CORRECTION NOTICE

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The cold-induced lipokine 12,13-diHOME promotes fatty acid transport into brown adipose tissue

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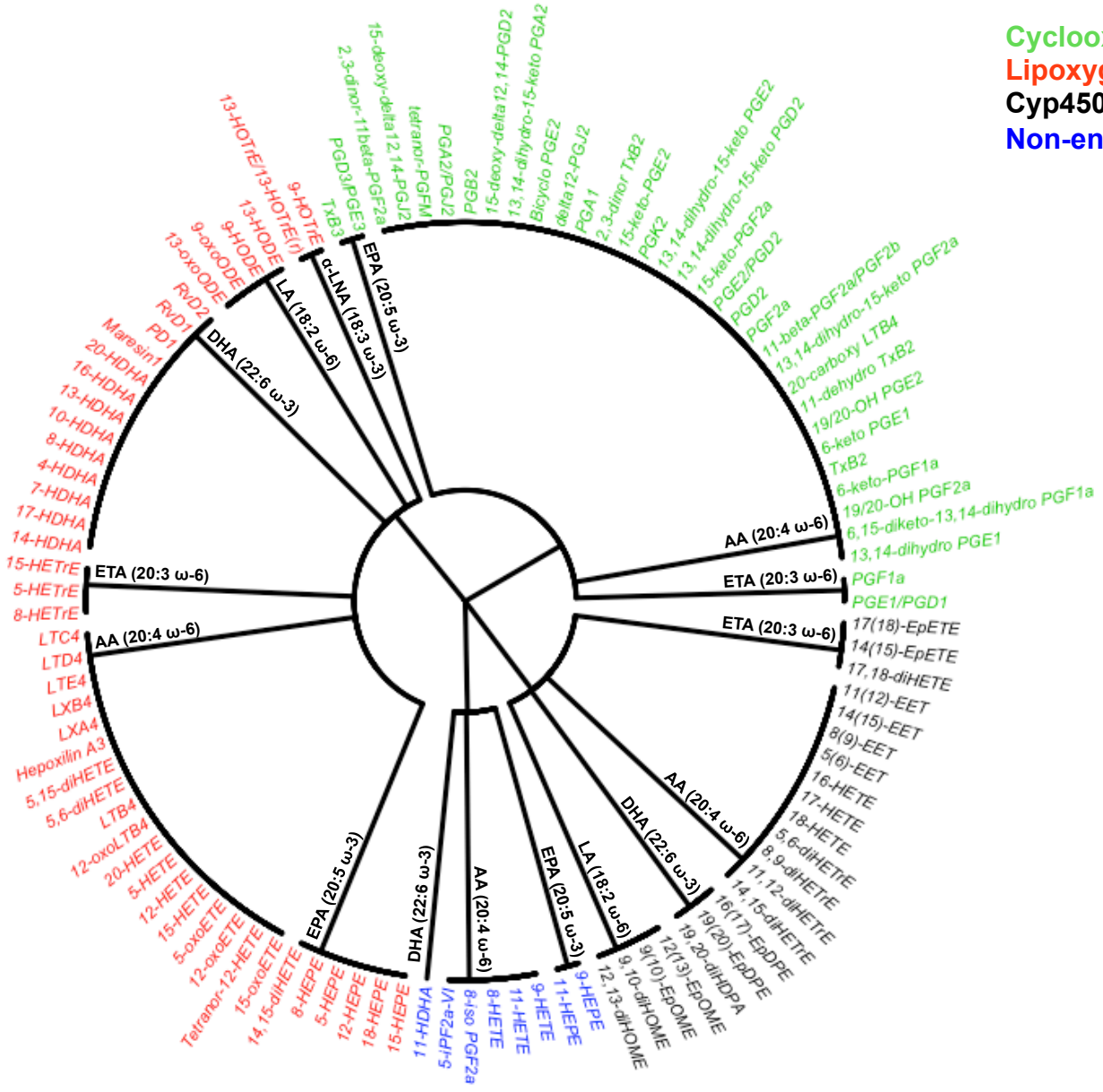
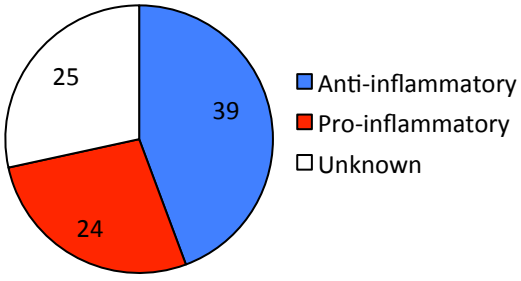
The incorrect raw western blot was used in Supplementary Figure 7 to reflect the blot for FATP1 in Figure 4e. Rather than simply replacing the Supplementary Information with the correct raw western blot, the authors provided all three replicates.

a



b Inflammatory effect



Supplementary Figure 1

Annotation of lipid species profiled by LC-/MS in human and mouse serum and mouse adipose tissues. (**a**) Dendrogram of all lipids included in the initial screen according to their original fatty acid and enzymatic pathway. (**b**) For all lipid species measured by LC-MS/MS annotation of, whether the lipid was pro- or anti-inflammatory.

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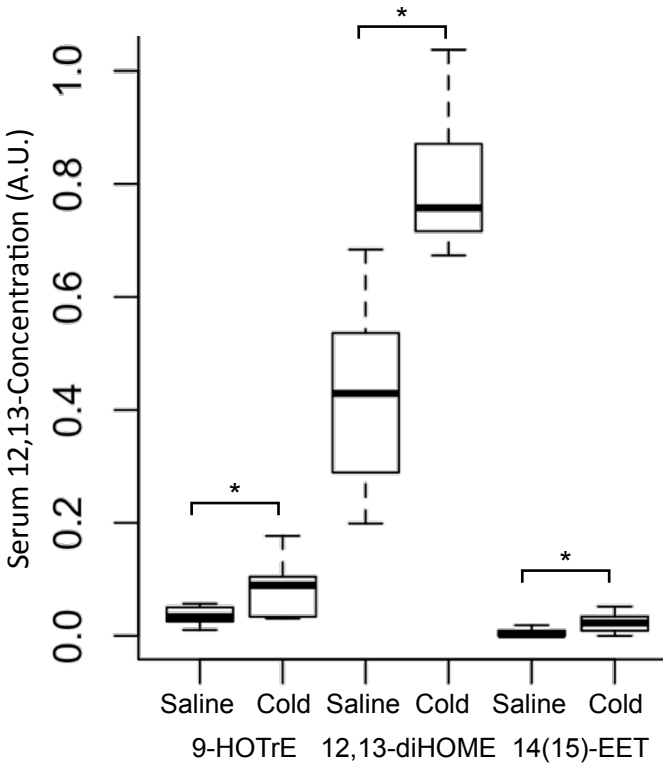
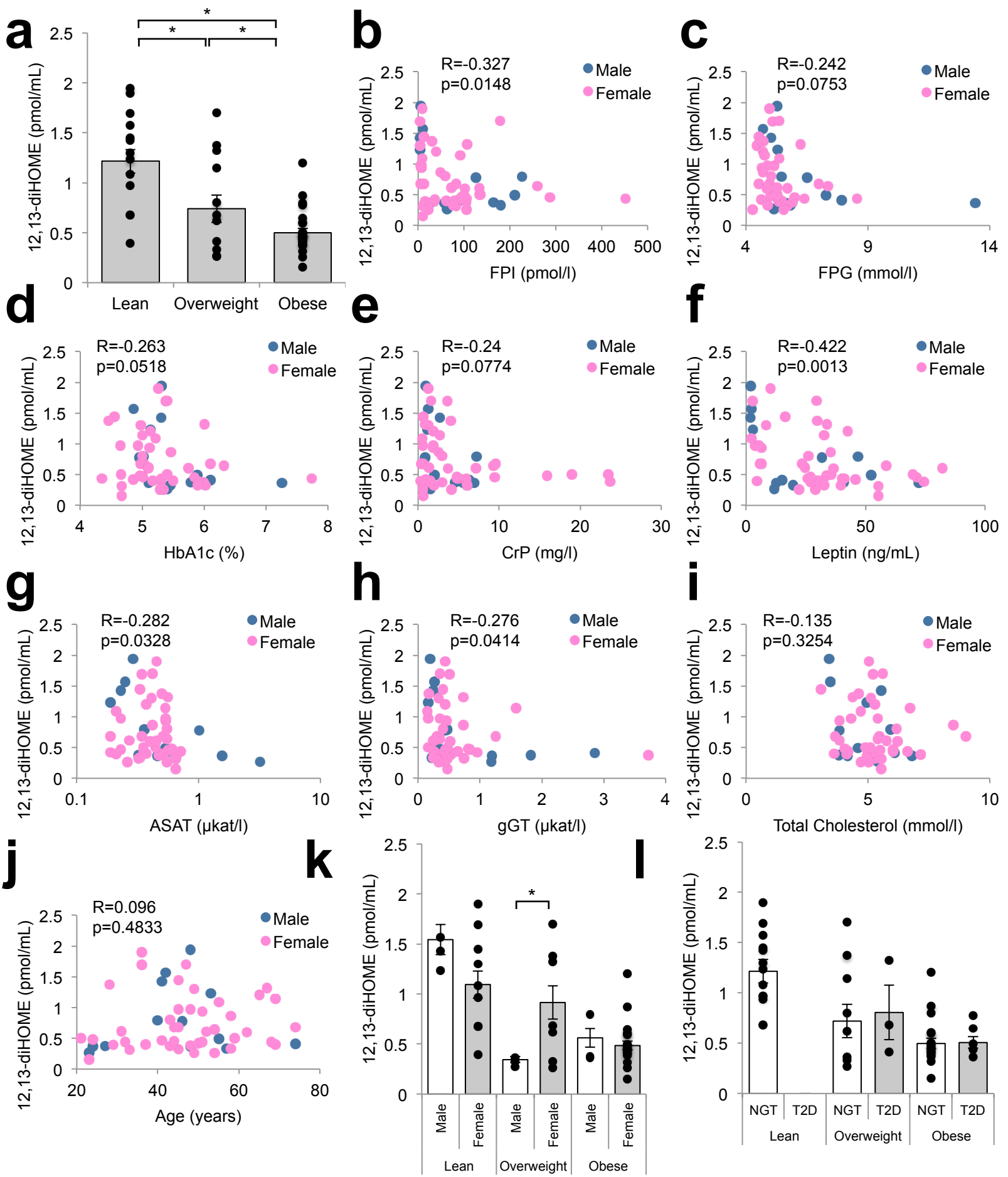


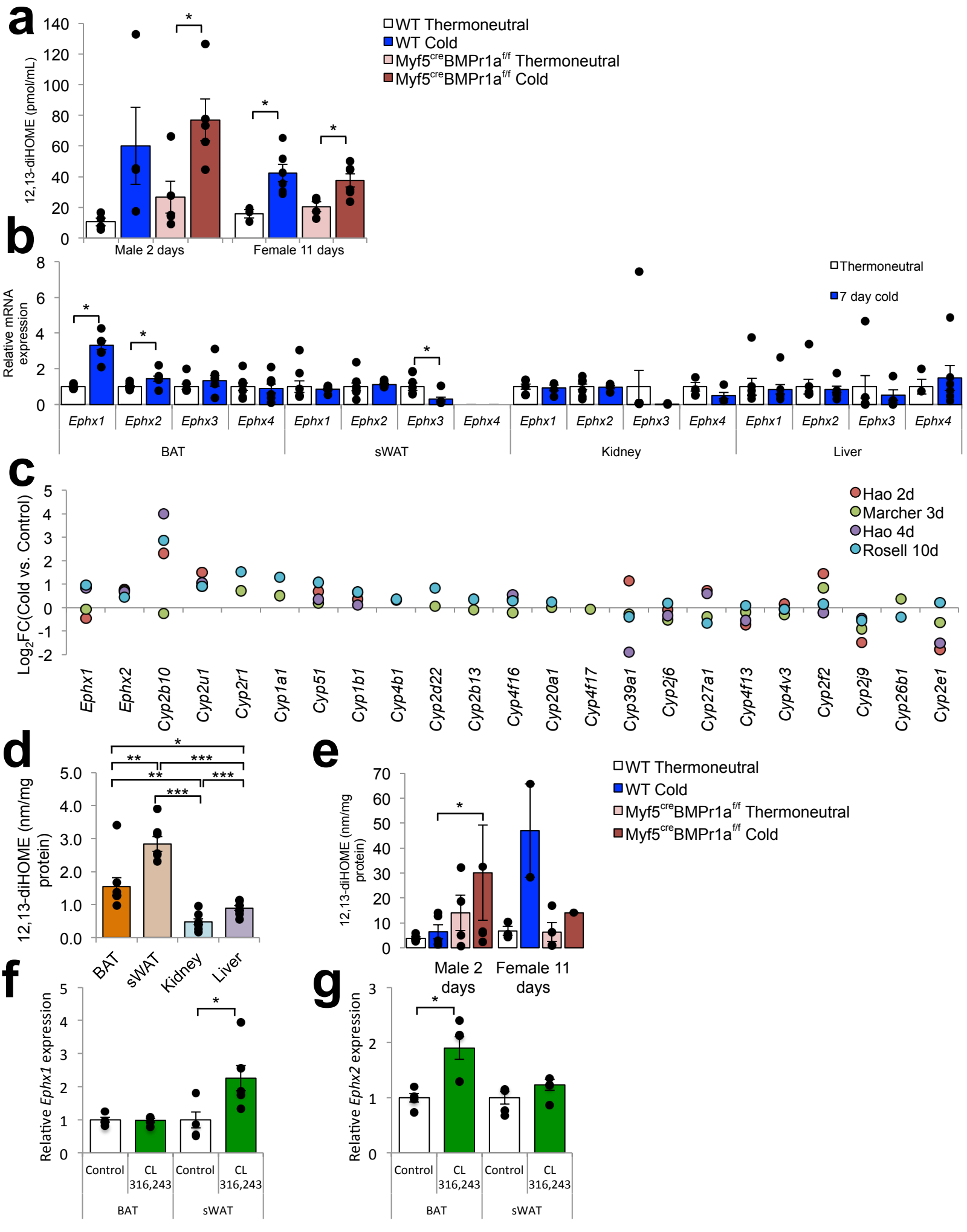
Supplementary Figure 2

Lipid species increased by a one-hour cold challenge. The increase in abundance of three lipid species reached a nominal *P* value of 0.05 after cold exposure. The two species with lower significance were only detectable after cold exposure. Data are means +/- s.e.m.; *n* = 9 individual subjects; **P* < 0.05 by paired Student's *t*-test.


a
b
c
d
e
f
g
h
i
j
k
l
12,13-diHOME (pmol/mL)
Lean
Overweight
Obese
R=-0.327
p=0.0148
FPI (pmol/l)
R=-0.242
p=0.0753
FPG (mmol/l)
R=-0.263
p=0.0518
HbA1c (%)
R=-0.24
p=0.0774
CrP (mg/l)
R=-0.422
p=0.0013
Leptin (ng/mL)
R=-0.282
p=0.0328
ASAT (µkat/l)
R=-0.276
p=0.0414
gGT (µkat/l)
R=-0.135
p=0.3254
Total Cholesterol (mmol/l)
R=0.096
p=0.4833
Age (years)
Male
Female
NGT
T2D

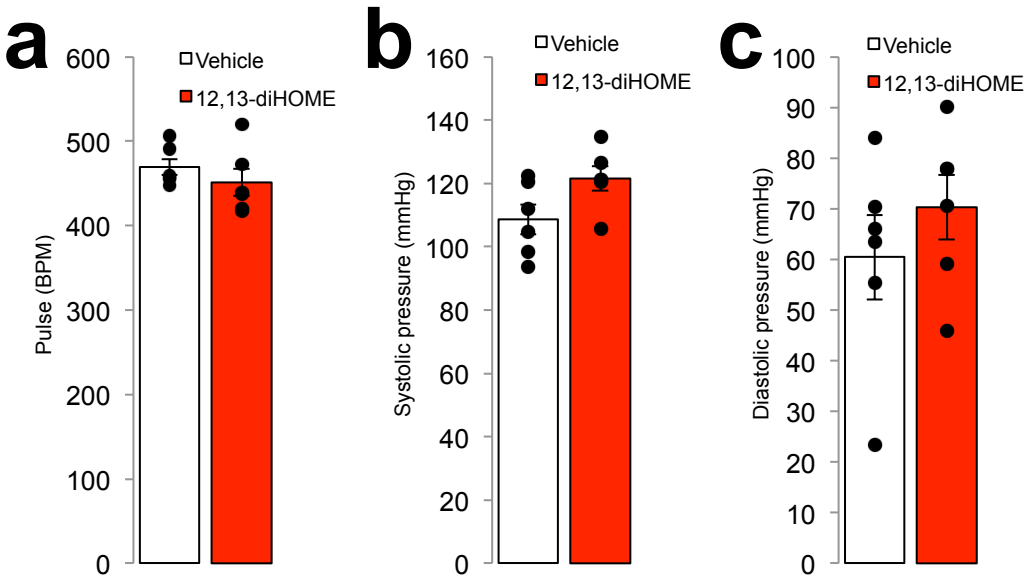
Supplementary Figure 3

Anthropometric correlates of 12,13-diHOME. (**a**) Circulating 12,13-diHOME in each body mass index (BMI) category. Data are presented as normalized means ± s.e.m.; *n* = 15 lean, 13 overweight and 27 obese subjects. (**b-j**), Circulating 12,13-diHOME concentration plotted against fasting plasma insulin (FPI) (**b**), fasting plasma glucose (FPG) (**c**), hemoglobin A1c (HbA1c) (**d**), C-reactive protein (CrP) (**e**), circulating leptin (**f**), circulating aspartate transaminase (ASAT) (**g**), and circulating gamma-glutamyl transpeptidase (gGT) (**h**)**,** circulating total cholesterol (**i**) and age (**j**). In each panel, R is the Spearman correlation coefficient and males are shown in blue while females are shown in pink; *n* = 55 individual subjects (13 M/42 F). (**k**) Circulating 12,13-diHOME in each BMI category of males and females. Data are presented as normalized means ± s.e.m.; *n* = 15 lean (4 M/11 F), 13 overweight (4 M/9 F) and 27 obese subjects (5 M/22 F); **P* < 0.05 by Student's *t*-test. (**l**) Circulating 12,13-diHOME in each BMI category of subjects with normal glucose tolerance (NGT) or Type 2 diabetes (T2D). Data are presented as normalized means ± s.e.m.; *n* = 15 lean, 13 overweight (10 NGT/3 T2D) and 27 obese subjects (20 NGT/7 T2D).


a
12,13-diHOME (pmol/mL)
WT Thermoneutral
WT Cold
Myf5cre BMPr1af/f Thermoneutral
Myf5cre BMPr1af/f Cold
Male 2 days
Female 11 days
b
Relative mRNA expression
Thermoneutral
7 day cold
Ephx1
Ephx2
Ephx3
Ephx4
BAT
sWAT
Kidney
Liver
c
Log2FC(Cold vs. Control)
Hao 2d
Marcher 3d
Hao 4d
Rosell 10d
Ephx1
Ephx2
Cyp2b10
Cyp2u1
Cyp2r1
Cyp1a1
Cyp51
Cyp1b1
Cyp4b1
Cyp2d22
Cyp2b13
Cyp4f16
Cyp20a1
Cyp4f17
Cyp39a1
Cyp2j6
Cyp27a1
Cyp4f13
Cyp4v3
Cyp2f2
Cyp2j9
Cyp26b1
Cyp2e1
d
12,13-diHOME (nm/mg protein)
BAT
sWAT
Kidney
Liver
e
12,13-diHOME (nm/mg protein)
WT Thermoneutral
WT Cold
Myf5cre BMPr1af/f Thermoneutral
Myf5cre BMPr1af/f Cold
Male 2 days
Female 11 days
f
Relative Ephx1 expression
Control
CL 316,243
BAT
sWAT
g
Relative Ephx2 expression
Control
CL 316,243
BAT
sWAT

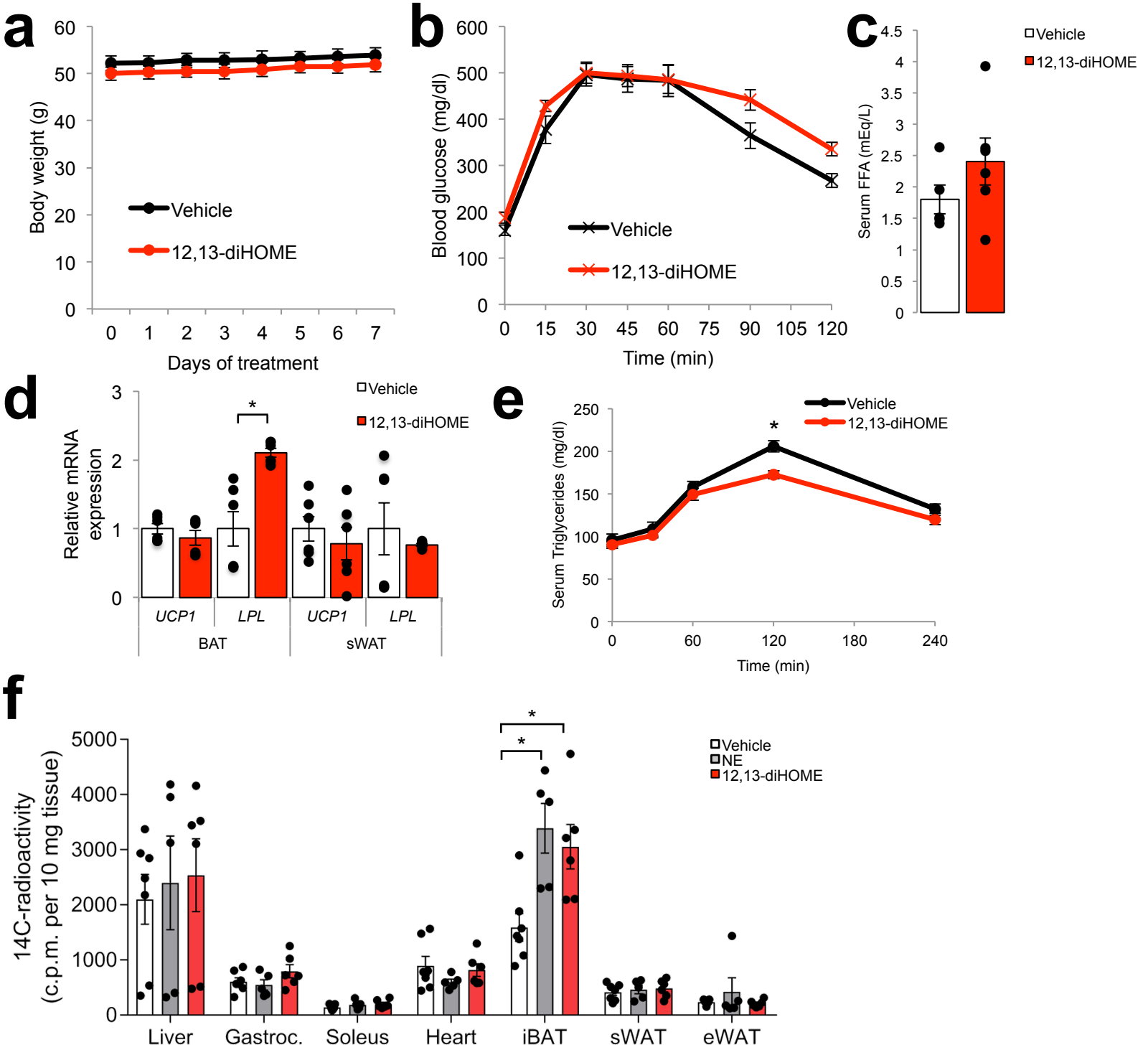
Supplementary Figure 4

12,13-biosynthesis in cold activated adipose tissue. (**a**) 12,13-diHOME concentrations measured by LC-MS/MS in serum from wild type and *Myf5*^{cre}*BMPr1a*$^{f/f}$ mice housed at cold or thermoneutral for 2 or 11 days. Data are plotted as the normalized means ± s.e.m.; *n* = 5 WT thermoneutral males, 3 WT cold males, 4 *Myf5*^{cre}*BMPr1a*$^{f/f}$ thermoneutral males, 5 *Myf5*^{cre}*BMPr1a*$^{f/f}$ cold males, 3 WT thermoneutral females, 5 WT cold females, 3 *Myf5*^{cre}*BMPr1a*$^{f/f}$ thermoneutral females, 4 *Myf5*^{cre}*BMPr1a*$^{f/f}$ cold female; **P* < 0.05 by Student's *t*-test. (**b**) *Ephx* family gene expression measured by qPCR in different tissues from mice housed at cold or thermoneutrality for 7 days. Data are plotted as the means normalized to thermoneutrality ± s.e.m.; *n* = 8 per group; **P* < 0.05 by Student's *t*-test. (**c**) Meta-analysis of 4 publically available BAT gene expression datasets from mice exposed to cold for different lengths of time for genes in the 12,13-diHOME biosynthetic pathway. The induction by cold of each gene after cold exposure is shown by increased fold change on the y axis. (**d**) 12,13-diHOME concentrations measured in different mouse tissues. Data are means +/- s.e.m.; *n* = 8 mice; **P* < 0.05, ***P* < 0.005 , ****P* < 0.0005 by Student's *t*-test. (**e**) 12,13-diHOME concentrations measured by LC-MS/MS in sWAT from wild type and *Myf5*^{cre}*BMPr1a*$^{f/f}$ mice housed at cold or thermoneutral for 2 or 11 days. Data are plotted as the normalized means ± s.e.m.; *n* = 5 WT thermoneutral males, 5 WT cold males, 4 *Myf5*^{cre}*BMPr1a*$^{f/f}$ thermoneutral males, 5 *Myf5*^{cre}*BMPr1a*$^{f/f}$ cold males, 3 WT thermoneutral females, 2 WT cold females, 4 *Myf5*^{cre}*BMPr1a*$^{f/f}$ thermoneutral females, 1 *Myf5*^{cre}*BMPr1a*$^{f/f}$ cold female; **P* < 0.05 by Student's *t*-test. (**f**) *Ephx1* gene expression measured by qPCR in BAT and sWAT from mice treated daily with 1 mg/kg body weight CL316,243 intraperitoneally for 10 days. Data are presented as normalized means ± s.e.m.; *n* = 6 per group; **P* < 0.05 by Student's *t*-test. (**g**) *Ephx2* gene expression measured by qPCR in BAT and sWAT from mice treated daily with 1 mg/kg body weight CL 316,243 intraperitoneally for 10 days. Data are presented as normalized means ± s.e.m.; *n* = 6 per group; **P* < 0.05 by Student's *t*-test.



Supplementary Figure 5

Physiologic effects of acute 12,13-diHOME treatment in mice. (**a**) Pulse measured in the tail after pretreatment with 12,13-diHOME or vehicle. Data are means ± s.e.m.; *n* = 6 per group. (**b**) Systolic pressure measured in the tail vein after pretreatment with 12,13-diHOME or vehicle. Data are means ± s.e.m.; *n* = 6 per group. (**c**) Diastolic pressure measured in the tail after pretreatment with 12,13-diHOME or vehicle. Data are means ± s.e.m.; *n* = 6 per group.


a
Body weight (g)
Days of treatment
Vehicle
12,13-diHOME
b
Blood glucose (mg/dl)
Time (min)
Vehicle
12,13-diHOME
c
Serum FFA (mEq/L)
Vehicle
12,13-diHOME
d
Relative mRNA expression
Vehicle
12,13-diHOME
UCP1
LPL
UCP1
LPL
BAT
sWAT
e
Serum Triglycerides (mg/dl)
Time (min)
Vehicle
12,13-diHOME
f
14C-radioactivity (c.p.m. per 10 mg tissue)
Vehicle
NE
12,13-diHOME
Liver
Gastroc.
Soleus
Heart
iBAT
sWAT
eWAT

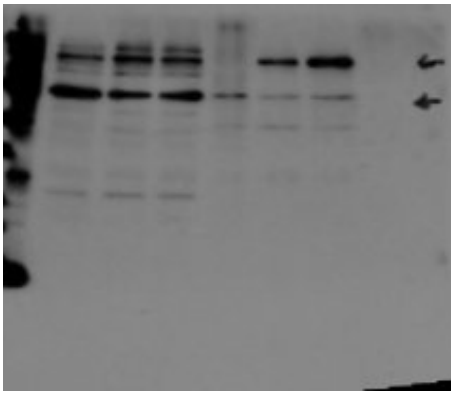
Supplementary Figure 6

Physiologic effects of daily 12,13-diHOME injections. (**a**) Body weights over 7 day course of daily injection treatment. Data are means +/- s.e.m.; *n* = 6 treated vs. 5 controls. (**b**) Glucose tolerance test of a separate cohort of diet-induced obesity mice treated every other day for 2 weeks with either 12,13-diHOME or vehicle. Data are means +/- s.e.m.; *n* = 5 per group. (**c**) Serum non-esterified free fatty acids (FFA) of mice treated daily for one week with either 12,13-diHOME or vehicle. Data are means +/- s.e.m.; *n* = 6 treated vs. 5 controls. (**d**) mRNA expression measured by qPCR of *UCP1* and *LPL* in tissue from mice treated every other day for two weeks with either 12,13-diHOME or vehicle. Data are means +/- s.e.m.; *n* = 6 treated per group; **P* < 0.05 by Student's *t*-test . (**e**) Oral lipid tolerance test showing serum triglyceride concentration from mice treated with vehicle or 12,13-diHOME and then given an oral bolus of triglyceride. Data are means ± s.e.m.; *n* = 6 per group; **P* < 0.05 by ANOVA with post-hoc Bonferroni test. (**f**) Radioactivity per 10 mg of tissues from mice treated with vehicle, Norepinephrine (NE) or 12,13-diHOME and then given a bolus of radiolabeled glucose. Tissues were measured by scintillation counting in liver, gastrocnemius muscle (Gastroc), soleus muscle, heart, BAT, sWAT, and epididymal white adipose tissue (eWAT). Data are means ± s.e.m.; *n* = 8 per group; **P* < 0.05 12,13-diHOME vs. Vehicle by ANOVA with post-hoc Bonferroni test.

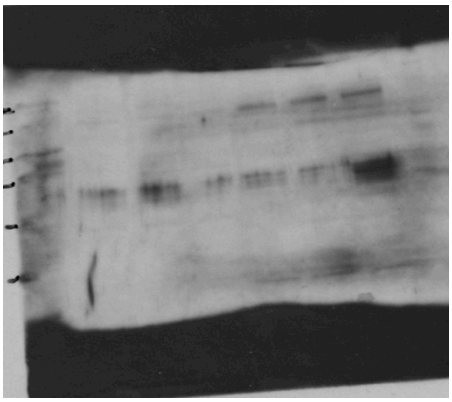
a

Cytosol Membrane

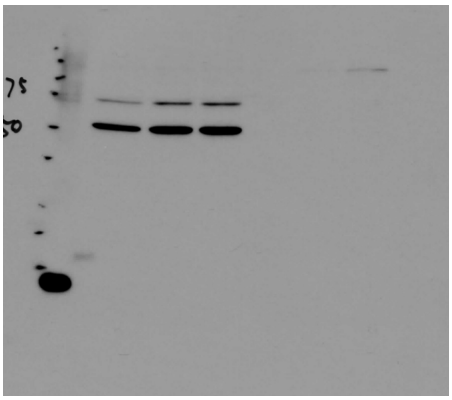
Control Insulin 12,13-diHOME Control Insulin 12,13-diHOME



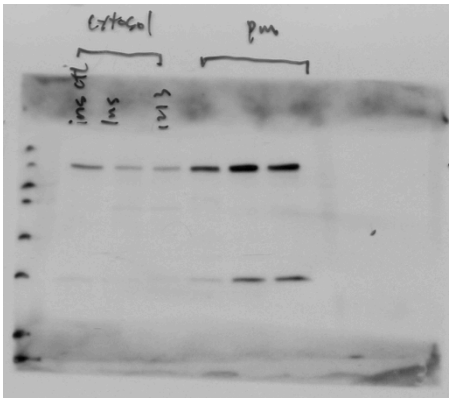
FATP1



CD36



Tubulin

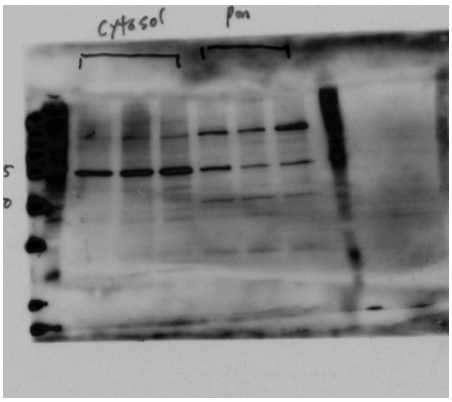


Cadherin

b

Cytosol Membrane

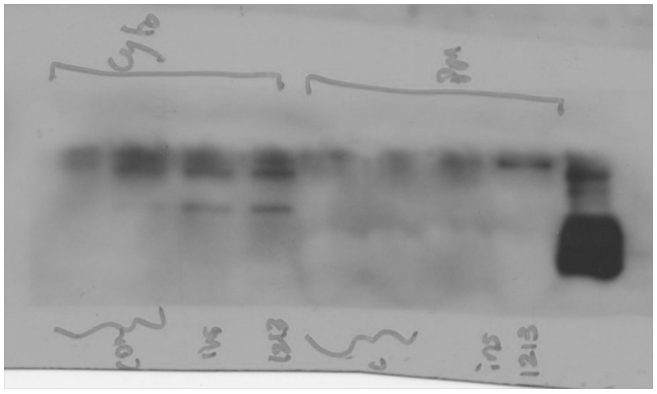
Control Insulin 12,13-diHOME Control Insulin 12,13-diHOME



c

Cytosol Membrane

Control Control Insulin 12,13-diHOME Control Control Insulin 12,13-diHOME



Supplementary Figure 7

Un-cropped immunoblots shown in this manuscript. (**a**) Experiments shown in Figure 4 (**b**) An independent experimental replicate of the FATP1 immunoblot shown in **a**. (**c)** A third independent experimental replicate of the FATP1 immunoblot shown in **a**. The experimental replicates in **b** and **c** were used to quantify FATP1 translocation as described in the online methods.

Supplementary Table 1
Lipid profiling by LC-MS/MS in human plasma after saline or cold challenge.

	Subject	341-01	341-02	341-03	341-04	341-05	341-06	341-07	341-08	341-09	341-01	341-02	341-03	341-04	341-05	341-06	341-07	341-08	341-09
	Treatment	Cold	Cold	Cold	Cold	Cold	Cold	Cold	Cold	Cold	Saline	Saline	Saline	Saline	Saline	Saline	Saline	Saline	Saline
	Code	341-01-C	341-02-C	341-03-C	341-04-C	341-05-C	341-06-C	341-07-C	341-08-C	341-09-C	341-01-S	341-02-S	341-03-S	341-04-S	341-05-S	341-06-S	341-07-S	341-08-S	341-09-S
	Species																		
	IS-d4-9-HODE	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9-oxoODE	0.8820752	0.13772466	0.30110357	0.40821832	0.46119151	0.38578526	0.53432263	0.11439154	1.66230684	0.22070346	0.13464997	0.67824337	0.33963432	0.12871609	0.16220992	0.06446726	0.36655777	0.6221771
	13-oxoODE	0.84687575	0.23180595	0.08310963	0.37735672	0.44132719	0.37386546	0.38222553	0.13517607	1.23434785	0.14931878	0.16398264	0.44110481	0.29814292	0.11087036	0.14897919	0.03521053	0.18031766	0.47868483
	9-HOTrE	0.17697993	0.03389002	0.09420009	0.10592884	0.0370685	0.03113476	0.10456824	0.03061817	0.09664619	0.05040424	0.03213139	0.03560318	0.05618638	0.0291903	0.01039693	0.02553466	0.04993029	0.05675979
	13-HOTrE/13-HOTrE(r)	0	0.00212058	0.08444003	0.05244116	0.03325706	0.02123659	0.08367766	0.08187226	0.01455282	0.07389398	0.03267962	0.31266571	0.09382568	0.00671887	0.01854387	0.0355627	0.04223872	0.12527225
	9-HODE	3.91943541	1.22345046	0.67334838	1.31061089	1.86791051	1.0102823	1.96652953	0.94789946	5.64421903	1.59699636	0.42535328	3.18619718	1.30629673	0.52118429	0.54076628	0.56493647	0.95049219	4.60993797
	13-HODE	5.12097498	1.12833588	0.82558584	1.75618796	2.63683682	1.34057854	2.45533991	1.16158199	8.28243273	1.62602974	0.47028437	3.37096622	2.23948275	0.54787381	0.62625744	0.67280668	1.20385351	2.7311558
	9(10)-EpOME	2.20215408	0.74125195	0.31476495	0.27484368	0.53126437	0.37912148	0.71423327	0.49946771	1.97850056	0.40949975	0.28451051	1.80132934	0.83020776	0.21822925	0.12019162	0.05716339	0.50686715	0.24733913
	12(13)-EpOME	1.87320275	0.79379427	0.41317053	0.4362924	0.57413432	0.47966661	0.80479263	0.54021352	2.49837296	0.4873635	0.46113654	1.67584874	0.91390139	0.25161919	0.24222062	0.0865	0.60470406	1.58567437
	9,10-diHOME	3.3272534	0.90768129	0.99019041	0.57254189	0.87079847	0.56103895	0.98862293	1.19871882	1.18568809	0.49795281	1.162309	0.52972917	0.8081577	0.41988789	0.24595267	0.35718634	1.2049586	0.77173535
	12,13-diHOME	1.46875726	0.71652283	0.73638901	0.77912647	0.7267959	0.44177781	0.87098188	1.03721686	0.84714557	0.4575017	0.53594509	0.36370236	0.67222662	0.28907866	0.19869644	0.23709389	0.48616595	0.6838185
	18-HEPE	0.03482791	0.0226062	0.01393433	0.00128854	0.00452034	0.04189755	0.01187777	0	0.01691096	0	0.01633175	0.03412209	0.04322722	0.00749832	0	0	0	0.00599058
	15-HEPE	0.03995867	0	0.02781801	0.00839931	0.00649814	0.01278576	0.02861311	0.03783117	0.01252254	0.00648206	0.07548249	0.00512205	0.0336037	0.00278939	0.0487373	0.03779358	0.01255589	0.01465769
	12-HEPE	0.03797506	0	0.00669321	0.00331692	0	0	0.00649222	0	0.0059629	0.01480579	0	0	0.02927001	0	0.01122213	0.03477062	0	0.00410264
	5-HEPE	0.01443379	0.0089581	0.00591013	0.00831136	0	0.03951262	0.03103896	0	0	0.02850702	0.02693501	0.01779496	0.00432579	0	0.00423175	0.02931917	0.00846928	0.00333205
	11-HEPE	0.02045306	0	0	0.00310293	0	0.01149639	0.00475933	0	0.0039127	0	0.01437334	0	0.01895096	0	0	0	0.01279124	0.00417701
	8-HEPE	0.01577257	0.02781498	0	0	0.00814537	0.02094913	0	0.01078564	0	0	0	0	0.0086514	0	0.00862009	0.02288272	0.0084697	0
	15-oxoETE	0.01796359	0.00426954	0	0.00675241	0	0.0153798	0.00570874	0.03426826	0	0	0.04323442	0	0	0.00548504	0.00458438	0	0	0.0038982
	9-HEPE	0	0	0	0	0	0	0	0	0.00426522	0	0	0	0	0.00354795	0	0	0	0
	14(15)-EET	0.02118569	0.05183913	0	0.00918021	0	0.00997707	0.024636	0.03407762	0.04587191	0.00648871	0	0	0.00432557	0	0.01722086	0	0.00919167	0
	11(12)-EET	0.01578896	0.034617	0.04466404	0	0.02181022	0	0.00640353	0.05752618	0.05576792	0.01881642	0.04062346	0.00531622	0.00168112	0.00278909	0.02441701	0.02822197	0	0.00961029
	8(9)-EET	0	0.05018695	0.00929148	0.01584103	0	0.04858976	0.02459868	0.00464922	0	0.0345319	0.10462385	0.02023739	0	0.00957971	0.03720013	0.00530879	0.01693959	0.00449927
	5(6)-EET	0.00643152	0.00161645	0	0	0.00800458	0.01278646	0.03103985	0.03556599	0.0229632	0.01482362	0.05393147	0.01920405	0.00432579	0.00154816	0	0	0.03802619	0.00381695
	15-HETE	0.07191695	0.04967329	0.05489717	0.02421615	0.0182332	0.03551278	0.06858253	0.13475127	0.04767125	0.08072385	0.11617988	0.01358925	0.04751897	0.02529085	0.02811637	0.03147345	0.01461535	0.03664841
	12-HETE	0.1665798	0.08207757	0.04170098	0.03502899	0.04040702	0.14849331	0.27205378	0.11740046	0.04314802	0.04076668	0.24696941	0.02658043	0.08995519	0.02911897	0.0248371	0.92245723	0.00872025	0.05640258
	5-HETE	0.14201379	0.15667264	0.11004592	0.0491466	0.02794356	0.20771158	0.24605791	0.23871839	0.20932031	0.19722658	0.31201862	0.08347809	0.04301536	0.02577249	0.05942672	0.08752551	0.12765647	0.09497188
	20-HETE	0.05374696	0.13715509	0.02223985	0.01021937	0.00608212	0.01917904	0.01598946	0.00464922	0.08172544	0.06587482	0.07824381	0	0	0.00294681	0.02229653	0.00535926	0.00768525	0.01374217
	11-HETE	0.15478346	0.11454226	0.01821948	0.04501689	0.02968725	0.10309355	0.06475798	0.18665149	0.15898088	0.11062228	0.09429788	0.01316201	0.29821177	0.07710361	0.07707103	0.70649298	0.08582017	0.04986108
	16-HETE	0.04581254	0.00849749	0.03481581	0.01900474	0	0.02185598	0.01627169	0.01175279	0.0177593	0.01206397	0.02780117	0.00960223	0.00397036	0	0.03448142	0	0.01086333	0.00711744
	17-HETE	0	0.11589514	0.0831147	0.01190338	0.02470268	0.0416021	0	0.07104636	0	0.04626907	0.20026577	0.06238974	0.12378804	0.02452737	0.04716968	0.01727634	0.24170241	0.02718897
	18-HETE	0.02976464	0.03681365	0.00921048	0.01917963	0	0.07672836	0	0.10356622	0.07710787	0.07537659	0.19277452	0.03436163	0.03017551	0.04201908	0.05321102	0	0	0.01730326
	9-HETE	0.00643083	0.04239607	0	0	0	0.0055111	0	0	0.00913759	0.03682737	0.02874102	0.00531599	0.00432558	0.00393721	0	0.03985586	0	0.01199032
	8-HETE	0.0336904	0.04170806	0	0.01531632	0.00899042	0.00850767	0.00991709	0.03182722	0.00539254	0	0.05428681	0.01801625	0.07517357	0	0	0.06338788	0.03307261	0.01220137
	all trans-LTB4	0.01327579	0.03598697	0	0	0.00501076	0.00775905	0	0.00218906	0.02369955	0.01036466	0	0	0.0087393	0.00843015	0	0	0.0038656	0
	LTB4	0.01327579	0.00520328	0	0	0.00501076	0.00775905	0	0.01285761	0	0	0	0.00249753	0.00708181	0	0	0	0	0
	5,6-diHETE	0.04434704	0.01750288	0.0114727	0.00961816	0	0.01576784	0	0	0.00801009	0.01258684	0	0.00082286	0	0	0.00878691	0.00395142	0	0.00109043
	5,15-diHETE	0	0	0	0	0	0	0	0	0.0049252	0	0.00752271	0	0	0	0.00570484	0	0	0
	Hepoxilin A3	0.01265234	0	0.01071905	0	0	0	0	0	0	0	0.01362103	0	0	0	0	0.00452613	0.00386563	0.00766148
	17-HDHA	0.13086115	0.03094994	0	0	0	0	0.0633934	0.14383265	0	0	0	0.02119478	0	0.08715058	0	0	0.01418545	0.008345
	14-HDHA	0.01104692	0.03963729	0.00923092	0.00331692	0.00223335	0.02095718	0.00401189	0.04854841	0.00596288	0.03129745	0.03253428	0	0	0.00787485	0	0.1217398	0	0.00435603
	7-HDHA	0	0.00520821	0	0.00371737	0	0.03399313	0.02354642	0	0	0	0	0.00512305	0.00432564	0	0	0	0	0.00435581
	4-HDHA	0.0222041	0	0.00925261	0.00780255	0.00606823	0.02094808	0.02561428	0	0.01192581	0	0.02693615	0	0.0231951	0.00546205	0.02171119	0.02822318	0.01547035	0.00416748
	8-HDHA	0.01626243	0	0	0	0	0.02094824	0.03876309	0	0.02739624	0	0	0.00450554	0.01895612	0	0	0	0	0.00416525
	10-HDHA	0.0157719	0.02205848	0.03543268	0	0.00904059	0	0	0.03117691	0	0	0.01484626	0.01491797	0.00432579	0.00812764	0.01425676	0.00531269	0	0
	11-HDHA	0	0	0.01846295	0	0	0	0	0.00881858	0	0	0.05170875	0	0	0.00278911	0	0.02888005	0	0.00434652
	13-HDHA	0.02699201	0	0.00923194	0.00331681	0.00608207	0	0.01280712	0.04021322	0.00596318	0	0.04690383	0	0.06286332	0.00920093	0	0.0884625	0.0311973	0
	16-HDHA	0	0.01402686	0.00923179	0.00521808	0.00452035	0.00787255	0.00946175	0.03556135	0	0	0.05051611	0.00669153	0.00222847	0.00932429	0.00860048	0.07601718	0.00846921	0.00600437
	20-HDHA	0	0.00519654	0.03543118	0.01199923	0	0.03154359	0.00476209	0.01793754	0.0229103	0.06892118	0.05129034	0.00888749	0	0.01044571	0	0.0244436	0.01040728	0.01345364
	19(20)-EpDPE	0	0.00519654	0.00477116	0	0	0	0	0.01286167	0	0.06750689	0	0	0	0.00934214	0	0.02291146	0	0
	16(17)-EpDPE	0	0.00169609	0	0	0	0	0	0.04020443	0	0.01480579	0	0.02451986	0.00419905	0.00492333	0	0.02291011	0.01471839	0
	PGE2/PGD2	0.03237649	0.03311641	0.00162726	0	0.00263481	0.0154526	0	0.01966326	0.00613352	0.00180509	0.00403581	0.00601951	0.00436398	0.02118443	0.00148337	0.04024763	0.00934356	0.00283751
	PGD2	0.05110797	0	0.00299722	0.00310629	0	0.00786371	0.00534238	0.00539098	0.00955062	0	0.00382797	0.0020889	0.00276077	0	0.00328019	0.02318241	0	0.0032589
	LXA4	0.03969985	0.01253619	0.00335969	0	0	0	0	0	0.0033298	0.00564954	0	0.00862614	0.00766044	0.00323691	0	0	0	0.00104566
	LXB4	0.00214888	0.00283358	0.00318569	0.0060449	0.00517021	0.00518695	0.01116179	0	0.00194575	0.01881837	0.02066103	0	0	0.02335869	0	0.01220011	0	0.001208
	15-keto-PGF2a	0	0	0.00368083	0	0	0.00353299	0.01212309	0	0.01668138	0.018012	0.0028776	0.00166392	0	0.00866126	0.00045731	0.00204585	0.0031371	0.00216842
	13,14-dihydro-15-keto PGE2	0.00476807	0.01285741	0	0.00697658	0	0	0.00825804	0.00278101	0.00666099	0.00853768	0.00553044	0	0.00455911	0.0030836	0	0.02082041	0	0.00262427
	13,14-dihydro-15-keto PGD2	0.04834704	0.00998238	0.00162723	0.00546839	0.00189556	0.00537476	0.01599245	0.00789616	0.00666484	0.0107805	0.01515891	0	0.00227298	0	0.00244245	0.01225892	0.00175041	0
	PGF2a	0.03029478	0.00848361	0.00318834	0.00894722	0.00526992	0.00342366	0.02811518	0.00521461	0.01039009	0	0.0056297	0.00713767	0.00867168	0.00962842	0	0.01013146	0.00171746	0.00444059
	PGE1/D1	0.0047708	0.02794274	0	0.00681215	0	0.00518683	0.01599794	0.00821993	0.02295678	0.00281416	0.02229943	0	0.00658218	0.00961785	0.00618589	0.03967214	0.00548882	0.00763858
	8-iso PGF2a	0.0329723	0.00848361	0.00318834	0.00894392	0.00526964	0.00247984	0.02182173	0.00432122	0.00780757	0	0.0056297	0.00601947	0.00746147	0.00769415	0	0.00362795	0.00174637	0.00652314
	5-iPF2a-VI	0.01220498	0.01362698	0.00184412	0.00970778	0	0.00353314	0.01108831	0	0.01640537	0	0.01698265	0.00206176	0.00435662	0	0.00444197	0	0.00175036	0
	Maresin1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	PD1	0	0.00258433	0.00318108	0.00310627	0.0029401	0	0	0.00666235	0	0	0.00562975	0	0.0013633	0.00962882	0.00407104	0.006565	0	0.00241397
	TxB2	0.15578249	0.01980041	0.01436194	0.00537447	0.04811491	0.00586518	0.17335966	0.00958853	0.0562911	0	0.01535797	0	0.02116264	0.10979916	0.00296675	0.42155733	0.02836876	0.00853881
	6-keto-PGF1a	0	0.00848333	0	0	0.00294026	0	0.00316439	0.01108041	0	0	0	0.00601946	0	0.0032766	0	0.01927389	0.00524866	0.00114938
	19/20-OH PGF2a	0	0	0.00162726	0.00402614	0	0.00600204	0.0031643	0	0	0.00281505	0	0.00206177	0	0	0	0	0	0.00340826
	RvD1	0	0	0	0	0.00263174	0	0.00311709	0.0020744	0.00286939	0	0	0	0	0.00814485	0	0	0	0
	RvD2	0	0	0	0	0	0	0.0069399	0.00207584	0	0.00274752	0.00675513	0	0	0.0032766	0.00144572	0	0	0.00761101
	LTE4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	LTD4	0.00603215	0	0	0	0.00209026	0	0	0	0	0	0	0	0	0	0	0.00319376	0	0
	LTC4	0	0.00374594	0	0.00310614	0	0	0.00251544	0	0	0	0	0	0	0	0.00148337	0	0.00206371	0
	PGF1a	0	0.0028265	0.05960986	0.00379564	0	0	0	0	0	0	0.07473816	0.00860168	0.05117547	0	0	0	0	0.06129607
	15-keto-PGE2	0.00603215	0	0	0	0	0.00518699	0	0	0	0	0	0	0	0	0	0	0	0
	PGD3	0	0.01622295	0.00481326	0.00402611	0.00558118	0	0	0.00562756	0	0	0.00470715	0	0.00240464	0.00327344	0	0.02094648	0	0.00253709
	PGA2/PGJ2	0.01048766	0.01085063	0.00318108	0.00703436	0.00153868	0.00336492	0.0054352	0.0081337	0	0.00074161	0.01062494	0.00650242	0.00892767	0.00962882	0	0	0.00116949	0
	PGB2	0.00477386	0.00515664	0	0.01023857	0	0	0	0.00262997	0	0.00514772	0	0.00470749	0	0.00327646	0	0.00428663	0.0024919	0
	15-deoxy-delta12,14-PGD2	0.00880852	0.00284002	0	0	0.01155394	0.01012046	0.01599827	0.00521788	0	0	0	0.00465665	0.00276347	0.01978713	0.00296673	0.02575126	0.00350073	0.00374253
	5,6-DiHETrE	0.0034526	0.00266656	0.01071895	0.01428401	0.06458497	0.00775866	0.04597991	0	0.0105659	0.03623538	0.02660184	0.00935528	0.00465124	0	0.02635985	0.00644169	0	0.00190449
	8,9-DiHETrE	0.01894492	0.02246293	0	0.00211861	0.00193267	0	0.00602079	0.01210574	0.01377357	0.02176487	0.02713225	0.02691133	0.0098876	0.03365783	0.01879593	0.00584746	0.02920653	0.00761823
	11,12-DiHETrE	0.13832154	0.01530025	0.02961696	0.03621561	0.0679621	0.14266708	0.18449487	0.03568834	0.13386157	0.16961684	0.11246387	0.04509038	0.02393381	0.02095105	0.17118215	0.01979974	0.05983042	0.01741919
	14,15-DiHETrE	0.25314244	0.2851802	0.08407026	0.06673701	0.08865614	0.20891383	0.14621531	0.08789911	0.17444377	0.18282615	0.17465069	0.15817538	0.0427578	0.20256671	0.22901717	0.04850597	0.10086025	0.07283636
	5-HETrE	0	0.02911327	0.02872587	0.00412028	0	0.02094915	0	0.0354841	0.03483118	0.11552983	0	0.00532609	0	0	0	0	0.04721793	0.01008503
	8-HETrE	0.07079045	0.07777401	0.04262773	0.00667031	0	0.05226377	0	0	0.13868969	0.02130126	0.02693501	0	0.03359437	0	0.03115187	0.07847393	0.00846921	0.0417684
	15-HETrE	0.12283663	0.1338614	0.03874481	0.0717968	0.07878727	0.14105611	0.04945661	0.41635866	0.32535658	0.32187915	0.91450788	0.05276736	0.33742994	0.04114536	0.0662108	0.36815073	0.26520039	0.02333672
	19,20-DiHDPA	0.19657519	0.0148816	0.09533832	0.01938806	0.09466181	0.15260692	0.1294652	0.05666532	0.10466447	0.21054674	0.16100974	0.03036406	0.04923989	0.17368477	0.18713177	0.0622569	0.06385036	0.10421156
	2,3-dinor-11beta-PGF2a	0	0	0.00162726	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	15-deoxy-delta12,14-PGJ2	0	0.03392007	0.01693021	0.00315956	0.01354647	0.03424425	0.02280314	0.00578632	0.01711792	0.01633068	0.04838009	0.01499458	0.00112402	0.02377063	0.01067354	0.00773433	0.00431489	0.00253698
	TxB3	0	0	0.00235668	0.00310616	0.00263493	0.00353314	0	0.00655911	0.00801773	0.00654388	0	0.00157938	0	0.00584882	0	0.04531966	0	0
	Tetranor-12-HETE	0.01286271	0.02285245	0.00923179	0.03868014	0.02395912	0.07868379	0.06323881	0.02416028	0.02974028	0.09532808	0.05031429	0.02126462	0.09187375	0.02698304	0	0.04328249	0	0.02259983
Precursors	Docosanoids	0.44457102	0.15078243	0.24057397	0.06849294	0.12523814	0.29840486	0.32919493	0.39769005	0.19809762	0.38108731	0.46634915	0.09580794	0.16949095	0.33154691	0.23614217	0.46277348	0.14919596	0.1644754
	Eicosanoids	3.16430801	2.065358	1.35995176	1.21503573	1.24483445	1.68986643	2.3451846	2.42629028	2.37806793	1.94569993	3.00003896	0.95737846	1.52644377	0.91967462	1.04405385	2.54916794	1.32541319	1.11153383
	Octadecanoids	9.30854111	2.84614814	2.19653918	2.17518185	2.91578437	2.21061251	3.52876524	2.51858581	8.65586249	1.81524255	2.23872005	5.16185862	3.24623048	1.15851309	0.92995095	0.62606218	2.91333553	3.76237058
Inflammatory	Anti-inflammatory	7.77025571	3.0421212	2.15121665	2.91924816	3.49962083	2.8753129	4.31060166	3.40145576	8.8932373	3.45884187	3.29394784	4.5228972	3.12171484	1.61600558	1.77581688	1.94358209	2.35996116	6.20284882
	Pro-inflammatory	13.9253286	4.20927298	3.12483579	3.62302841	5.20165711	3.60107252	6.17272985	4.04290409	16.0258439	3.71776977	3.23782076	8.5178867	5.38231456	1.70707805	1.53655225	2.42593049	4.11130551	6.26715966
Enzymatic	COX	0.39802421	0.11483448	0.10184432	0.06980047	0.07050444	0.05878489	0.2740405	0.1192454	0.13405346	0.08429828	0.18105493	0.0779488	0.12147372	0.20968652	0.01914308	0.59547977	0.06969611	0.09098157
	CYP450	14.2303109	4.34536852	3.26474616	3.66621017	5.38027009	3.97172755	6.26394498	4.06039291	16.3664167	4.14311064	3.46957095	8.41098624	5.30341928	2.01566371	2.131215	1.51813757	4.27567713	6.27617438
	LOX	8.2450646	2.92829671	2.30022923	3.25252239	3.81652389	2.91246982	4.69918886	3.41448326	10.2797602	3.3016972	3.06819946	5.27858119	3.55813921	1.36076381	1.37873527	2.82287832	2.59977874	6.80387067

Supplementary Table 2

P values for linear model of relationship between each phenotype with BMI as covariate.

Covariate	p
Age	0.191
FPG	0.507
FPI	0.747
HOMA-IR	0.643
HbA1c	0.48
CrP	0.73
Leptin	0.154
Total.Cholesterol	0.674
HDL.Cholesterol	0.392
LDL.Cholesterol	0.788
Triglycerides	0.0463
ALAT	0.0494
ASAT	0.0274
gGT	0.138

Supplementary Table 3
Primer Sequences.

Primer	Sequence	Gene
ARBPfor	TTTGGGCATCACCACGAAAA	ARBP
ARBPrev	GGACACCCTCCAGAAAGCGA	
Ephx1for	GGAGACCTTACCACTTGAAGATG	Ephx1
Ephx1rev	GCCCGGAACCTATCTATCCTCT	
Ephx2for	ACCACTCATGGATGAAAGCTACA	Ephx2
Ephx2rev	TCAGGTAGATTGGCTCCACAG	
Ephx3for	CAGTGGACTCCGATAGCACG	Ephx3
Ephx3rev	TGGGACGACTACAGAGCCG	
Ephx4for	TCCCTGGTGTACGGCTACTG	Ephx4
Ephx4rev	ATCTTAACCCGGAGTCCTTGA	
UCP1for	AGGCTTCCAGTACCATTAGGT	UCP1
UCP1rev	CTGAGTGAGGCAAAGCTGATTT	
LPLfor	GCCCAGCAACATTATCCAGT	LPL
LPLrev	GGTCAGACTTCCTGCTACGC	

Supplementary Table 4
Antibodies.

Antibody List	Vendor	Catalog #
FATP1(ALSVL5, m-100)	Santa Cruz Biotechnology	sc-25541
Pan-Cadherin(H-300)	Santa Cruz Biotechnology	sc-10733
β-Tubulin	Cell Signaling Technology	2146
HRP conjugated anti Rabbit IgG	Cell Signaling Technology	7074
Anti-CD36	Santa Cruz Biotechnology	sc-9154

Supplementary Video 1
Representative imaging of FFA-SS-Luc uptake in UCP1cre$^{+/-}$Rosa(stop)Luc$^{+/-}$ injected intravenously with luciferin-conjugated fatty acid and 12,13-diHOME or vehicle. Data from individual images using sequential one-minute exposures over approximately 50 minutes was stacked into a movie. The animal on the left is the vehicle treated and the mouse on the right is treated with 12,13-diHOME.

Supplementary Video 2
Representative imaging of FFA-SS-Luc uptake in CAG-Luc$^{+/+}$ brown adipocyte cells treated with 12,13-diHOME or vehicle and then incubate with luciferin-conjugated fatty acid. Data from individual images using sequential 30 second exposures over approximately 50 minutes was stacked into a movie. The well on the left is vehicle treated and the well on the right is treated with 12,13-diHOME.