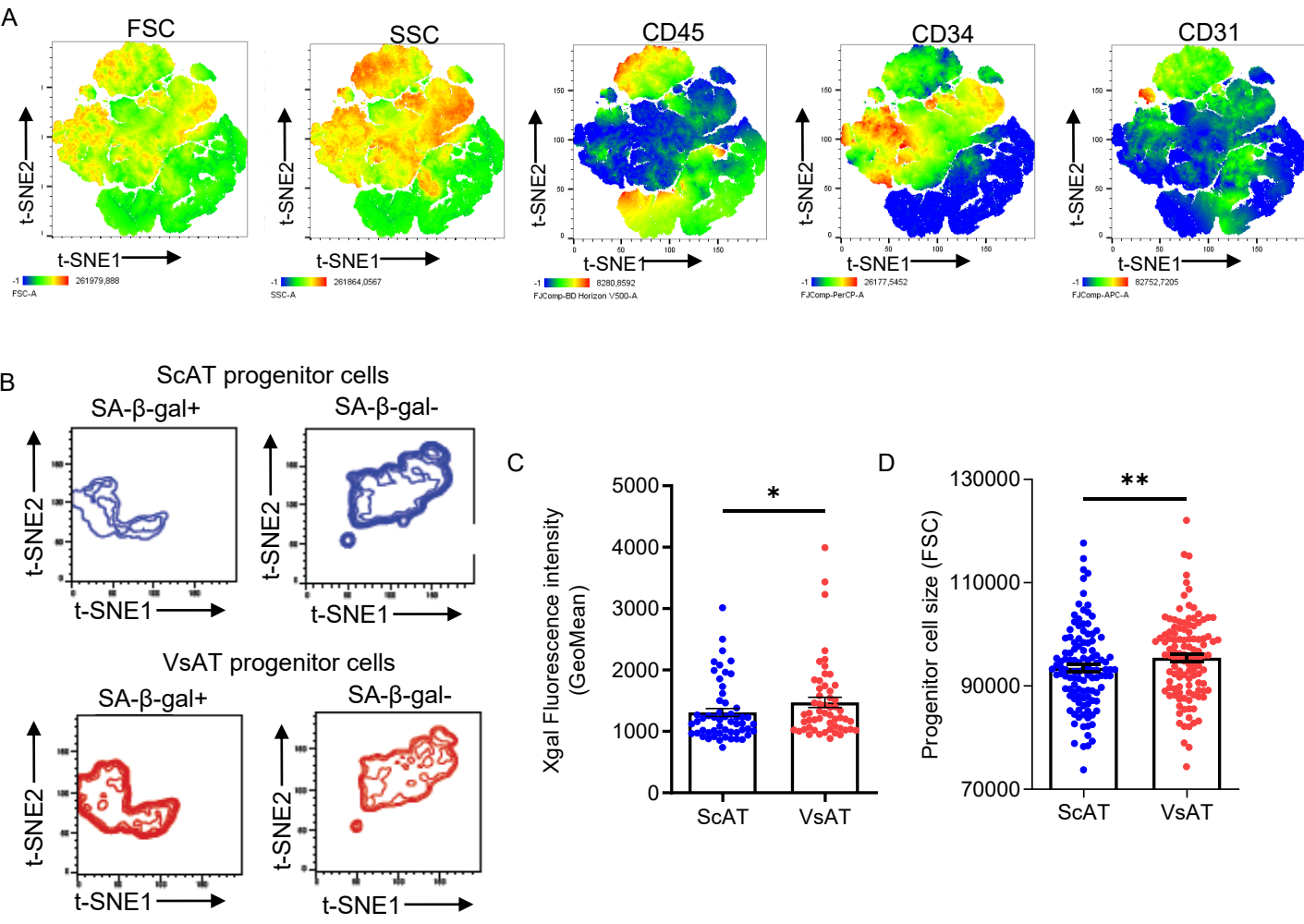


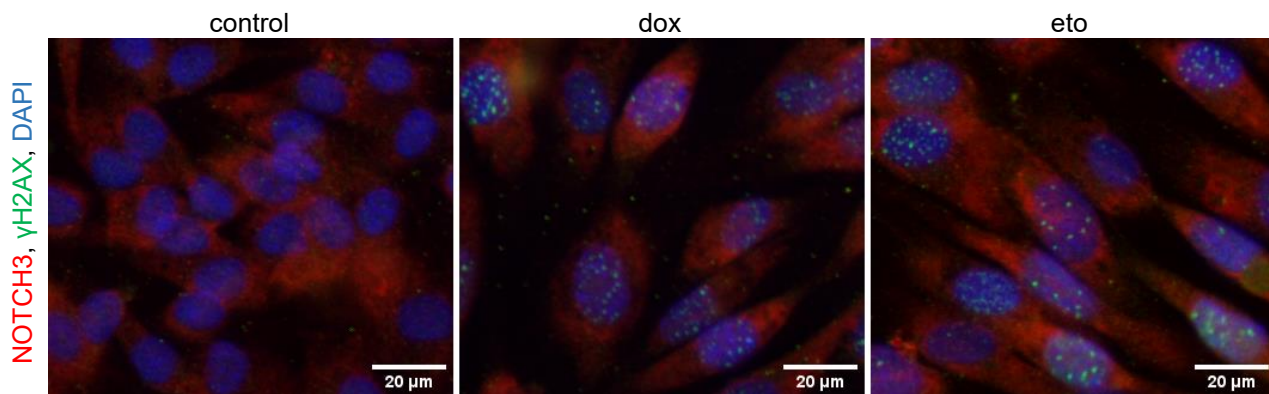
Supplementary Figure 1



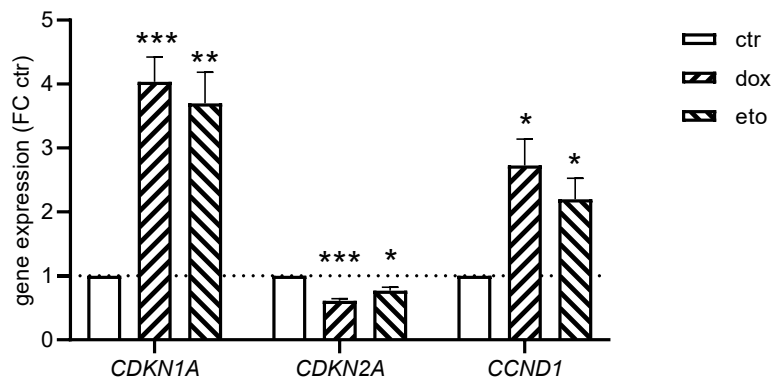
Supplementary Figure 1: **Characterization of ScAT and VsAT progenitor senescence by flow cytometry.**
 A) Paired ScAT and VsAT stroma-vascular cells from 55 subjects were analysed by flow cytometry. tSNE of flow cytometry data after downsampling and concatenation of the FSC (Forward Scatter), SSC (Side Scatter), CD45, CD34 and CD31 fluorescence intensities. B) Density plot of the SA-β-gal+ and SA-β-gal- ScAT and VsAT progenitor clusters. C) Geometric mean of the SA-β-gal fluorescence intensity in SA-β-gal+ progenitor cells of ScAT and VsAT from 55 subjects. D) Progenitor cell size determined with the FSC in ScAT and VsAT by supervised analysis of the SA-β-gal+ progenitor cells. Results are expressed as means +/- sem.

Supplementary Figure 2

A



B

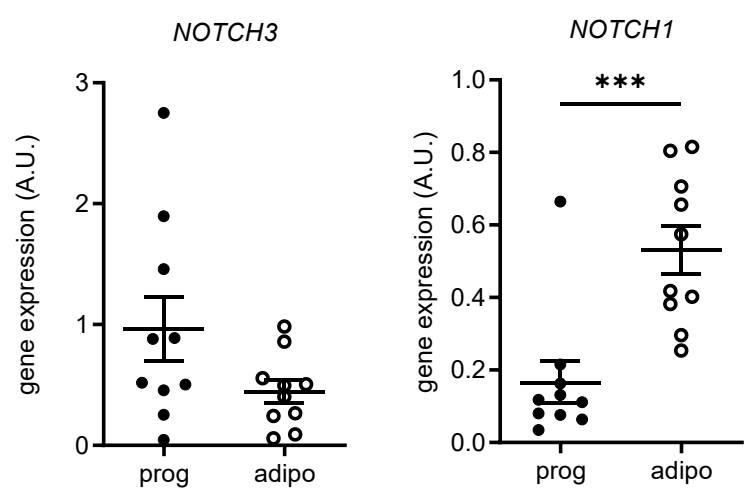


Supplementary Figure 2: DNA damage-induced senescence in ScAT progenitors.

A) Representative photomicrographs of NOTCH3 (red), γ H2AX (green) and DAPI (blue) stainings in progenitor cells treated with doxorubicin (dox) or etoposide (eto) or not (control) during 72h (scale bar = 20 μ m).

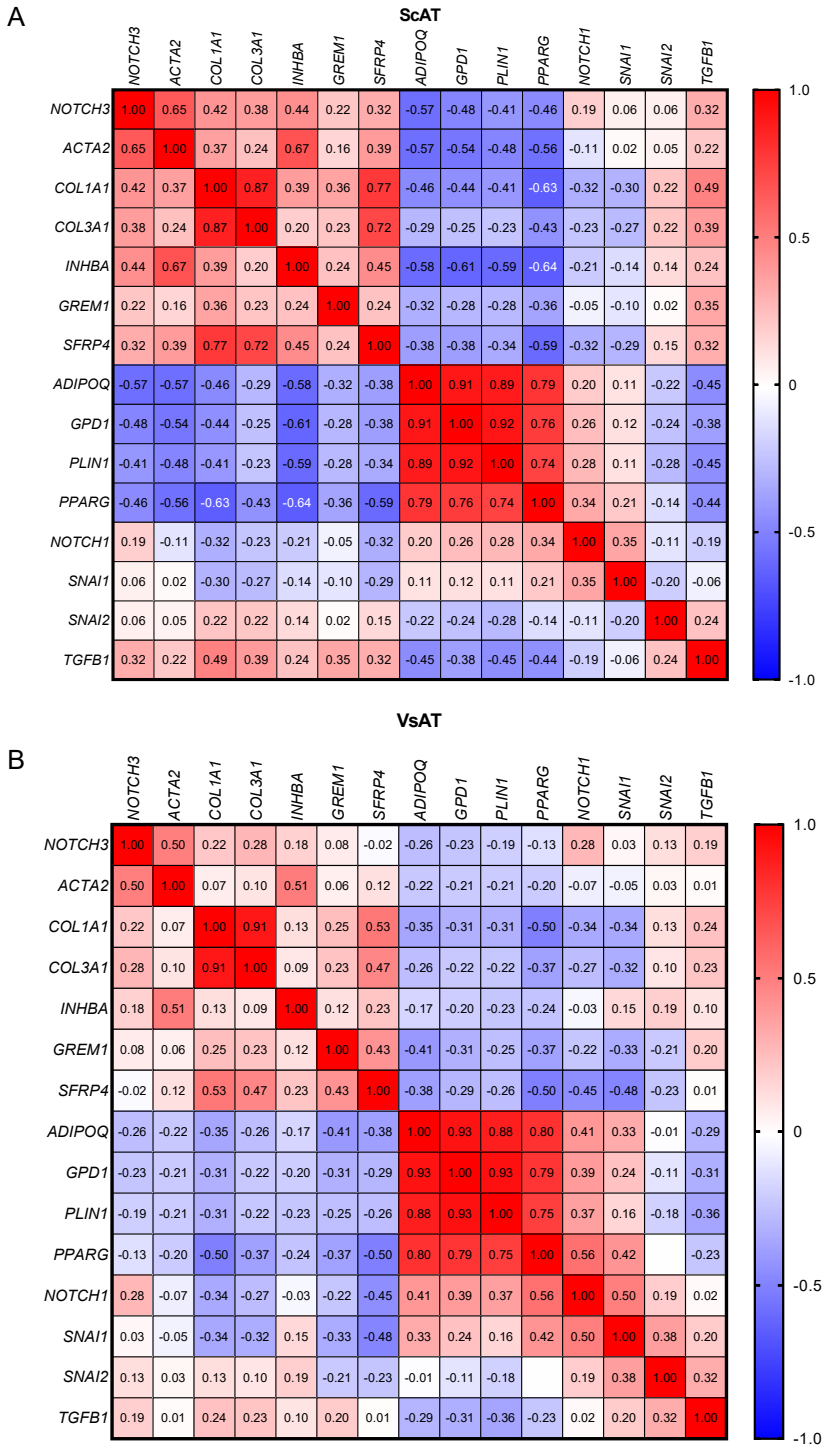
B) *CDKN1A*, *CDKN2A* and *CCND1* mRNA levels in progenitor cells after 72 hours of doxorubicin (dox) or etoposide (eto) treatment determined by RTqPCR. Results are expressed as fold change over control cells, means +/- sem of n=3 donors (two-way ANOVA, Dunnett's post-test, * p<0,05, ** p<0,01, *** p<0,001 compared to control).

Supplementary Figure 3



Supplementary Figure 3: **Distinct expression of NOTCH1 and NOTCH3 according to obesity and cell type.** NOTCH3 and NOTCH1 mRNA levels in isolated progenitor cells (prog) and mature adipocytes (adipo) determined by RTqPCR. Values are means +/- sem of n=10 donors.

Supplementary Figure 4

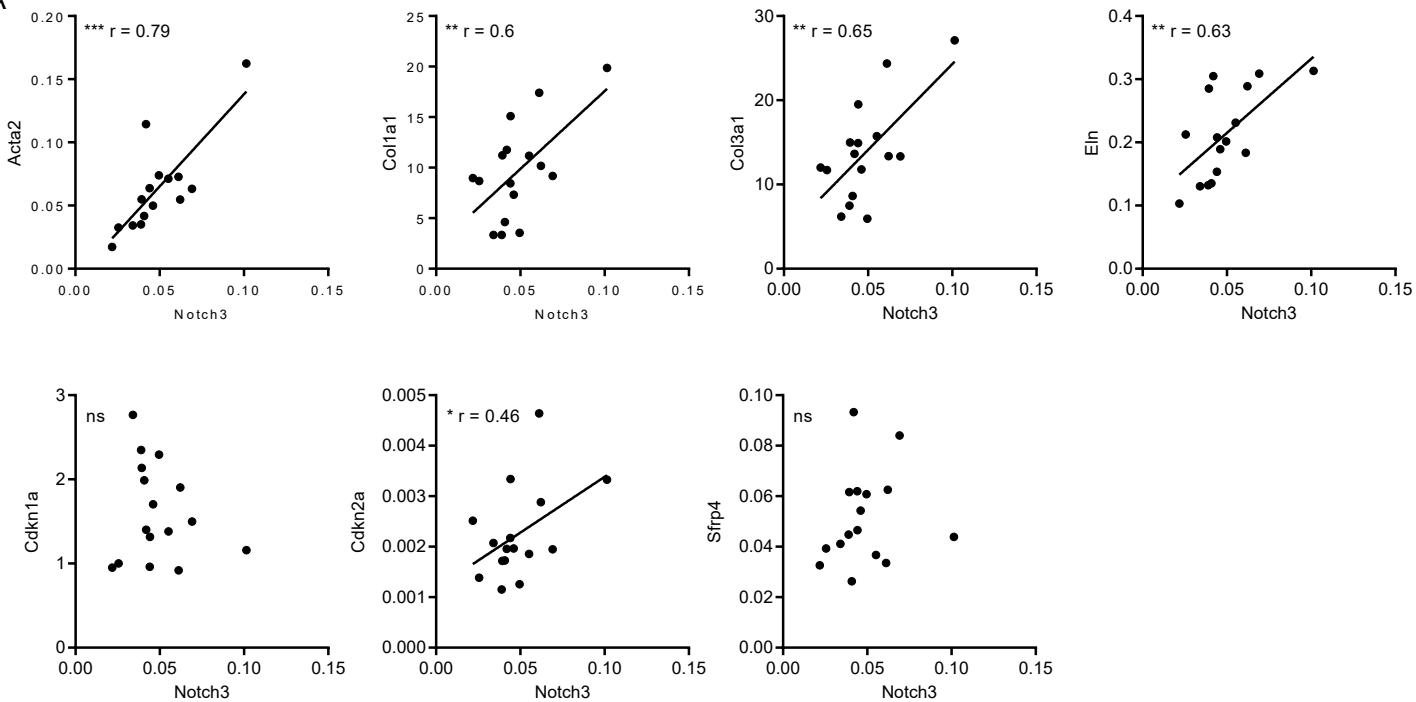


Supplementary Figure 4: **Correlation between NOTCH3 and NOTCH1 with fibrosis-, adipogenic- and TGFβ-related genes in ScAT and VsAT.**

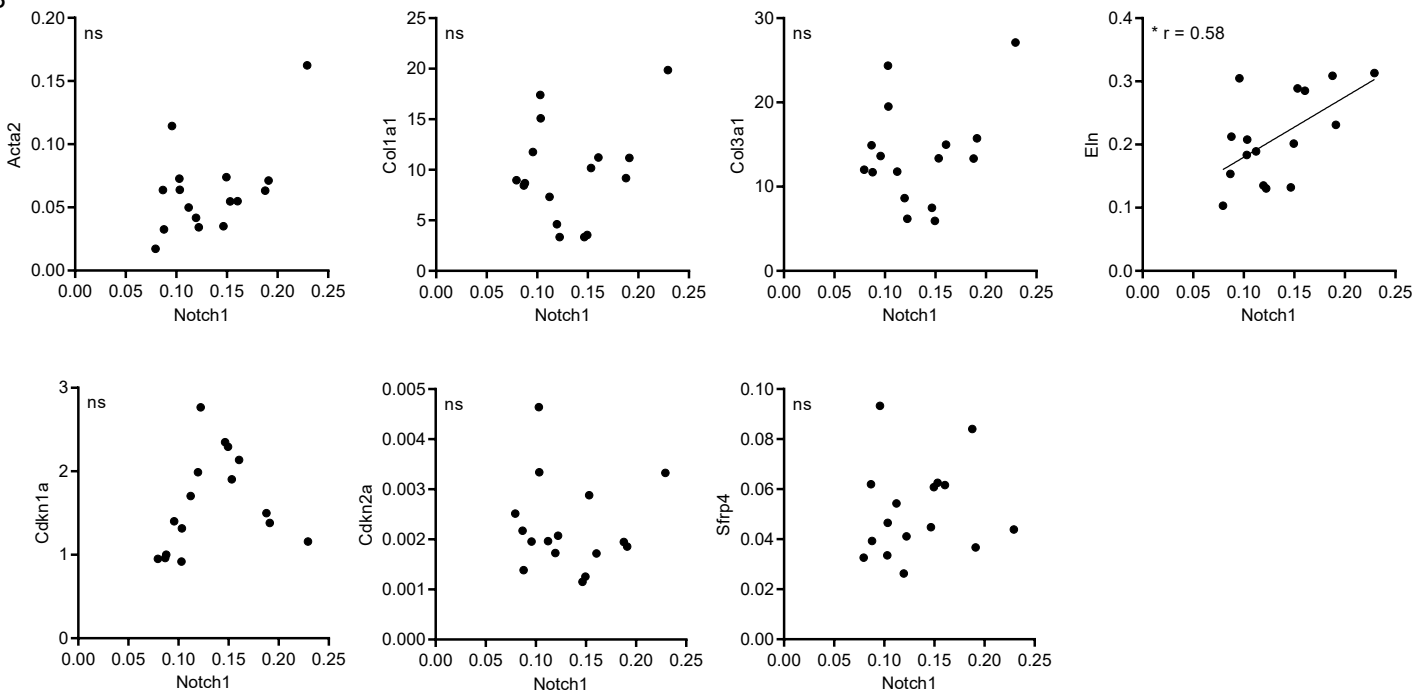
Correlation matrix showing the Spearman r between NOTCH3, NOTCH1 and fibrosis-related (ACTA2, COL1A1, COL3A1), SASP-related (INHBA, GREM1, SFRP4), adipogenic-related (ADIPOQ, GPD1, PLIN1, PPARG) and TGFβ-related genes (SNAI1, SNAI2, TGFβ1) transcript levels in A) ScAT and B) VsAT from the GTEx RNA-seq database performed on whole AT samples. ScAT n=663, VsAT n=541, Spearman correlation test.

Supplementary Figure 5

A



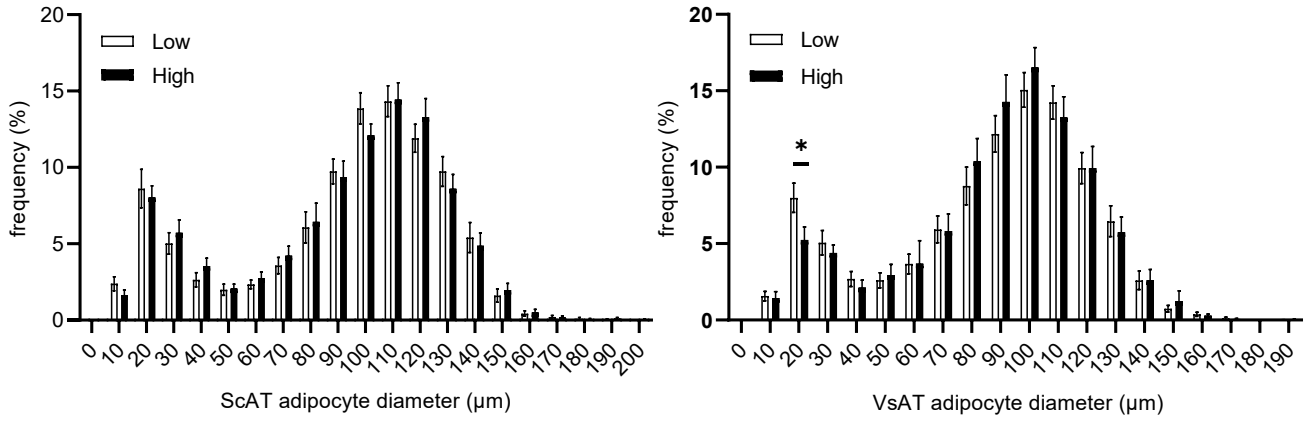
B



Supplementary Figure 5: ***Notch3* gene expression is positively correlated with fibrosis-related genes in VsAT stroma-vascular cells of C3H/HeOuJ mice.**

Correlations between A) *Notch3* or B) *Notch1* and fibrosis-related genes (*Acta2*, *Col1a1*, *Col3a1*, *Eln*) and senescence-related genes (*Cdkn1a*, *Cdkn2a*, *Sfrp4*) in stroma-vascular fraction cells isolated from perigonadal AT of mice fed 0, 2, 4 and 6 weeks with 45% high fat diet, determined by RTqPCR. n=16, Pearson correlation test.

Supplementary Figure 6



Supplementary Figure 6: **ScAT and VsAT adipocyte diameter in low and high senescence groups.** Distribution of mature adipocyte diameter in ScAT (left panel) and VsAT (right panel) in low and high VsAT progenitor senescence groups. Attention to the VsAT 20 μm diameter position where the only significant difference was observed between the low and high tertiles. Results are expressed as means +/- sem of n=30 low and n=24 high donors per group (two-way ANOVA, Tukey's post-test).

Supplementary Table 1: Human and murine Assay on Demand (Thermofisher)

Human target gene	AOD
<i>ACTA2</i>	HS00909449-m1
<i>ADIPOQ</i>	Hs00605917-m1
<i>CCND1</i>	Hs00277039-m1
<i>CDKN1A</i>	Hs00355782-m1
<i>CDKN2A</i>	Hs00923894-m1
<i>CITED1</i>	Hs00918445-g1
<i>COL1A1</i>	Hs00164004-m1
<i>COL3A1</i>	Hs00943809-m1
<i>CYCS</i>	Hs01588973-m1
<i>DIO2</i>	Hs00988260-m1
<i>ELN</i>	Hs00355783-m1
<i>ELOVL3</i>	Hs00537016-m1
<i>GPD1</i>	Hs00193386-m1
<i>GREM1</i>	Hs01879841-s1
<i>HES1</i>	Hs00172878-m1
<i>HEYL</i>	Hs01113778-m1
<i>INHBA</i>	Hs00170103-m1
<i>NGFR</i>	Hs00182120-m1
<i>NOTCH1</i>	Hs00413187-m1
<i>NOTCH2</i>	Hs01050702-m1
<i>NOTCH3</i>	Hs01128537-m1
<i>PLIN1</i>	Hs00160173-m1
<i>PPARGC1A</i>	Hs01016719-m1
<i>PPARGC1b</i>	Hs00991677-m1
<i>PPARG2</i>	Hs01115510-m1
<i>PPIB</i>	Hs00168719-m1
<i>SFRP4</i>	Hs00180066-m1
<i>SNAI1</i>	Hs00195591-m1
<i>SNAI2</i>	Hs00161904-m1
<i>TFAM</i>	Hs01082775-m1
<i>UCP1</i>	Hs00222453-m1

Murine target gene	AOD
<i>Acta2</i>	Mm01546133-m1
<i>Cdkn1a</i>	Mm00432448-m1
<i>Cdkn2a</i>	Mm00494449-m1
<i>Col1a1</i>	Mm00801666-g1
<i>Col3a1</i>	Mm00802300-m1
<i>Eln</i>	Mm00514670-m1
<i>Notch1</i>	Mm00627185-m1
<i>Notch3</i>	Mm01345646-m1
<i>Sfrp4</i>	Mm00840101-m1