

Supplementary Figures and Tables

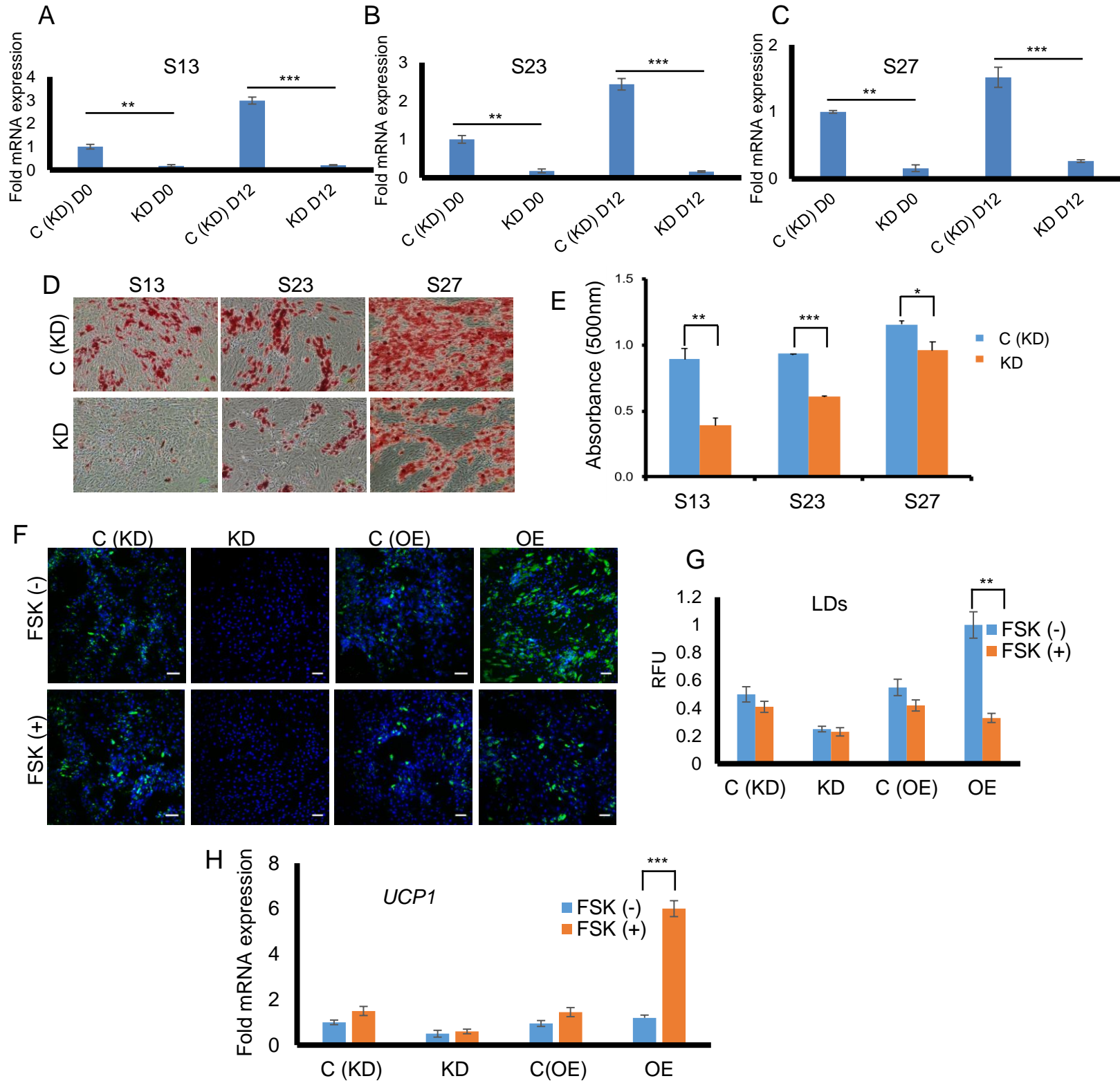


Fig. S1

Fig. S1. CD10 determines adipogenic maturation and browning capacities of ASCs. Relative mRNA levels of CD10 of (A) S13 (B) S23 and (C) S27 are quantified by qRT-PCR normalized to RPL27. Fold expression changes are compared to control cells at D0 for each subject. Each value is the mean \pm SEM from three independent replicates. (D) Representative brightfield images of Oil Red O staining (in red) of CD10 KD and control ASCs are shown. The scale bar represents 100 μ m. (E) Quantification of Oil Red O staining is shown. Reduced lipid accumulation in CD10 KD ASCs is observed compared to the controls in all 3 subjects. Each value is the mean \pm SEM from three independent replicates. (F) Representative merged images of Adipored staining of lipids (in green) and Hoechst 33342 staining of nuclei (in blue) in CD10 knock-down (KD) and over-expression (OE) cells with controls with(out) forskoline treatment. The scale bar represents 100 μ m. (G) The LDs are quantified by using MATLAB analysis as described in Experimental Procedures. The values are normalized to CD10 OE ASCs. Each value is the mean \pm SEM from three independent replicates. (H) Relative mRNA levels of browning marker gene UCP1 are quantified by qRT-PCR normalized to RPL27. Fold expression changes are compared to CD10 OE cells before forskolin treatment. Each value is the mean \pm SEM from three independent replicates. All statistical significance was assessed by using Student's paired t-test: ***p <0.001, **p <0.01, *p <0.05.

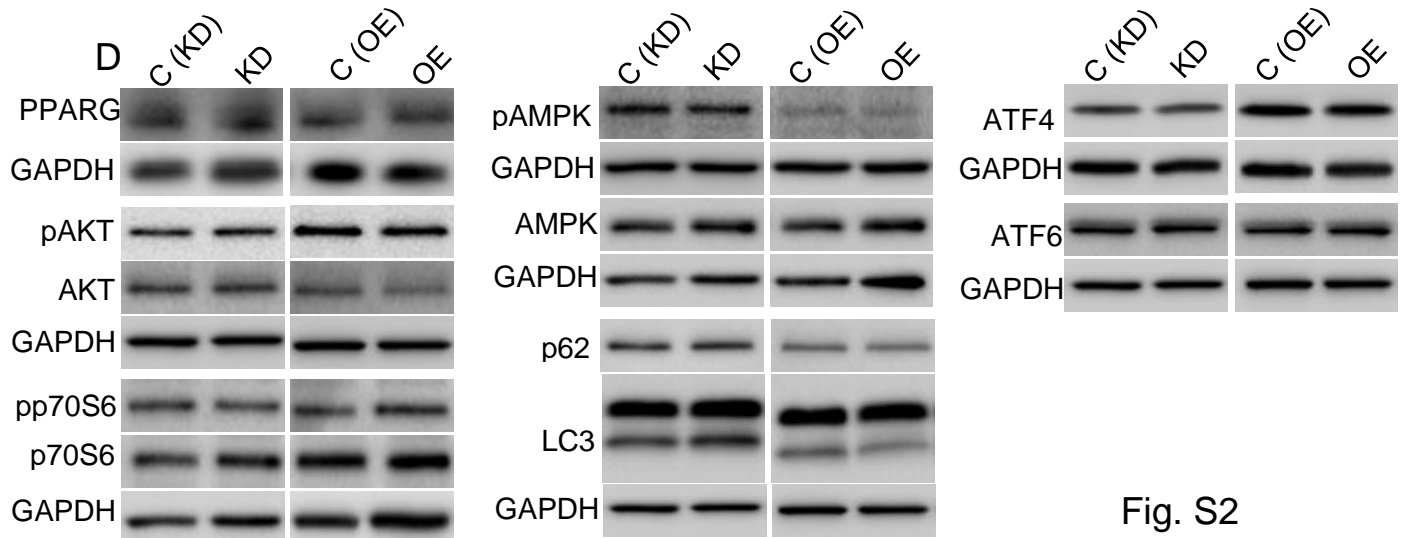
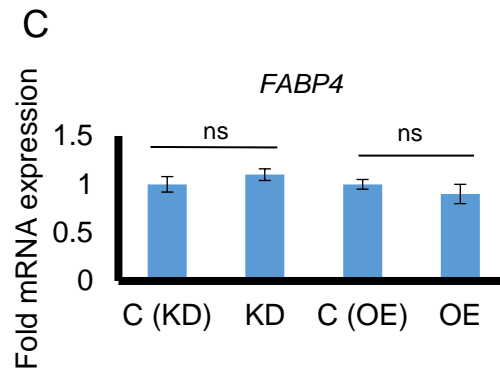
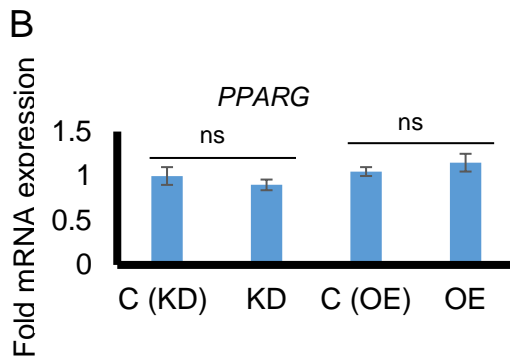
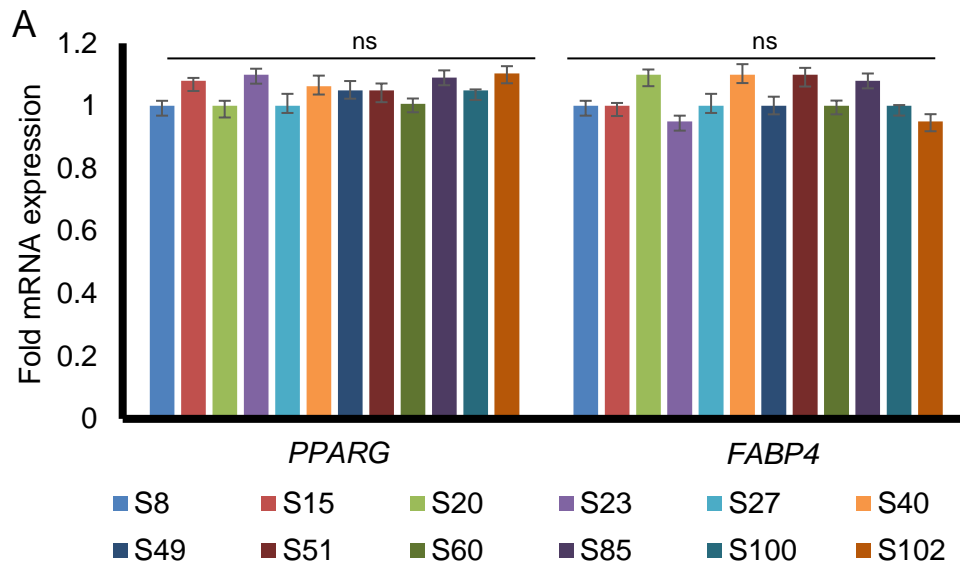


Fig. S2

Fig. S2. CD10 functions non-canonically independent of classical adipogenic pathways. (A)

Relative mRNA levels of *PPARG* and *FABP4* quantified by qRT-PCR normalized to *RPL27* are shown for differentiated ASCs from 12 subjects. Fold expression changes are compared to S8. ns denotes non-significant, $p > 0.05$. Relative mRNA levels of **(B)** *PPARG* and **(C)** *FABP4* are displayed for differentiated CD10 KD, OE and control cells from qRT-PCR analysis normalized to *RPL27*. ns denotes non-significant. **(D)** Western blot analysis shows expression of PPARG, phospho-AKT (P-S473), total AKT, phospho-p70S6 (P-T470, P-T389), p70S6 (P-T470), phospho-AMPK (P-T172), total AMPK, p62, LC3, ATF4 and ATF6 proteins in CD10 KD and OE cells compared to the controls. GAPDH was used as internal control.

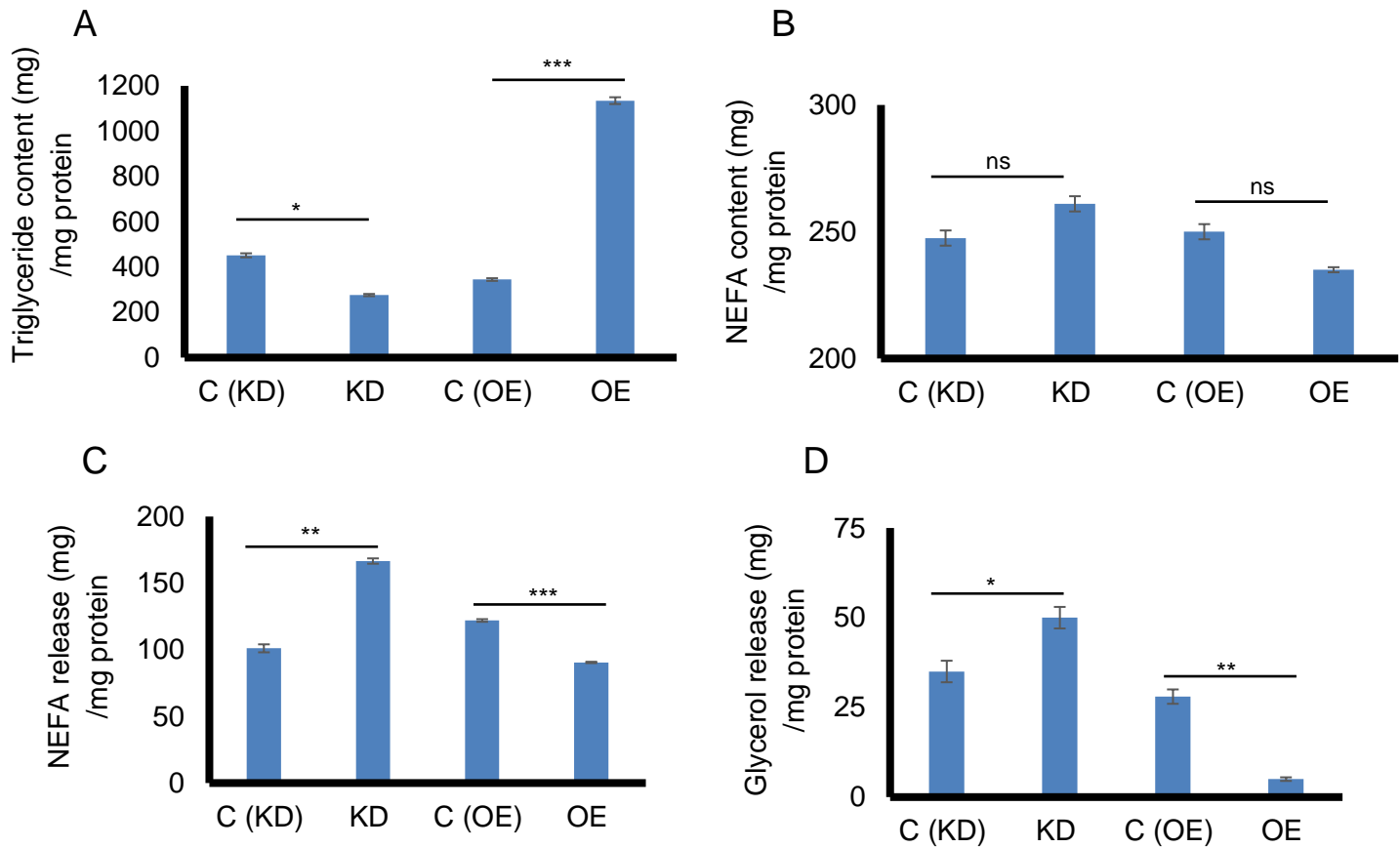
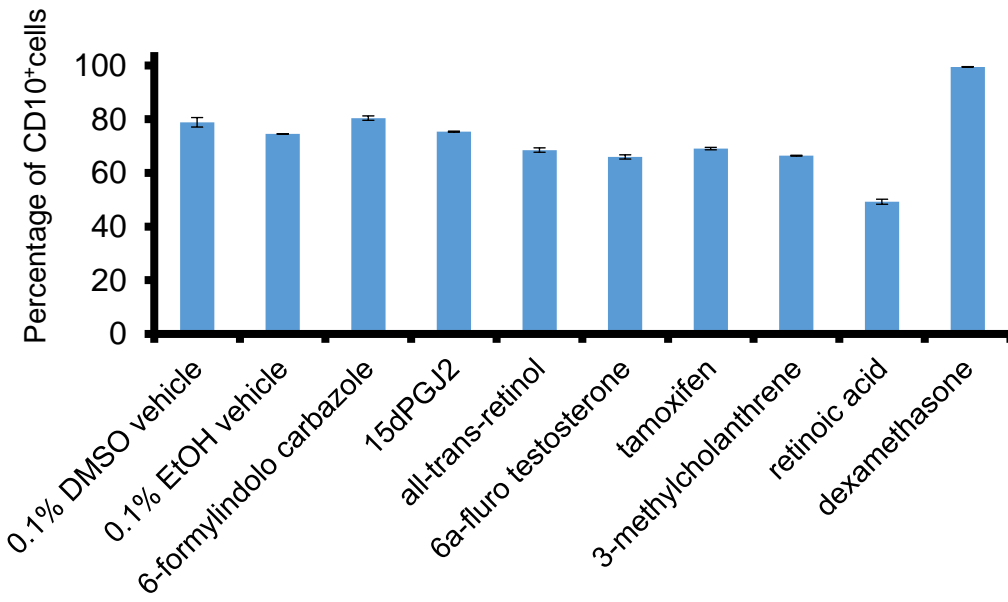


Fig. S3

Fig. S3. CD10 exerts reduced hydrolysis of lipid TGs into FAs and Glycerol. (A) TGs content of mature CD10 KD, OE and control cells are shown normalized to the total protein levels. (B) Intracellular and (C) Secreted levels of Non-esterified FAs (NEFAs) are shown normalized to the total protein levels. (D) The amount of glycerol released into the medium are quantified from CD10 KD, OE and control cells normalized to intracellular protein values. All statistical significance was assessed by using Student's paired t-test, *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$, ns; non-significant, $p > 0.05$. All the measurements are taken from each of six replicate wells.

A



B

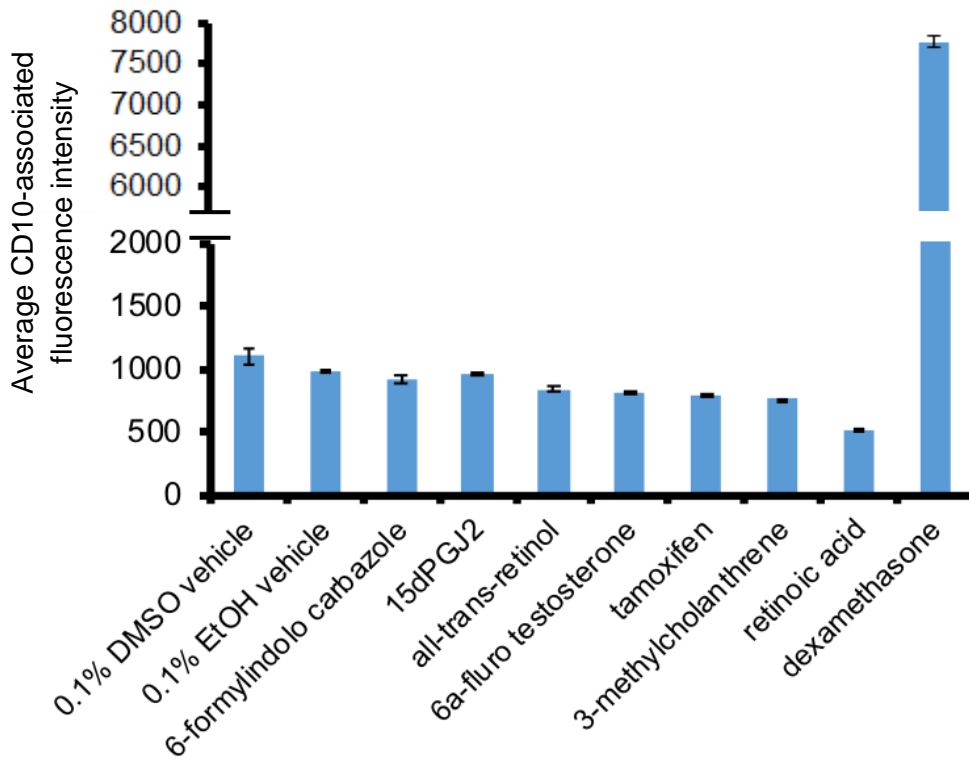


Fig. S4

Figure S4. Effects of selected hits from nuclear receptor ligand library on expression of CD10 in ASCs. (A) Percentage of CD10 positive cells and (B) Average CD10-FITC intensity are assessed by flow cytometry analyses. Each value is the mean \pm SEM from 3 separate wells of cells cultured under the same specified condition. Nuclear receptor ligand library screening identifies dexamethasone as a stimulator and retinoic acid as an inhibitor of CD10 expression.

Table S1: Donor information

Subject	Age	Sex	Height (m)	Weight (kg)	BMI	T2DM/ NDM
S8	42	F	163.8	130.5	48.64	T2DM
S13	35	F	1.5	101.1	44.93	T2DM
S15	24	F	1.67	149.4	53.6	T2DM
S20	26	F	173	113	37.76	T2DM
S23	37	M	160	144.2	56.33	NDM
S27	25	F	160	98	38.28	NDM
S29	34	F	1.59	88.7	35.09	NDM
S40	51	F	1.66	95	37.1	NDM
S49	56	F	1.56	66	27.1	NDM
S51	36	F	1.6	95	37.1	NDM
S60	24	F	1.76	174.55	56.4	NDM
S85	51	F	1.49	87.6	39.4	NDM
S100	54	F	1.64	116.9	42.4	T2DM
S102	54	F	1.59	85.1	33.6	NDM

Table S2: Primers used in this study

Gene	Forward	Reverse
RT RPL27	GGGTGGTTGCTGCCGAAATG	TGGCTGTAGGGGCGATCTGA
RT UCP1	ACGGGTCTTTGGAAAGGGACTA	GCGATAAGAGCCGACACCAA
RT CD10	GTCTTCCCAGCCGGCATTCT	AGTTTCTGCCATTGTCATCGA GC
RT PPARG	GACAGGAAAGACAACAGACA AATC	GGGGTGATGTGTTTGAAGTTG
RT FAPB4	CCTTTAAAAATACTGAGATTT CCTTCA	GGACACCCCCATCTAAGGTT
iRFP720	ACAAGCTAGCGCCACCATGGCG GAAGGATCCGTC	ACAAGCGGCCGCTCAAGGTCC AGGGTTCTCTCCACGTCTCCA GCCTGCTTCAGCAGGCTGAAG TTAGTAGCTCCGCTTCCCTCTT CCATCACGCCGATCTG
CD10	ACAAGCTAGCACAAAGGGTCGA CGCCACCATGGCAAGTCAGAA AGT	ACAAGCGGCCGCTCACCAAAC CCGGCACTTC
iRFP720-P2A	ACAAGCTAGCGCCACCATGGCG GAAGGATCCGTC	ACAAGCGGCCGCGAGGTCCAGG GTTCTCCTCCACGTCTCCAGCC TGCTTCAGCAGGCTGAAGTTA GTAGCTCCGCTTCCCTCTTCCA TCACGCCGATCTG
CD10 shRNA	<i>GATCCAGAACAGTAGGTGACACTATACTCGAGAATAGTGTAC CTACTGTTCTTTTTCCAAG</i>	

Table S3: Antibodies used in this study

Antibodies	Source	Identifier
Mouse monoclonal CD10 (Clone 56C6)	Leica Microsystems	Cat# CD10-270-L- CE
phospho-AKT (S473)	Cell Signaling Technology	4058S
AKT	Cell Signaling Technology	9272S
phospho-p70S6 (T389)	Cell Signaling Technology	9205S
p70S6	Cell Signaling Technology	9202S
phospho-AMPK (T172)	Cell Signaling Technology	2535S

AMPK	Cell Signaling Technology	5831S
p62	Cell Signaling Technology	5114S
LC3	Cell Signaling Technology	2775S
ATF4	Cell Signaling Technology	11815S
ATF6	Novus Biologicals	NBP1-40256
COXIV	Cell Signaling Technology	4850P
phospho-HSL (S660)	Cell Signaling Technology	4126S
HSL	Cell Signaling Technology	4107S
phospho-ATGL (S406)	Abcam	ab135093
ATGL	Abcam	ab99532
GAPDH	Cell Signaling Technology	2118L

Table S4: First screening results of nuclear receptor ligand library using CD10 as a marker with flow cytometry analysis and ImageExpress analysis.

Ligand	Flow Cytometry Analysis							ImageExpress Analysis						
	Well Location	P2 #Event	P2 %Parent	P2 FITC-A Mean	% Fluor Intensity relative to Control (A2&A3)	P3 #Event	P3 %Parent	Fluor 1	Fluor 2	Fluor 3	Fluor 4	Mean Fluor Intensity	% Fluor Intensity relative to Control (A2&A3)	
(empty)	A1	306	89	108	81.8	0	0.0	2.49	8.82	5.47	6.22	5.8	27.6	
DMSO (control)	A2	462	97.5	132	100.0	9	1.9	20	26.82	22.88	20.44	22.5	108.0	
Ethanol (control)	A3	141	100	132	100.0	2	1.4	17.29	20.88	13.21	25.37	19.2	92.0	
25-Hydroxyvitamin D3	B1	95	82.6	167	126.5	5	5.3	18.07	24.28	29.47	17.72	22.4	107.3	
Retinoic acid, all trans	B2	167	77.7	144	109.1	7	4.2	19.19	9.63	8.91	32.9	17.7	84.6	
9-cis Retinoic acid	B3	148	80	135	102.3	6	4.1	16.66	23.52		28.79	23.0	110.2	
13-cis Retinoic acid	B4	296	78.9	125	94.7	4	1.4	18.46	19.11	14.65	14.94	16.8	80.5	
4-Hydroxyphenylretinamide	B5	372	58.7	152	115.2	19	5.1	30.91	29.38	9.81	22.11	23.1	110.5	
AM-580	B6	442	79.2	140	106.1	14	3.2	17.79	15.81	16.44	13.86	16.0	76.6	
TTNPB	B7	366	79.6	128	97.0	11	3.0	18.25	12.86	20.33	18	17.4	83.2	
Methoprene acid	B8	941	80.4	139	105.3	29	3.1	24.2	25.24	27.9	25.64	25.7	123.4	
WY-14643	B9	574	74.1	143	108.3	29	5.1	20.37	18.08	23.46	21.22	20.8	99.6	
Ciglitazone	B10	481	78.2	141	106.8	14	2.9	25.18	23.77	15.44	22.53	21.7	104.2	
Tetradecylthioacetic acid	B11	862	75.2	137	103.8	38	4.4	18.54	15.77	17.89	16.96	17.3	82.9	
5,8,11,14-Eicosatetraynoic acid	B12	383	68.3	168	127.3	30	7.8	15.13	15.71	100.8	11.11	35.7	171.0	
6-Formylindolo [3,2-B] carbazole	C1	735	66.5	443	335.6	486	66.1	73.16	66.87	56.74	64.49	65.3	313.1	
Diindolylmethane	C2	441	80.3	135	102.3	7	1.6	17.42	18.41	21.64	20.82	19.6	93.8	
Acetyl-S-farnesyl-L-cysteine	C3	325	80.2	134	101.5	12	3.7	21.21	14.56	16.97	23.67	19.1	91.6	
S-Farnesyl-L-cysteine methyl ester	C4	694	79.6	155	117.4	53	7.6	32.26	33.37	41.64	35.31	35.6	170.9	
N-Acetyl-S-geranygeranyl-L-cysteine	C5	825	78.6	144	109.1	36	4.4	23.75	28.52	36.27	33	30.4	145.7	
AGC (Acetyl-geranyl-cysteine)	C6	681	80	118	89.4	17	2.5	17	17.61	12.84	12.6	15.0	72.0	
Farnesylthioacetic acid	C7	398	82.4	120	90.9	8	2.0	12.73	15.04	10.51	20.45	14.7	70.4	
Bezafibrate	C8	1061	77.9	142	107.6	47	4.4	18.55	20.23	21.02	26.97	21.7	104.0	
LY 171883	C9	382	74	152	115.2	21	5.5	18.47	21.15	17.49	17.29	18.6	89.2	
15-Deoxy-D12,14-prostaglandin J2	C10	275	59.1	179	135.6	34	12.4	17.06	22.64	17.74	20	19.4	92.8	
Troglitazone	C11	630	73.8	138	104.5	25	4.0	15.25	17.91	12.65	19.16	16.2	77.9	
CITCO	C12	471	80.2	139	105.3	15	3.2	13.97	20.89	17.44	12.02	16.1	77.1	
Paxilline	D1	801	84.9	149	112.9	39	4.9	15.04	26.6	28.07	25.31	23.8	113.9	
24(S)-Hydroxycholesterol	D2	7	58.3	119	90.2	0	0.0	19.66	23.64	23.23	29.41	24.0	115.0	
24(S),25-Epoxycholesterol	D3	127	81.4	130	98.5	1	0.8	21.15	37.87	23.72	30.51	28.3	135.7	
Pregnenolone-16(alpha)-carbonitrile	D4	1185	79.9	142	107.6	56	4.7	23.12	24.31	28.29	25.6	25.3	121.4	
Carbacyclin	D5	512	83.5	152	115.2	26	5.1	29.27	32.82	35.88	29.47	31.9	152.7	
Clofibrate acid	D6	1079	79.5	130	98.5	36	3.3	21.18	21.41	34.62	22.5	24.9	119.5	
BADGE	D7	370	81.9	121	91.7	8	2.2	13.41	11.5	4.35	9.24	9.6	46.1	
GW 9662	D8	997	74.8	140	106.1	52	5.2	21.1	18.37	18.17	22.27	20.0	95.8	
Gemfibrozil	D9	833	80.6	136	103.0	34	4.1	21.9	14.51	16.92	22.06	18.8	90.3	
GW 7647	D10	834	82.3	136	103.0	18	2.2	17.96	14.97	12.7	19.98	16.4	78.6	
3,5-Diiodo-L-thyronine	D11	1003	80	147	111.4	52	5.2	22.21	21.87	20.09	12.27	19.1	91.6	
3,5-Diiodo-L-tyrosine	D12	411	76	148	112.1	24	5.8	28.95	19.11	36.95	13.52	24.6	118.1	
all-trans-Retinol	E1	152	74.1	322	243.9	72	47.4	41.95	41.91	24.25	31.63	34.9	167.5	
13-cis-Retinol	E2	699	84	139	105.3	32	4.6	24.39	21.3	22.99	23.75	23.1	110.8	
Retinyl acetate	E3	790	81.6	135	102.3	20	2.5	16.58	16.02	16.84	18.01	16.9	80.8	
3,5-Diiodo-4-hydroxyphenylpropionic acid	E4	1036	78.5	132	100.0	30	2.9	21.45	21.04	26.08	21.93	22.6	108.5	
Cholic acid	E5	1061	83.2	136	103.0	47	4.4	21.52	23.59	21.26	26.44	23.2	111.2	
Deoxycholic acid	E6	1148	80.4	141	106.8	63	5.5	23.91	22.38	27.12	22.91	24.1	115.4	
Chenodeoxycholic acid	E7	1402	81.8	130	98.5	39	2.8	23.59	27.52	22.81	23.22	24.3	116.4	
Glycocholic acid	E8	1174	78.7	136	103.0	30	2.6	25.67	21.93	24.05	20.12	22.9	110.0	
Glycodeoxycholic acid	E9	1068	77.9	134	101.5	26	2.4	25.18	24.69	18.31	14.93	20.8	99.6	
Taurocholic acid	E10	981	80.5	129	97.7	16	1.6	16.14	16.69	18.54	22.27	18.4	88.2	
Taurodeoxycholic acid	E11	954	78.9	137	103.8	38	4.0	16.31	16.41	24.32	21.75	19.7	94.4	
Rifampicin	E12	413	78.8	136	103.0	14	3.4	13.01	11.15	15.86	21.76	15.4	74.0	
Dexamethasone	F1	157	56.9	578	437.9	114	72.6	65.27	59.53	67.78	61.69	63.6	304.7	
Lithocholic acid	F2	752	80.8	139	105.3	38	5.1	28.02	23.66	23.22	26.51	25.4	121.5	
5b-Pregnan-3,20-dione	F3	1171	80.9	148	112.1	71	6.1	17.53	24.96	23.36	25.76	22.9	109.8	
Adapalene	F4	270	87.9	148	112.1	10	3.7	12.49	18.47	11.18	11.84	13.5	64.7	
Farnesol	F5	964	84.7	140	106.1	33	3.4	22.08	21.98	17.33	26.5	22.0	105.3	
3a, 5a-Androstenol	F6	1237	80.5	145	109.8	65	5.3	17.06	21.78	16.18	17.81	18.2	87.3	
3o, 5a-Androstanol	F7	889	82.1	131	99.2	27	3.0	24.18	16.08	19.85	16.53	19.2	91.8	
Z-Guggulsterone	F8	1036	80.7	143	108.3	51	4.9	24.71	19.76	27.06	23.4	23.7	113.8	
TCPOBOP	F9	1042	78.1	141	106.8	58	5.6	23.37	24.5	23.06	23.2	23.5	112.8	
N-Oleylethanolamide	F10	764	82.6	124	93.9	17	2.2	18.57	16.53	10.72	15.7	15.4	73.7	
GW4064	F11	679	79.4	147	111.4	32	4.7	16.66	22.1	19.1	13.16	17.8	85.1	
Geranylgeraniol	F12	326	76.9	136	103.0	4	1.2	13.23	10.54	16	17.85	14.4	69.1	
6a-Fluorotestosterone	G1	55	56.7	350	265.2	33	60.0	59.64	49.72		52.55	54.0	258.7	
Tamoxifen	G2	381	89.2	178	134.8	30	7.9	32.14	19.96	22.31	27.72	25.5	122.4	
Mifepristone	G3	650	80.5	153	115.9	39	6.0	24.31	30.46	26.74	23.25	26.2	125.5	
Estrone	G4	932	78.7	125	94.7	22	2.4	16.97	19.64		19.22	18.6	89.2	
13(S)-Hydroxy-9Z,11E-octadecadienoic acid	G5	657	82.2	132	100.0	14	2.1	22.66	26.68	24.51	16.28	22.5	108.0	
Cortisone	G6	1175	81.1	136	103.0	40	3.4	23.68	25.7	20.8	29.91	25.0	119.9	
Progesterone	G7	749	85.3	156	118.2	51	6.8	22.16	24.25	25.2	30.19	25.5	122.0	
17b-Estradiol	G8	881	80.9	127	96.2	25	2.8	17.18	13.61	17.98	17.51	16.6	79.4	
Pregnenolone	G9	867	81	137	103.8	36	4.2	24.26	26.82	19.41	17.54	22.0	105.5	
Androstenedione	G10	887	80.5	152	115.2	45	5.1	26.71	20.63	19.45	16.11	20.7	99.3	
1a,25-Dihydroxyvitamin D3	G11	151	87.8	151	114.4	4	2.6	13.08	16.02	8.54	6.76	11.1	53.2	
Docosa-4Z,7Z,10Z,13Z,16Z,19Z-hexaenoic acid	G12	287	74.2	148	112.1	10	3.5	19.41	14.09	27.72	13.64	18.7	89.7	
3-Methylcholanthrene	H1	74	75.5	221	167.4	13	17.6	22.23	21.21	29.72	13.49	21.6	103.7	
Acitretin	H2	106	79.7	131	99.2	4	3.8	11.95	19.67	39.7	24.53	24.0	114.9	
Pioglitazone	H3	321	84.9	155	117.4	26	8.1	12.06	15.43	22.95	19.81	17.6	84.2	
4-Hydroxyretinoic acid	H4	185	85.6	129	97.7	5	2.7	6.09	9.79	6.06	32.85	13.7	65.7	