipoprotein from Human Plasma, (OxLDL)	Thermo Fisher Scientific	L34357
Recombinant Mouse IFN-γ (carrier-free)	BioLegend	575302
Lipopolysaccharides from Escherichia coli	Sigma-Aldrich	L4391
Critical commercial assays		
PrimeScript™ RT Master Mix (Perfect Real Time)	Takara Bio	RR036A
BCA assay kit	Thermo Fisher Scientific	#23227
ECL western blotting substrate	Thermo Fisher Scientific	#32106
Picrosirius Red Stain Kit	Polysciences	24901-500
Hydroxyproline Assay Kit	BioVision	K555
Total Cholesterol kit	Wako	439-17501
Triglyceride Colorimetric Assay Kit	Cayman	10010303
Free cholesterol Kit	Wako	994-02501
Human/Mouse/Rat Activin A Quantikine ELISA Kit	R&D	DAC00B
Human Follistatin Quantikine ELISA Kit	R&D	DFN00
Mouse Osteoactivin/GPNMB DuoSet ELISA	R&D	DY2330
AST/GOT LIQUID(KINETIC) Kit	Teco Diagnostics	A559150
ALT/SGPT COLOR ENDPOINT Kit	Teco Diagnostics	A526120
Senescence Cells Histochemical Staining Kit	Sigma-Aldrich	CS0030
Deposited data		
RNA-seq	NCBI GEO database	GSE221443
Experimental models: Cell lines		
Hepa 1-6	ATCC	CRL1830 (lot#70031235)
L929	ATCC	CCL-1(lot# 70026472)
Experimental models: Organisms/strains		
Mouse: C57BL/6J	The Jackson Laboratory	000664 age: 8–10 wks
Oligonucleotides		
See supplemental Table 1 for RT primer		
AAV8-shRNA SC	5'CACCACCTAAGGTTAAGTCGCCCTCGCTCGAGCGAGGGCGAC TTAACCTTAGG-3',	
AAV8-shRNA Gpnmb	5'CACCAGGAGCTTTGTCTACGTCTTTCCTCGAGGAAAGACGTAG ACAAAGCTCC-3',	
AAV8-shRNA Activin A	5'CACCACCTTCCACTCAACAGTCATTACTCGAGTAATGACTGTTG AGTGGAAGG-3'	
Recombinant DNA		
AAV8-TBG-GFP	This paper	N/A
AAV8-TBG-Activin A	This paper	N/A
AAV8- RSV-GFP-H1	Gifted by Dr. Ira Tabas	N/A
AAV8-shRNA SC	This paper	N/A
AAV8-shRNA Gpnmb	This paper	N/A

AAV8-shRNA Activin A	This paper	N/A
Software and algorithms		
ImageJ/Fiji	This paper	https://imagej.net/software/fiji/
PRISM GraphPad	Version 8	N/A
Flow Jo	Version.10.8.0	https://www.flowjo.com/
Image studio	Version 5.2	N/A
R version 4.0.5	R Core Team	https://www.R-project.org/
RStudio	RStudio Team	http://www.rstudio.com
R package DESeq2	Version1.30.00	N/A
R package ggplot2	Version 3.3.5.9000	N/A
R package ClusterProfiler	Version 3.8	N/A
R package Heatmap	Version1.0.12	N/A
R package stats	Version 3.6.2	N/A
R package ggvenn	Version 0.1.9	N/A
Other		
AAV8-TBG-GFP virus	This paper	Customized
AAV8-TBG-Activin A virus	This paper	Customized
AAV8-H1-shRNA SC virus	This paper	Customized
AAV8-H1-shRNA Gpnmb virus	This paper	Customized
AAV8-H1-shRNA Activin A virus	This paper	Customized
Standard laboratory diet	Pro-lab	irradiated Prolab Isopro RMH 3000
MASH (NASH) diet	Envigo	TD.160785
BG1000 Blood Glucose Meter and Strips	Clarity	CD-BG5

Supplemental Table 2: RT-PCR primers for mice

Primer name	Primer sequence
mHRPT-RT-F	ACTGTAATGATCAGTCAACGGG
mHRPT-RT-R	GGCCTGTATCCAACACTTCG
Activin A-RT-F	ACGACATTGGCAGGAGG
Activin A-RT-R	GCTGAAATAGACGGATGGTG
Col1a1-RT- F	GCTCCTCTTAGGGGCCACT
Col1a1-RT- R	CCACGTCTCACCATTGGGG
Col1a2-RT- F	GTAACCTTCGTGCCTAGCAACA
Col1a2-RT- R	CCTTTGTCAGAATACTGAGCAGC
Col3a1-RT-F	CTGTAACATGGAACTGGGGAAA
Col3a1-RT- R	CCATAGCTGAACTGAAAACCACC
Srebp2-RT-F	CCAAAGAAGGAGAGAGGCGG
Srebp2-RT-R	CGCCAGACTTGTGCATCTTG
Srebp1-RT-F	CAAGGCCATCGACTACATCCG
Srebp1-RT-R	CACCACTTCGGGTTTCATGC
FST-RT-F	TGCTGCTACTCTGCCAGTT
FST-RT-R	CAACACTCTTCCTTGCTCAGT
ACVR1a-RT-F	GGCTGCTTTCAGGTTTATGA
ACVR1a-RT-R	GGACTTCCCTTTAGTGGGC

ACVR1b-RT-F	CGTCTTCCTGGTCATCAACTAT
ACVR1b-RT-R	GCGTCTTGTCTTTGGAGAGA
ACVR1c-RT-F	CAAGGTAAGCCTGCTATTGC
ACVR1c-RT-R	GGTTCCCACTTTAGGATTCTG
Acta2-RT- F	ATGCTCCCAGGGCTGTTTTCCCAT
Acta2-RT- R	GTGGTGCCAGATCTTTTCCATGTCTG
Tnf α -RT- F	CTTCTGTCTACTGAACTTCGGG
Tnf α -RT-R	CAGGCTTGTCACTCGAATTTTG
Mcp1/CCL2-RT-F	TTAAAAACCTGGATCGGAACCAA
Mcp1/CCL2-RT-R	GCATTAGCTTCAGATTTACGGGT
CCL3-RT-F	TGTACCATGACACTCTGCAAC
CCL3-RT-R	CAACGATGAATTGGCGTGGA
CCL4-RT-F	AAACCTAACCCCGAGCAACA
CCL4-RT-R	CCATTGGTGCTGAGAACCCT
CCL5-RT-F	TGCCCACGTCAAGGAGTATTT
CCL5-RT-R	TCCTAGCTCATCTCCAAATAGTTGAT
Ccl6-RT-F	AAGAAGATCGTCGCTATAACCCT
Ccl6-RT-R	GCTTAGGCACCTCTGAACTCTC
CCL7-RT-F	CTGTGCCTGCTGCTCATA
CCL7-RT-R	AGGGACACCGACTACTGGT
CCL9-RT-F	CCCTCTCCTTCCTCATTCTTACA
CCL9-RT-R	AGTCTTGAAAGCCCATGTGAAA
Ccl22-RT-F267	CAGGCAGGTCTGGGTGAA
Ccl22-RT-R413	TAAAGGTGGCGTCGTTGG
CCR1-RT-F144	AGTGGTGGGCAATGTCCT
CCR1-RT-R292	CGTCTTTCAACTTGTAGTCAATCC
CCR2-RT-F	TGTGGGACAGAGGAAGTGG
CCR2-RT-R	GGAGGCAGAAAATAGCAGCA
CXCL1-RT-F	GGCTGGGATTACCTCAA
CXCL1-RT-R	GCTTCAGGGTCAAGGCAA
CXCL9-RT-F	TCCTCTTGGGCATCATCTTCC
CXCL9-RT-R	TTGTAGTGGATCGTGCCTCG
CXCL10-RT-F	TGCTGGGTCTGAGTGGGACT
CXCL10-RT-R	AGGATAGGCTCGCAGGGATG
Cxcr4-RT-280	CCCTTCTGGGCAGTTGAT
Cxcr4-RT-433	TGGTGGCGTGGACAATAG
CD68-RT-F	ACCACAAATGGCACTGCT
CD68-RT-R	CTGAACACAAGGCTGGGA
Lgals3-RT-F	AACACGAAGCAGGACAATAACTGG
Lgals3-RT-R	GCAGTAGGTGAGCATCGTTGAC
Mpeg1-RT-F181	CGGGTGATGGACTTGACA
Mpeg1-RT-R361	GGGCGAGTTCTGTGTTGA
TLR1-RT-F	TCAGCACTACGATCGGTTTG

TLR1-RT-R	TGTTTCCACATTGTTTCAGGG
TLR2-RT-F	GCGACATCCATCACCTG
TLR2-RT-R	TCATCTACGGGCAGTGG
TLR13-RT-F1511	TTCGGACTCTCAACCACG
TLR13-RT-R1644	CATCAGGTCAAGGGAACG
ITGB2-RT-F662	TCGGCAAGCAACTGATTT
ITGB2-RT-R796	CATCGTCTGTGGCAAACA
ITGAX-RT-F365	TGACAGGGCTCTGCTTTC
ITGAX-RT-R495	GGAAGTATGCTACCCGA
Ly6D-RT-F	ATGCAACGAGAGGCTGGTCA
Ly6D-RT-R	ACTAGAAGGGAAGGGGCAAG
Lyz2-RT-F	TGTGAATGCCTGTGGGA
Lyz2-RT-R	AGACTCCGCAGTTCCGA
Fcgr1-RT-F	ACCTGAGTCACAGCGGCATCTA
Fcgr1-RT-R	TGACACGGATGCTCTCAGCACT
Irf5-RT-F	CCTACAGAACCACTCTTGCCTG
Irf5-RT-R	CCTTGTGGGTTGCTGATGGTGA
Irf7-RT-F	GAGTTTCGGGCTCGGAG
Irf7-RT-R	GGACACACCCTCACGCT
Lcn2-RT-F276	ATGTCACCTCCATCCTGGTCAG
Lcn2-RT-R420	GCCACTTGCACATTGTAGCTCTG
H2-Ab1-RT-F39	TGTGGTGGTGCTGATGGT
H2-Ab1-RT-R144	CGTCCCGTTGGTGAAGTA
H2-Eb1-RT-F	GCGGAGAGTTGAGCCTACG
H2-Eb1-RT-R	CCAGGAGGTTGTGGTGTTC
H2-Aa-RT-F	TCAGTCGCAGACGGTGTTCAT
H2-Aa-RT-R	GGGGGCTGGAATCTCAGGT
IL-1 β -RT-F	TGCCACCTTTTGACAGTGATG
IL-1 β -RT-R	TGATGTGCTGCTGCGAGATT
Fabp3-RT-F247	AGAGTTCGACGAGGTGACAGCA
Fabp3-RT-R350	TTGTCTCCTGCCCGTTCCACTT
Fabp4-RT-F64	AAAGAAGTGGGAGTGGGC
Fabp4-RT-R234	GTCGTCTGCGGTGATTTC
Fabp5-RT-F	GCCTGATGGAAAGCCAC
Fabp5-RT-R	CCGTGATGTTGTTGCCA
Cd36-RT-F	CGTGGCAAAGAACAGCA
Cd36-RT-R	GGCTCAAAGATGGCTCC
Gpnmb-RT-F	AGAAATGGAGCTTTGTCTACGTC
Gpnmb-RT-R	CTTCGAGATGGGAATGTATGCC
TREM2-RT-F	ATGCCAGCGTGTGGTGA
TREM2-RT-R	GACGGTTCCAGCAAGGG
CD9-RT-F	TGCTGGGATTGTTCTTCGGG
CD9-RT-R	GCTTTGAGTGTTTCCCGCTG

Mmp12-RT-F	TTTGATGAGGCAGAAACGTG
Mmp12-RT-R	AGAGAGGCGAAATGTGCT
Adgre1 (F4/80)-RT-F	ACCACAATACCTACATGCACC
Adgre1 (F4/80)-RT-R	AAGCAGGCGAGGAAAAGATAG
Timp1-RT-F	CCAGAACCGCAGTGAAGAG
Timp1-RT-R	CTCCAGTTTGCAAGGGATAGA
Cidec-RT-F	TCGTGTTAGCACCGCAGA
Cidec-RT-R	ATCTTCCTCCAGCACCGAG
mCdkn2a (p16)-RT-F	GCTCAACTACGGTGCAGATTC
mCdkn2a (p16)-RT-R	GCACGATGTCTTGATGTCCC
mCdkn1a (p21)-RT-F	CGAGAACGGTGGAACCTTGAC
mCdkn1a (p21)-RT-R	CCAGGGCTCAGGTAGACCTT
mTp53-RT-F	ATCGCCTTCGACATCATCGC
mTp53-RT-R	CCCCATGCGTACTCCATGAG
mGlb1 (β-gal)-RT-F	CTGCCCAAGATGAAGCC
mGlb1 (β-gal)-RT-R	CCCAGATGGTAGCGGAA
mBasp1-RT-F	GCGAGGCCAAAAAGACTGAG
mBasp1-RT-R	CCGCGCTGCTAGGTTTAGAG
mNrg1-RT-F	CTGTTGGTGGTCGGCAT
mNrg1-RT-R	CTGGTGGTGGGTTTGGA
mSirpa-RT-F	GGCGTGTGCTTTGCTCGTA
mSirpa-RT-R	TTCCCTGGCGTTCTTCTCG
mPlau-RT-F	CCTGGTTCGCAGCCATCTA
mPlau-RT-R	TTCTTTGGGAGTTGAATGAAGC
mSh3bgrl3-RT-F	AGGTGACCCGCATCCTA
mSh3bgrl3-RT-R	GGTTGCCAGCCAAGGTT
mCol5a2-RT-F	GGGTTTCCTGGTTCTGC
mCol5a2-RT-R	TATCTCCCACTCGCCCA
mCD14-RT-F	TGTGCTCGGGATTTCCG
mCD14-RT-R	CCTTGTTGCCACGACA

Supplemental Table 3: SASP genes (total 105) upregulated by sugar water-FPC diet.

Gene name	Average FPC	Average Chow	log2FoldChange	padj
Lgals3	496.968585	40.91124193	3.609664214	1.55E-33
Anxa2	1820.02561	200.2442981	3.187112509	1.27E-28
Mmp12	355.429392	2.396829861	7.247920265	6.56E-27
Vcam1	775.527679	147.9749437	2.390227635	2.72E-26
Sirpa	919.024931	197.5873283	2.221002503	1.47E-24
Iqgap1	638.754635	134.2496268	2.254459663	3.06E-21
Colla1	939.2413	152.051837	2.627480957	1.80E-20
Gpc1	911.721751	151.0373937	2.591989118	2.88E-20
Axl	964.60582	256.1653195	1.915632291	4.46E-18
S100a11	608.356566	78.20409487	2.961524027	3.43E-17

Anxa5	5348.85508	1354.385265	1.981993435	6.15E-17
H2ab1	1558.59665	368.18867	2.082620886	7.14E-17
Col1a2	975.026019	227.5969463	2.098430678	4.77E-16
Col3a1	2411.31953	568.4390015	2.084945518	7.15E-16
Ccdc80	571.382764	116.6685525	2.297631849	2.51E-15
Nid1	907.096429	210.1295084	2.11134147	9.86E-15
Serpine1	189.805535	23.81718436	3.016618995	2.28E-13
Nrg1	103.942685	7.190489583	3.879501289	1.29E-12
App	2425.12614	942.2162719	1.364595557	2.30E-12
Vim	952.145481	349.9703194	1.445083199	9.15E-12
Msn	924.892786	313.0445071	1.565408848	2.01E-11
Csflr	1310.69507	446.323384	1.555633182	1.44E-10
Igfbp1	4736.46179	1605.310524	1.560850619	1.94E-10
Lgals1	1105.77121	280.3305792	1.982005197	2.42E-10
Spp1	3159.50953	885.8562375	1.834459521	3.67E-10
Cd44	337.783139	75.56923864	2.168439465	3.68E-10
Lum	453.295502	130.8494725	1.79044614	1.46E-09
Pkm	708.085126	271.7155223	1.383808267	1.68E-09
Mmp13	64.1039457	2.26475954	4.790272523	5.92E-09
Mmp7	103.957541	0.346638924	7.9534031	2.01E-08
Cxcl16	256.831781	82.11121247	1.640696266	2.55E-08
Col14a1	1764.57713	779.3936442	1.17962364	3.20E-08
Dkk3	126.555475	27.07228864	2.228816588	3.22E-08
Tmsb4x	3252.49542	1195.180099	1.444487633	3.32E-08
Thbs2	182.142209	48.41455869	1.91423136	5.58E-08
Flna	1177.81875	469.4477321	1.328773361	5.68E-08
Il1rn	176.3138	36.57382616	2.281814322	7.95E-08
Mfge8	482.15717	183.0861454	1.398557092	7.97E-08
Thbs1	141.650714	28.02656122	2.351858249	1.36E-07
Tagln2	562.780516	193.7357092	1.539662587	1.43E-07
Col4a1	1854.82783	798.8465063	1.214958985	1.57E-07
Postn	363.160364	108.9358993	1.742225467	1.58E-07
Selplg	104.618957	23.40835901	2.162483698	3.79E-07
Tgfb1	286.158396	104.7508657	1.455574715	3.88E-07
Sparc	1840.02882	757.6394928	1.280981552	7.40E-07
Fstl1	302.094441	107.8466552	1.486315376	9.59E-07
Cd14	181.354602	48.09985354	1.915839722	1.06E-06
Loxl2	128.436223	32.1280733	2.004752569	1.13E-06
Mmp2	183.397914	53.60696524	1.768643432	1.57E-06
Cd9	604.806731	243.6707127	1.311567654	2.14E-06
Timp2	588.306458	252.7498772	1.220494364	3.14E-06
Bgn	2653.53367	1315.392187	1.01270203	3.80E-06
Col5a1	348.486198	150.6705807	1.210872059	9.93E-06

Emilin1	650.665146	324.3631603	1.003680379	1.15E-05
Baspl	101.869631	23.17676219	2.156644543	1.59E-05
Hspb1	1469.60553	609.6970953	1.270384562	2.31E-05
Ccl2	45.2491196	5.587349579	3.037914429	2.69E-05
Jun	1667.5514	833.4013094	1.001733146	2.85E-05
Man1c1	114.303537	36.35321044	1.654501137	2.94E-05
Csrp1	384.66847	165.0657176	1.221384562	4.02E-05
Col5a2	206.040669	61.98065064	1.737153914	4.14E-05
Cx3cl1	61.3394271	10.40535257	2.556510889	5.19E-05
Ehd2	209.697231	68.87233309	1.610396121	5.22E-05
Csf2rb	249.522169	96.46470246	1.370664494	5.68E-05
Gsn	992.850142	448.7675289	1.144947288	6.36E-05
Cxcl9	280.651716	95.26042993	1.567214566	8.91E-05
Ccl5	53.1524676	9.059038161	2.530726566	9.06E-05
Fscn1	139.787242	44.22651693	1.66417866	0.000118
Anxa1	175.336655	68.65246515	1.358862477	0.000124
Efemp2	123.975922	43.29545741	1.520866329	0.000134
Spon2	416.974814	193.9997428	1.105542423	0.000141
Fbln2	113.394265	33.68365697	1.756513007	0.00019
Lamc1	607.192268	289.3611504	1.069588366	0.000195
Col6a3	466.35591	198.3736723	1.233952787	0.000233
Col6a2	244.908338	104.3972942	1.229941056	0.000287
Rps6ka1	478.624674	227.3712896	1.076078927	0.0003
Pgm1	156.78673	63.49552071	1.302903191	0.000315
Esm1	58.8836737	8.645798976	2.776193742	0.000315
Col16a1	154.534454	65.32457577	1.247325094	0.000336
Fbn1	161.855288	58.87188143	1.455550556	0.000356
Gdf15	1029.22083	435.8511581	1.240690464	0.000363
Sh3bgrl3	217.299337	95.19205866	1.196575602	0.000598
Ube2c	42.5117253	5.119239015	3.061263874	0.000609
Hexb	234.271971	110.1612315	1.083414934	0.000615
Loxl1	133.158312	46.82000166	1.506806825	0.000634
Tnc	78.5732237	21.97424698	1.845364639	0.000785
Sema3f	206.803528	95.91296342	1.112422976	0.000789
Areg	13.9826938	0	6.017166569	0.001023
Pamr1	153.433465	66.11724239	1.212937267	0.001035
Bcl2	69.4496118	19.93995407	1.804447111	0.001118
Lama5	158.899644	66.31591297	1.257482059	0.001197
Ltbp3	134.772575	51.19826877	1.396852452	0.001256
Tpm4	731.693561	356.8356258	1.038216637	0.001596
Col12a1	130.924175	47.33327043	1.479115675	0.00232
Htra1	104.463357	33.95839629	1.626128158	0.002917
S100a6	80.6907768	27.06182769	1.579336426	0.003106

Mrc2	134.257963	49.81195777	1.419663865	0.00316
Plat	66.4182316	21.12568575	1.648531646	0.003406
Ckap4	102.099805	38.60938701	1.409398394	0.004101
Plaur	41.2853639	9.360136455	2.146254107	0.005009
Ccl22	14.7463859	0.346638924	5.132633123	0.005254
Fkbp10	44.5591497	11.26451248	2.001835288	0.005681
Cxcl10	82.6719509	33.93733666	1.291621524	0.005905
Plau	74.2259494	27.83633588	1.426008251	0.006173
Svep1	74.2918233	22.42444382	1.72895279	0.007576

Supplemental Table 4: SASP genes (total 10) downregulated by sugar water-FPC diet.

Gene name	Average FPC	Average Chow	log2FoldChange	padj
Gstp1	6947.958	28679.46	-2.04536	3.32E-28
Moxd1	0.900777	2434.029	-11.448	8.63E-14
Ang	1335.433	3629.997	-1.44309	4.01E-10
Tpst1	185.7701	487.3706	-1.39295	7.82E-09
Rnase4	7450.7	15784.97	-1.08321	3.20E-08
Egfr	5241.006	10656.24	-1.02383	6.64E-06
Col27a1	454.3214	1071.716	-1.23721	7.77E-06
Calr	8866.376	17889.44	-1.01261	9.79E-06
Pdia6	3292.882	6943.877	-1.07625	1.72E-05
Il18	82.97418	179.9712	-1.11478	0.0051

Supplemental Table 5: SASP genes (total 36) downregulated by Activin A in MASLD liver.

Gene name	Average Activin A	Average Control	log2FoldChange	padj
Vcam1	417.2931671	841.159413	-1.011243401	7.60E-09
Sh3bgrl3	117.0377874	235.6662804	-1.012490481	0.000697
Loxl2	66.17225923	139.2697736	-1.075003679	0.006248
Col5a2	102.8901496	223.4092717	-1.120734542	0.000918
Tmsb4x	1612.774387	3527.20307	-1.129277555	3.30E-11
Col1a2	482.2575772	1057.312803	-1.133074852	3.95E-08
Spon2	205.0756441	452.4560355	-1.14116018	1.31E-06
Cxcl9	137.8850356	304.412979	-1.144425051	4.67E-07
Anxa5	2614.92333	5800.262508	-1.14957518	2.08E-10
Sirpa	402.6079643	996.8599099	-1.308463305	1.10E-16
H2ab1	660.1814333	1689.982541	-1.356858085	5.86E-10
Pdgfb	38.66689747	99.27246644	-1.363977306	0.003998
Cd44	139.261661	366.3566223	-1.396704301	2.19E-09
Thbs2	74.27705142	197.529454	-1.411783953	7.38E-06
Col3a1	975.369588	2614.424637	-1.422838902	3.94E-10
Cxcl10	33.49155963	89.67094817	-1.423032707	0.001673
S100a6	32.14308493	87.5103448	-1.443194265	0.004299
Col15a1	84.39631995	231.6896791	-1.459988813	0.000158

Col1a1	345.9615912	1018.341008	-1.558440251	3.83E-10
Baspl	37.32468792	110.5174034	-1.570269247	0.000117
Ccl5	18.0544141	57.66775372	-1.675881374	0.003422
Tgfb2	12.91523761	47.33219417	-1.873879773	0.001973
Thbs1	41.32513878	153.5953176	-1.900417083	5.24E-07
Esm1	16.24487541	63.82264136	-1.981358031	0.005915
Serpine2	63.6574916	261.9866386	-2.040408482	6.37E-09
Plau	19.33829466	80.49605275	-2.067871103	4.37E-05
Ccl2	11.62056252	49.08076539	-2.085462099	0.000817
Cd14	46.15607058	196.7136345	-2.093286696	6.08E-12
Lgals3	122.0374361	538.9037448	-2.142686378	2.89E-20
Spp1	752.115964	3425.759889	-2.187408167	4.90E-07
Il1rn	38.07774304	191.2950971	-2.327258837	1.02E-13
Mmp12	60.02813893	385.5829964	-2.680626921	3.04E-28
Plat	10.57092754	72.01913031	-2.780099511	1.17E-06
Mmp13	9.913752277	69.52605817	-2.801283903	3.70E-07
Nrg1	15.84272383	112.7297456	-2.834278463	1.13E-11
Mmp7	3.681411651	112.6851165	-4.948482476	4.55E-05

Supplemental Table 6: SASP genes (total 3) upregulated by Activin A in MASLD liver.

Gene name	Average Activin A	Average Control	log2FoldChange	padj
Inhba	469.2757676	151.394253	1.632273	4.41E-19
Col27a1	1150.113031	492.628999	1.221222	4.47E-08
Fst	202.068477	91.72917107	1.141739	4.55E-05

Supplemental Table 7: SASP genes (total 37) downregulated by shRNA Gpnmb in MASLD liver.

Gene name	Average shRNA Gpnmb	Average shRNA SC	log2FoldChange	padj
Nid1	472.5962	962.8345	-1.02784	1.81E-08
Sh3bgrl3	97.19669	200.3697	-1.04495	1.51E-05
Sparc	919.3429	1920.573	-1.06375	1.65E-14
Rcn3	75.26957	157.0139	-1.06576	0.000152
Cd14	71.09759	148.7711	-1.07064	0.001238
Ccdc80	287.047	609.1702	-1.08513	2.20E-07
Serpinh1	192.915	425.8754	-1.14416	1.80E-08
Plau	40.04156	88.2592	-1.14447	0.006813
Tnc	40.527	89.63184	-1.15087	0.004766
Fos	132.7713	296.9208	-1.16407	4.13E-07
MyI9	24.59059	60.06191	-1.29202	0.00443
Cxcl1	56.46234	138.4001	-1.29322	1.41E-05
Loxl1	54.09793	132.624	-1.30087	3.64E-05
Cxcl10	42.24393	104.506	-1.31039	0.000391
Colla2	481.5175	1195.894	-1.31316	0.001402

S100a11	236.5751	592.3199	-1.32505	2.45E-08
Il1a	39.3691	99.41484	-1.34139	0.000354
Selplg	43.69099	112.8276	-1.36624	0.000371
Sirpa	439.2057	1143.509	-1.38199	1.35E-12
Hexb	131.0811	343.167	-1.38908	1.80E-13
Cx3cl1	20.64087	55.24197	-1.40896	0.005518
Col3a1	933.3454	2612.429	-1.48529	0.000268
Col5a2	80.73557	231.7103	-1.52671	4.80E-09
Baspl	30.23226	87.2495	-1.53061	0.000206
H2ab1	465.9999	1380.416	-1.56552	1.06E-21
Lox	12.37235	36.74071	-1.5789	0.008647
Anxa2	544.8601	1703.405	-1.64501	2.32E-05
Il15	15.24875	49.47425	-1.69537	0.00109
Colla1	384.5046	1281.597	-1.73762	2.10E-05
Lgals1	389.1031	1319.951	-1.76396	4.02E-35
Ccl2	13.80527	51.40555	-1.90092	0.00051
Nrg1	20.27071	90.5726	-2.16954	5.44E-05
Lgals3	94.81971	503.9981	-2.41549	3.13E-21
Mmp12	65.20975	481.6603	-2.88743	9.73E-05
Timp1	1.996592	35.34102	-4.19667	9.25E-06
Fgf9	0.418562	10.91781	-4.73104	0.009037
Ccl7	0.360675	15.70682	-5.25364	0.001787

Supplemental Table 8: SASP genes (total 4) upregulated by shRNA Gpnmb in MASLD liver.

Gene name	Average shRNA Gpnmb	Average shRNA SC	log2FoldChange	padj
Moxd1	167.7157	1.486805502	6.825857	0.009535
Igfbp1	5376.65	1178.326953	2.189598	7.35E-58
Gstp1	16079.25	5868.613057	1.454236	2.04E-42
Egfr	7794.302	3371.568682	1.209055	0.000228

Supplemental Table 9: SASP genes (total 15) upregulated by sugar water-FPC diet and downregulated by Activin A and shRNA Gpnmb in MASLD liver.

Gene name	FPC vs chow log2FoldChange	FPC vs chow padj	Activin A vs control log2FoldChange	Activin A vs control padj	shRNA Gpnmb vs shRNA SC log2FoldChange	shRNA Gpnmb vs shRNA SC padj
Baspl	2.156644543	1.59E-05	-1.57027	0.000117	-1.53061	0.000206
Ccl2	3.037914429	2.69E-05	-2.08546	0.000817	-1.90092	0.00051
Cd14	1.915839722	1.06E-06	-2.09329	6.08E-12	-1.07064	0.001238
Colla1	2.627480957	1.80E-20	-1.55844	3.83E-10	-1.73762	2.10E-05
Colla2	2.098430678	4.77E-16	-1.13307	3.95E-08	-1.31316	0.001402
Col3a1	2.084945518	7.15E-16	-1.42284	3.94E-10	-1.48529	0.000268
Col5a2	1.737153914	4.14E-05	-1.12073	0.000918	-1.52671	4.80E-09
Cxcl10	1.291621524	0.005905	-1.42303	0.001673	-1.31039	0.000391
H2ab1	2.082620886	7.14E-17	-1.35686	5.86E-10	-1.56552	1.06E-21

Lgals3	3.609664214	1.55E-33	-2.14269	2.89E-20	-2.41549	3.13E-21
Mmp12	7.247920265	6.56E-27	-2.68063	3.04E-28	-2.88743	9.73E-05
Nrg1	3.879501289	1.29E-12	-2.83428	1.13E-11	-2.16954	5.44E-05
Plau	1.426008251	0.006173	-2.06787	4.37E-05	-1.14447	0.006813
Sh3bgrl3	1.196575602	0.000598	-1.01249	0.000697	-1.04495	1.51E-05
Sirpa	2.221002503	1.47E-24	-1.30846	1.10E-16	-1.38199	1.35E-12