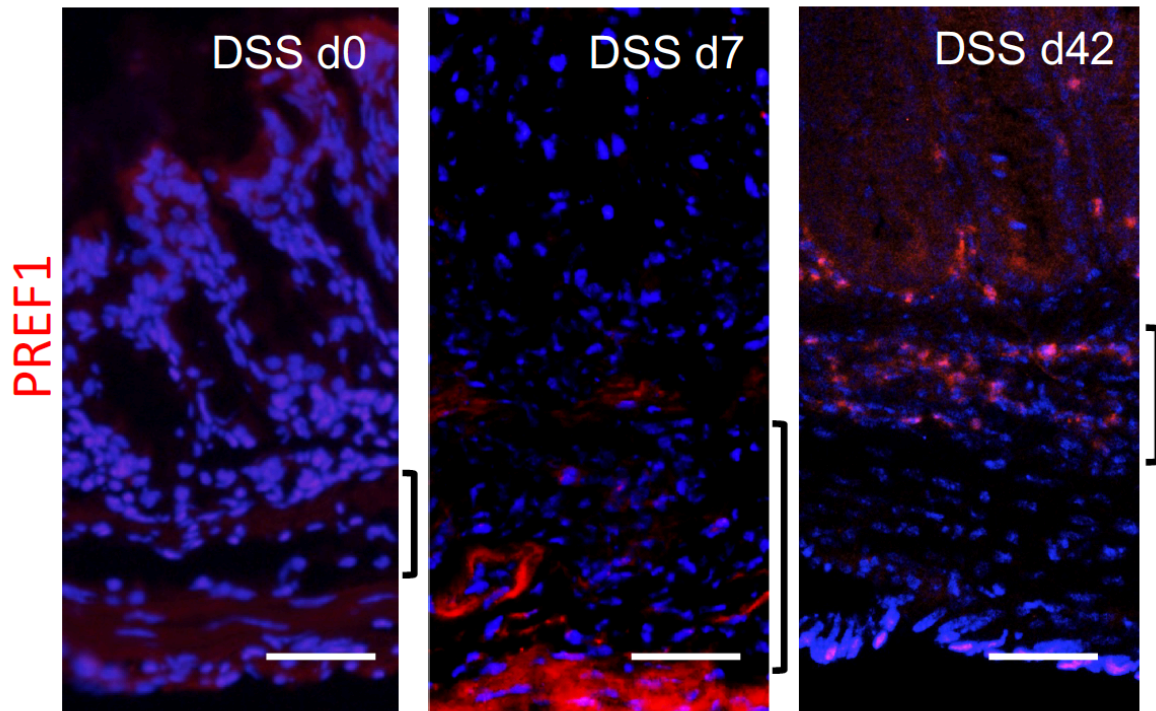


Supplemental Figure 1.

Adipogenesis is inhibited by hyaluronidase.

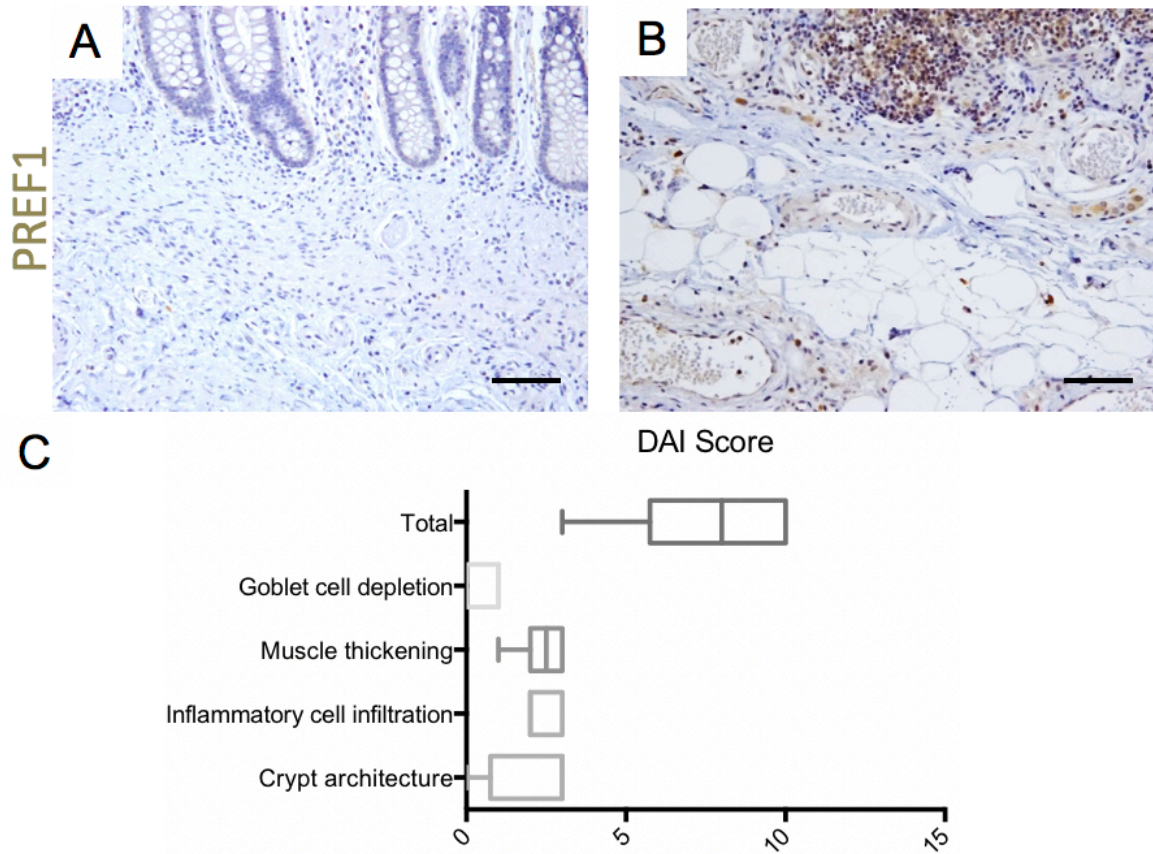
Mouse preadipocytes (3T3L1) were differentiated by the addition of adipocyte differentiation media (see methods) with or without the addition of 20 ug/ml of recombinant hyaluronidase (PEGPH20). (A) Cell numbers were analyzed by SRB assay and normalized to that of day 0 number. (B) Proliferative preadipocytes stained green with anti-BrdU. Scale Bar = 50 Microns. (C-E) Relative expression of mRNA for EBF1, Adipoq and Zfp521 at day 2 of differentiation. Data in A, C-E are represented using box-and-whiskers plots, with boxes representing the IQR, lines representing the median value, and whiskers representing minimum and maximum values, whereas data in D is represented as mean \pm SEM; * $P < 0.05$, ** $P < 0.01$ (t test).



Supplemental Figure 2.

Pref1 expression increases in colitis.

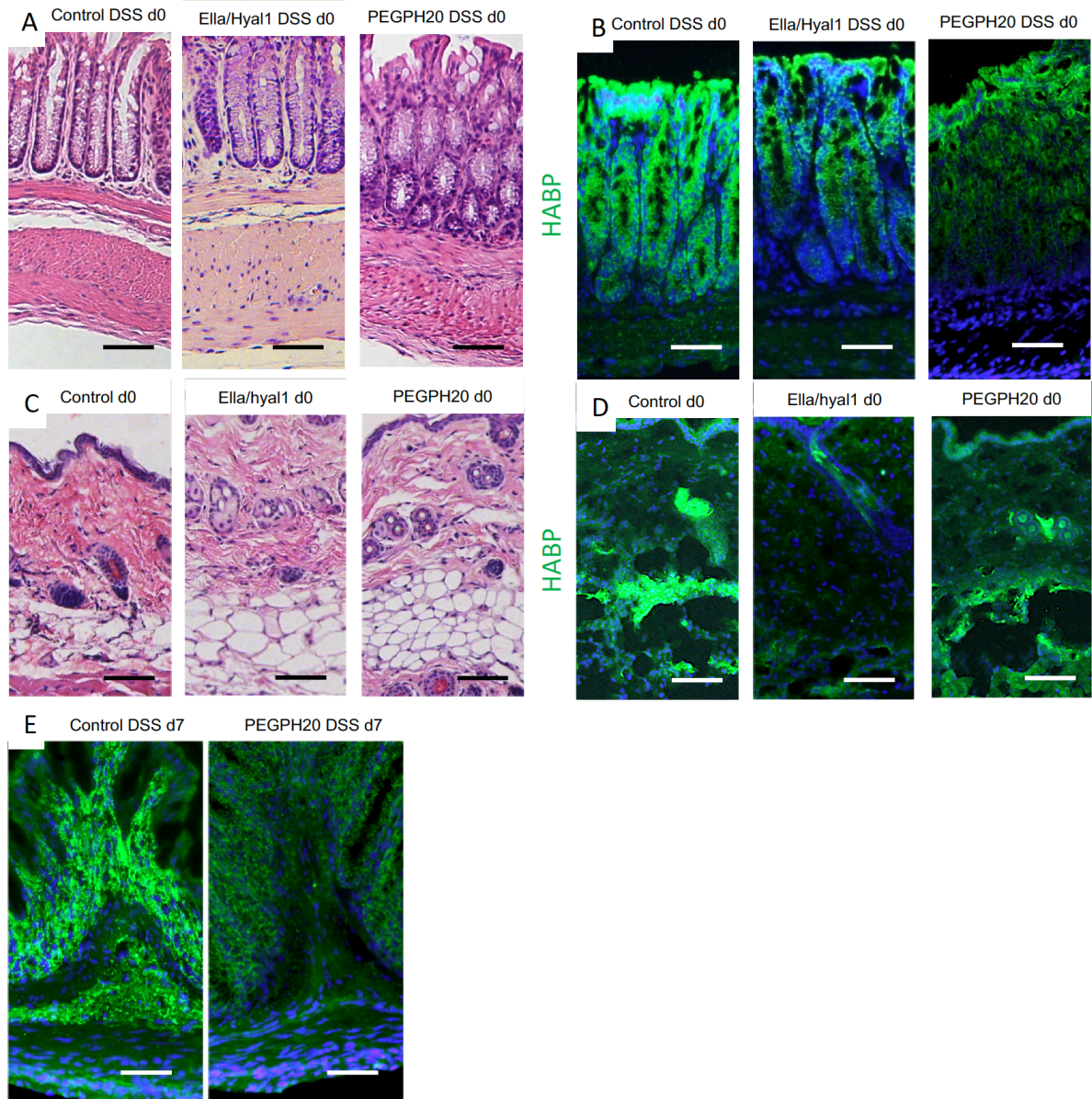
Representative histology stained with anti-PREF1/DLK of distal colon sections from control mice or mice at day 0 and 7 days or 42 days after being provided with 3% DSS colitis in drinking water. Brackets delineate submucosal region occupied by adipocytes. Scale Bar = 50 Microns.



Supplemental Figure 3

Adipogenesis is coincident with HA accumulation in IBD patients.

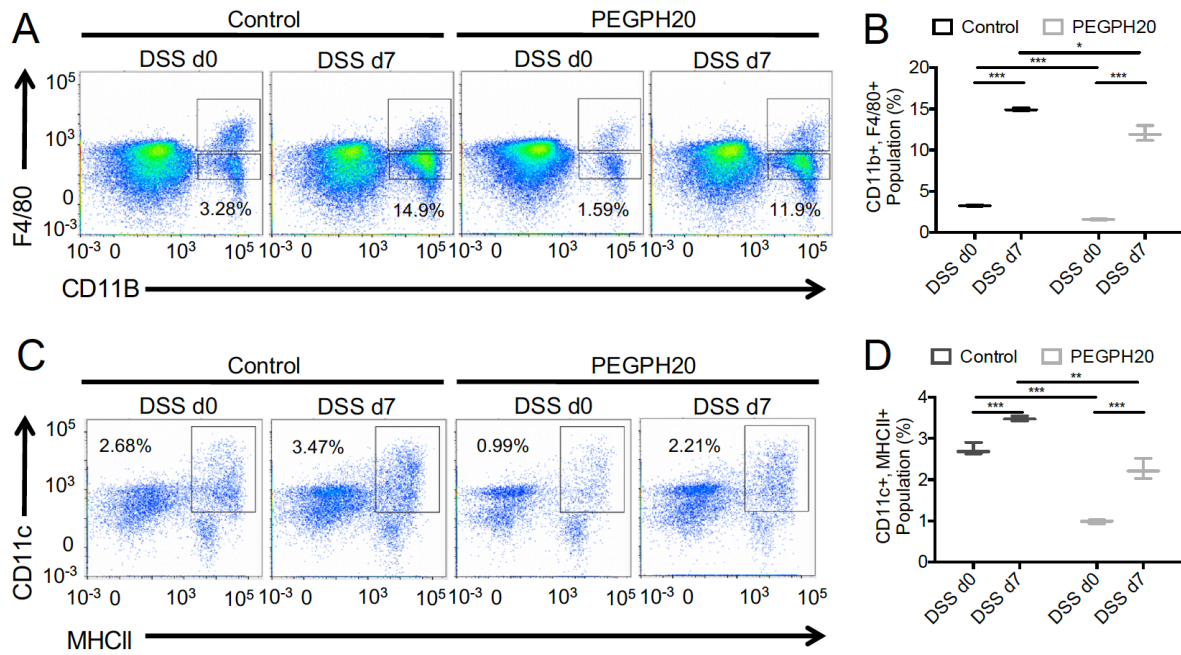
Representative histology from colon sections from Crohn's disease ((n=5). **(A)** Uninvolved section from subject stained for Pref1. **(B)** Inflamed colon from the same patient stained for Pref1. **(C)** Disease activity index score of IBD patients. Scale Bar = 20 Microns. Data in C is represented using box-and-whiskers plots, with boxes representing the IQR, lines representing the median value, and whiskers representing minimum and maximum values; ** P < 0.01, *** P < 0.001 (t test).



Supplemental Figure 4

Hyaluronidase is effective to digest HA in skin and colon.

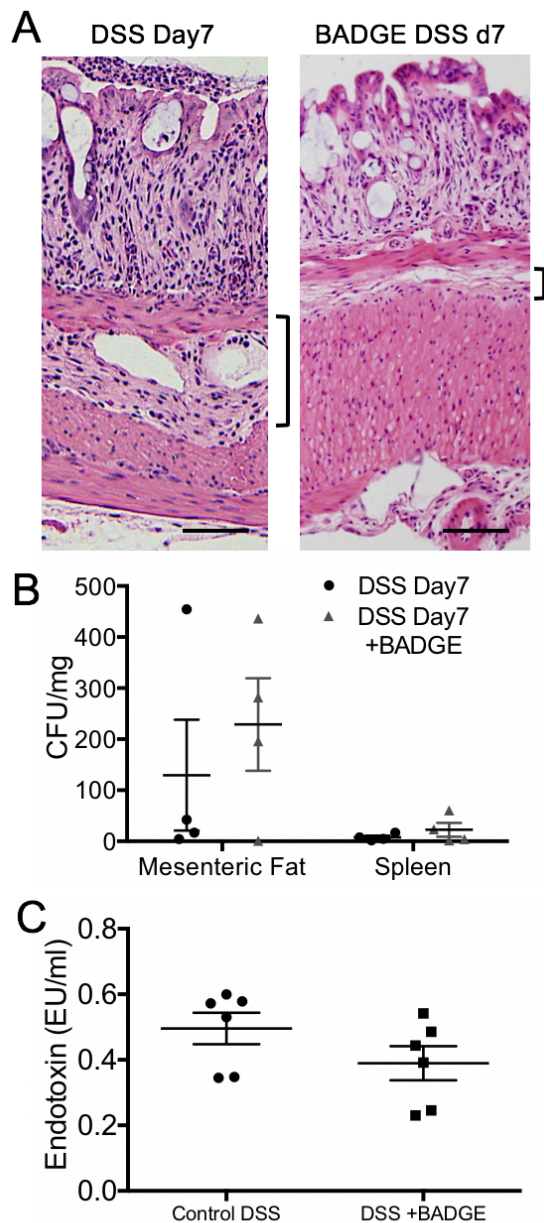
Representative histology of WT, Ella/hyal1 and PEGPH20 injected mice. (A, B) Normal distal colon section of WT, Ella/hyal1 and PEGPH20 injected mice stained with (A) H&E and (B) with HABP for HA. (C, D) Skin sections of WT, Ella/hyal1 and PEGPH20 injected mice stained with (C) H&E and (D) HABP for HA. (E) HABP staining of colon at day 0 (control) and 7 days after DSS administration and treated with PEGPH20



Supplemental Figure 5

Hyaluronidase results in decreased macrophages and dendritic cells during DSS colitis.

(A to D) Flow cytometry analysis of colon lamina propria single cell suspensions showing expression of (A, B) F4/80 and CD11B and (C, D) CD11C and MHC II from DSS d0 control, PEGPH20 d0, DSS d7 control and PEGPH20 treated DSS d7 mice. Numbers represent the percentage of the cells in the indicated gate. Data in B and D are represented using box-and-whiskers plots, with boxes representing the IQR, lines representing the median value, and whiskers representing minimum and maximum values ; ** $P < 0.01$, *** $P < 0.001$ (t test).



Supplemental Figure 6

Incomplete inhibition of inflammatory response by PPAR γ agonist.

(A) Representative histology of distal colon sections in colitis of WT and BADGE treated mice were stained with H&E. (B) Systemic bacteremia detected after colitis in mesenteric fat and spleen from WT and with BADGE treatment (N=4 mice/group). (C) Endotoxin concentration in the serum from WT and with BADGE treatment (N=4 mice/group). All error bars indicate mean \pm SEM; * P < 0.05, ** P < 0.01, *** P < 0.001 (t test).

Supplemental table 1	Up-regulated genes by DSS	Down-regulated genes by DSS
	Reg3b	Dbp
	Sptssb	Ciart
	Nos2	Lars2
	Plet1	Vaultrc5
	Apol10a	Fut9
	Mmp3	Npy1r
	Retnlb	Nxpe2
	Isx	Reg4
	Lbp	Cps1
	Clca4b	Ctnnbp2
	Cemip	Trf
	Socs3	Chodl
	Dhrs9	Tef
	Slpi	Ttr
	Tnf	Snora23
	Mfsd2a	Jchain
	Slc3a1	Smoc2
	Aldh1a3	Slc16a12
	Nfil3	Gjb4
	Mmp13	Per3
	Tac1	Mir6236
	Chn2	Itih2
	1810065E05Rik	Plk3
	Ly6c1	Cdo1
	Cxcl5	Axin2
	Adra2a	Snord22
	Acacb	Tmprss13
	Wfdc18	Rnf32
	B3gnt6	Kyat1
	Slc5a9	Trpv6
	Rian	Tppp3
	Serpina3n	Igsf10
	Meg3	Pyroxd2
	Dnah17	2310079G19Rik
	Duoxa2	Mptx2
	Duox1	Gsta3
	Car12	0610005C13Rik
	B4galnt1	Per2
	Ttyh1	Fzd7
	Gm12250	Ctgf
	Trim15	Tenm4
	Car8	Rn45s
	E2f2	Hopx
	Duox2	Gjb5

St3gal1
Mgat4c
Agpat9
Steap4
Plat
Hmgcs2
Ccl20
Cd177
Rnf150
Nlrc5
C2cd4b
Cmah
Gda
Shank3
Nupr1
ligp1
Mx1
Zbp1
Gm5431
Gm14137
Plaur
Col23a1
Ptk6
Syt6
Slc9a3
Ddah1
Gcg
Serpina3g
Ly6a
Zc3h12a
Cpn2
Gbp6
Il1rl1
Casc4
Gpnmb
Snhg11
Ifit1
Trim40
Ifit2
Osmr
Lpo
Il18bp
Cdhr1
Muc2
Muc1

Slc2a5
Timp4
Atp10a
Fam46c
Sstr1
Mptx1
Sorcs2
Spin4
Mir6516
Serpina9
Apobec2
Ces1f
2410006H16Rik
Prkar2b
Ace2
Gstm1
Csad
Hist3h2a
Terc
Car3
9230105E05Rik
Slc16a9
Arl4d
Nr1d2
Hist1h1a
Eda2r
Bambi
Tmem132c
Ptpro
Pdzd7
Hist2h2be
Scarna6
Hoga1
Gm14391
Cldn2
Glp2r
Cnn3
Ephb6
Hist4h4
Hist1h2bb
Ugt2b35
Aqp1
Celf4
Hykk
Cox7a1

Ffar4	5033404E19Rik
Cldn8	Il33
Casp4	Wee1
Adamts1	Ces1e
Ceacam10	Scarna13
Pla2g2a	Dnah8
Arhgap20	Col4a6
Wtip	Gm16576
Npas2	Hist1h3b
Prox1	Dok7
Rel	Prdx4
Apol6	Snora78
Myrip	Hist2h2bb
Bcl6	Rpph1
Csf2rb	Fam132a
Tdrd1	Csrnp1
Cpne8	Hist1h2bm
1700120E14Rik	Sun2
Ranbp17	Cenpp
Dmbt1	Epb41l4aos
Aqp4	Naaladl1
Rsad2	Ptpru
Ifi47	Snord17
Slc7a9	Per1
Cnn1	Amica1
Nov	Clec14a
B3galt5	Hist1h2bl
Fer1l4	Hist1h2bn
Appl1	Hist1h1b
Pfkfb3	Hist1h3a
Cpne2	Crip1
Igfbp5	Gstm6
Tmem181c-ps	Aldh1b1
Cd38	Smim24
Slc7a5	Paqr7
Gm13363	Acer1
Gm10400	Frem2
Sec1	Etv4
Zfhx2	Hist1h3e
Gbp5	Hist1h4h
Gbp4	Hist1h3c
Ypel2	Slc16a11
Gpr22	Hist1h2bq
Rdh16	Hist1h2br
C3	Hist1h2be

Lrp8
Ak4
Des
C4b
Tnfrsf1b
1700024P16Rik
Adora1
Ncoa7
F2rl2
Ttn
Slc51b
Nckap5
Tmigd1
Oasl2
Slc35d1
Nfasc
Bglap3
Cxcl13
Slc13a2
Slc13a2os
Pde9a
Htr2b
Dnm3os
Sulf2
Gna14
Wfdc17
Bhlha15
Ceacam2
Ereg
Csf2rb2
Mgll
Map3k8
Fam196a
Megf11
Fut2
Htra3
Mapre3
Cyp2c65
Lgals9
Clca3a1
Fkbp5
Sppl2a
Fcgr2b
Armcx4
Cp

Rgs10
Kyat3
Hist1h3g
Phlda3
Fgfr3
Hist1h2ad
Hist1h4c
Mycl
Tmem14a
Snora74a
Gstm3
Hist1h2ap
Hist1h2bk
Hist1h2bh
Itpripl2
Acyp1
Efna4
Hist1h3d
Hist1h4f
Lipt2

Pcsk5
Trim72
Ifit3b
C77370
Slc10a2
Lgmn
D730005E14Rik
Col8a1
Gm8615
Il4ra
Ceacam1
Tnip3
Tead1
Socs1
Synm
Bach2
Arhgap27os3
Gsdmcl-ps
Itgam
Gm19461
Tnfsf10
Paqr8
Mgp
Rassf4
Fam3b
Arhgap23
Xdh
Apol9a
Ogfrl1
Tgtp2
Ccl9
Mmp28
Actg2
Kcnn3
Stc2
Nlrp9b
Gnpda1
Prps1
Hspa1a
Tagln
Hmox1
Galnt18
Piezo1
Pclo
Sidt1

Gem
Lypd6b
Nt5c1a
Hcn2
Cwh43
Ttc7b
Kctd12
Hspa1b
4931406H21Rik
Ly6c2
AI661453
Mbd6
Itga2
Zdhhc13
Slc4a7
Pgap1
Pla2g5
Ang4
4930565N06Rik
Muc4
Ppm1l
Sgk2
Mospd3
Hcls1
Il18
Isg15
Arap3
Tmem139
Tmem38b
Emp1
Auts2
Kcnk6
Cd68
Pdlim3
Glipr2
Vcam1
Pde8a
Reln
Cry1
Slc30a10
Muc13
Sod3
Plekhm1
Tbc1d9
Pstpip2

Tgtp1
Arntl
Prr13
9930111J21Rik2
Tnfaip2
Tc2n
Slc2a4
Tpm2
Grin1os
Mboat2
Ermp1
Ido1
Ecscr
Satb1
Cdx2
Pag1
Oas3
Gramd3
2010016I18Rik
Nol4l
Fzd3
Nkain1
Slc36a4
Slc5a3
Insl3
Fam219a
Brd4
Gm13889
Igsf6
Themis2
D17H6S56E-5
Nfkbiz
Nlgn2
Evi2b
Tanc2
Stat2
Setd1b
Rrbp1
Rbms3
Tifa
Apob
Cnm2
Pappa
Fyb
Fgl2

Abca5
Gnao1
Slc28a3
Tnfsf13b
Cyp2d9
Pcdhgb2
Ffar2
Lrrc32
Hivep3
Igtf
Adrbk2
Pdpn
Galnt16
Plxnc1
Areg
Neat1
Lonrf3
Flt4
Prdm1
Ier5
Etnppl
Rdh18-ps
Tmcc3
Leo1
Icam1
Ttyh3
Lrrtm2
Dclk1
Daglb
Kmt2d
Syvn1
Slc8a1
A330023F24Rik
Eid3
Ifit3
AW112010
Atn1
2210407C18Rik
Mafb
Lhfpl2
Pgs1
Ehd4
Nbea
Cyp2d10
Dmxl2

H2-T24
Chad
Robo2
Grem1
Sema7a
Hyou1
Tifab
Cfh
Arid3a
Cd84
Ttc22
Gprc5a
Basp1
Hck
Laptm5
Adap2
Adcy2
Parp14
Ubd
Polq
Strip2
Pmepa1
Cntnap1
Rbpms
Pgm5
Ripk3
Cd47
2610528A11Rik
Crem
Arhgap35
Alox5
Camk2n1
4732471J01Rik
Macf1
Galnt3
Ralgapa2
Ccdc97
Zfp9
St8sia5
Cacna1b
Irgm2
Spon1
Slit2
Gbp2
Gm15708

Ano7
Tgm2
B3gnt5
Zfand5
Slc9a1
Pcp4l1
Ppp2r1b
Bmp7
Anks6
Bcl2l11
Srgap1
Abcc5
Itgb2l
Srrm2
Ptpn2
Tmc5
Atp8a1
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Abcg8
Kazn
Myo1d
Abhd6
Eif4g3
Proser1
Rims2
Hap1
Pom121
Fam124a
Efnb2
Ppy
Ttl10
Nus1
Fndc3b
Acadl
Exoc6b
Nos1
AW551984
Scarf2
Alg3
Tspan6
Plod2
Fam122a
6430548M08Rik
Ptafr
Scg3

Fbrs
Mpzl1
Dtx3l
Jak3
Ryr2
Fry
Cacna1h
Tlr4
Igf2bp2
Ifit1bl1
Arl14
Rdh19
Mroh3
Pnrc1
Tmem184c
Ifit1bl2
Pdlim7
Arhgap17
Cmtm8
Eif4e3
Psm8
Tbrg3
Dock4
Abi2
Tinagl1
Mvb12b
Rdh9
Srrm1
Hk2
Clec7a
Unc5a
Ripk2
C1galt1
Iqgap2
Rtp4
Rhoj
Slco3a1
Tmem220
Pcsk1n
Pcdhgb7
Prr12
Ppifos
Rnf44
Aoc2
Srgap3

Pglyrp1
Hipk2
Ssh2
Kdm7a
Rnf39
Pappa2
Hgf
Sema4a
Srcap
Celsr3
Bcl3
Krt84
Gdap10
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Sh3kbp1
1190002N15Rik
Trafd1
Atp10b
Klhdc8a
Fabp2
Tmem131
Stambp
Kmt2a
Dvl3
Trim12a
Mmp15
Mpp3
Kirrel3
Spen
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Plagl2
B4galnt2
A430088P11Rik
Hspa5
Acer2
St5
3110062M04Rik
Ncor2
Asap1
Grb10
Tprn
Plxna4
Itgav
Neto2
Ankrd22

Lpin2	
Osbp17	
Phactr2	
	10-Sep
Trim36	
Cyp2c55	
Tnfrsf11a	
Apol7a	
Zdhhc9	
5830444B04Rik	
1110059E24Rik	
Sema6b	
Pcdhga9	
Syn3	
Capn13	
Tex9	
Fth1	
Cd14	
Cpeb2	
Dcp2	
Slc16a6	
Creb3l1	
Ugt1a6b	
Gabbr1	
Zfp711	
Trp53i11	
Tlr2	
Ubqln2	
Rimbp2	
Apaf1	
Lgals3bp	
Col18a1	
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Ptpn23	
Tbc1d15	
Fgd5	
Ptpn	
Hip1	
2010109I03Rik	
Ms4a8a	
Ptp4a1	
Prom1	
Hkdc1	
Rab6b	
Fxyd6	

Nr1h4	
Galc	
Cnbd2	
Creld2	
Pyy	
Figl2	
Fscn1	
B130006D01Rik	
Abhd17b	
Nectin1	
Irf7	
Fas	
Ick	
Gan	
Rsc1a1	
Asap2	
Capg	
Sec24a	
Ankrd28	
Tcf23	
Prrc2a	
5330417C22Rik	

Supplemental table 2	Up-regulated genes by PEGPH20	Down-regulated genes by PEGPH20
	Lars2 Mir6236 Cxcl5 Rn45s Plat Hspa1a Hspa1b Trf Syt8 Chodl Ctnnb2 Tmprss13 Reg4 Slc16a12 Pyroxd2 Fam46c Ankrd37 Nxpe2 Fut9 Mptx2 Steap4 Hoxd10 Banp Snord22 Gatm Smoc2 Mptx1 Tmem173 Slc4a4 Dbp Fzd7 Ciart	Mmp13 Tmigd1 Sptssb Cemip Reg3b Gm13363 B3gnt6 Mmp3 Creb3l3 Cyp2c65 1810065E05Rik Ptgs2 Lpo Slc3a1 Mt2 Ido1 Ifit2 Retnlb Cmah Il1rl1 Rian Car8 Slc7a9 Gcg Cd177 Gchfr Ifit1 Adap2 Serpina3n Plet1 Ereg Cyp2d10 Ilgp1 Emp1 Slpi C4b Apol9a Ly6c1 Ccl20 Ccr2 St3gal1 Zfp37 Mgll Ncoa7

Adra2a
Cyp2d11
Hmgcs2
Ppy
Gm5431
Pappa
Chn2
Aldh1a3
Col18a1
Ccr1
Mboat2
Gadd45a
Tcf23
Pdpn
Cp
Acacb
Ms4a6c
Krt23
Cyp2d9
Igfbp5
Isg15
Adamts1
Zg16
Gpnmb
Rac2
B4galnt1
Spink1
Tnf
Myrip
Cyp4f14
Casc4
1500009L16Rik
Aldh3b1
Entpd1
Apold1
Bmp7
Nt5c1a
Fabp2
Itgam
Rsad2
Apol10a
Apol6
Gm14137
Ednrb
Dpep1

Fcgr3
C3
Ces2b
Mapre3
Hsd3b2
Mmp19
Rab37
Mep1b
Tex9
Sema3a
Ifi47
C77370
Ifit3
Slc2a4
Ccl9
Fkbp5
Ppfia3
Bglap3
Aqp8
Svep1
28-Feb
Hsd3b3
Pde4b
Gngt2
Srxn1
Ttyh1
Dcn
Mgat4c
Tek
Ptpro
Cdh13
Clec7a
Fbxo44
Ranbp17
Serpina3g
Nat8f2
Itgal
Aspa
Tmem37
Apobec1
1700052K11Rik
Ppp3cc
Pla2g15
Nat8f4
Neto2

9930111J21Rik2

Esam

Gm12250

Slfn5

Ccdc122

Hbb-b2

Hbb-bt

Tnfaip2

Gbp4

Ces2c

Gbp6

Apoc2

Dnase2a

Ugt1a1

Lama4

Car1

Ube2l6

Hba-a2

Clca4b

Antxr1

Prss30

Ccrl2

Ceacam10

Ces2d-ps

Ces2e

Lyve1

Prex1

Chst11

Rgs13

Plek

Dgat2

Hbb-b1

Hbb-bs

Ifit3b

Ggt1

2210407C18Rik

AW112010

Lepr

Ubd

St8sia4

Gm20939

Isx

Igfbp7

Lgals9

Prom1

Pdlim2
H2-Q1
Cfh
Rgl1
Capg
Mt1
Loxl2
Dhx58
Espn
Sgk1
Bik
Casp3
Zfp820
Alox5ap
Csf2rb
Car4
Sod3
Tyrobp
Agpat9
Arl14
Tstd3
Vav3
Gpt
Spata6
Mmrn1
Srgn
Tff3
Spns2
Gm3336
Btnl6
Adgrl3
Ppm1m
Tgm2
Kremen2
Pld4
Trim6
Mgp
Slc16a6
Sepp1
P3h4
Abcg2
Nrp1
Ly6a
Cd84
Ang4

Dusp10
Cxcl12
Alox5
Slc26a3
Cd53
Gm5141
Rtp4
Kctd18
Chic1
Slc25a34
Glrx
A630066F11Rik
Slc30a1
Col12a1
Cyp2c55
C1qtnf1
C1galt1c1
Gpcpd1
Sectm1b
Ogfrl1
Saa2
Sult1d1
Abhd6
Zfp52
Glipr2
Hkdc1
Lypd8
Ly6c2
Sla
Ggh
C2
Meg3
Pcsk5
Lrrc19
Zfp781
Clec2e
Vcam1
Bcap29
Herc6
AI507597
Sult1b1
Postn
Itga8
Pax8
Psmb8

Lyz2
Rbks
Gbp2
Slc34a2
Nceh1
Arntl
Igfbp4
Psmb9
BC021614
Rasgrf2
Itga4
Gem
Tspan6
Il10ra
Cwh43
Plekho2
Rbms3
Zfp994
Hip1
Sema7a
Car12
Dcxr
Hmox1
C2cd4b
Pla2g3
Hsd12
Lpin2
Tnfsf13b
Zfp995
Afmid
Sdhaf1
Gdpd2
Ifi2712a
H2-DMa
Cideb
Cd93
Icosl
Dock4
Pgap1
4931406C07Rik
Mmp2
Mrc1
St3gal3
Scarf2
Snx20

Dnajc27
Sirpa
Lamb1
Btn1
Oasl2
Fmo5
Col4a1
Fscn1
Rorc
Bola3
Oas1g
Prdm1
Selplg
Cdkn2b
Gm8909
Clca1
Csf2rb2
Tfpi2
A430105I19Rik
Tbc1d1
Ncf1
Tmsb4x
Ffar2
Pcsk1
Lrrc32
Htra1
Fbxw17
Hcls1
Tmem139
Grina
Prdx6b
Tgfb1
Saa1
Samhd1
Hba-a1
Guca2a
Fgl2
Rfk
Cyp3a13
Trpv6
Gm9833
Map10
B2m
Slc12a4
Vsir

Pglyrp1
Fgd2
2200002D01Rik
Golt1a
Cgrrf1
Fabp5
Syne3
Pdgfra
Sdcbp2
H2-Q2
Slc23a3
Mmrn2
Lpcat4
Acyp2
Nkx2-3
Acot4
Txn1
Cdhr2
Prdx6
Ifit1bl2
Rftn1
Mettl7b
Snrpn
Hcn2
Slc9a3r1
Col15a1
Bank1
Gprc5b
Rab31
Fam105a
P2ry4
Ptprc
Themis2
Slc30a10
Rhod
Prickle1
Oaf
Nov
Slc1a4
Dusp5
Atg4a
Scin
Pcdhgb2
Slc46a3
Rhobtb3

Rnf150
Irf7
Lyz1
Prex2
Ddah1
Cd36
Robo4
Bmp4
Syt15
Ddx60
Ceacam1
4-Sep
Tesk2
Muc2
Cyp2d22
Col23a1
Chmp1b
Aldh1a1
Fa2h
Lrrc8c
Pde9a
Dnm3os
Spata7
H1f0
Col5a2
H2-Q5
Reln
Celf2
Ephx2
Anapc10
Slc51b
Zfp677
Lacc1
Cybb
Trib2
Oasl1
Mmp15
Col5a1
Cxcl16
Adgrl4
Gcnt3
Arl4a
Sdk1
Car13
Adamts2

Fgfr1
Ermp1
Pde6d
Syap1
Maf
Cd44
Slc9a2
Slc43a3
Cyp2f2
Gcc2
B3gnt2
Palm
Plau
Mblac1
Rassf4
Zfp759
Mmp28
Vcan
Podxl
Cd34
Pecam1
Sowaha
Cyp2d12
Crispld2
Mpeg1
Pim1
Hdhd3
Stard3nl
Il18
Kdr
Fbxo25
Ethe1
Aqp4
4921531C22Rik
Sval1
Scand1
Slco3a1
Rab17
Cyp2c40
Csf1r
Slc25a40