SUPPLEMENTAL INFORMATION

Supplemental Figure Legends

Fig S1. Growth curve of male C57BL/6 mice that have been treated with 7,8-DHF and high fat diet for 22 weeks (n=8), related to Fig 1.

Fig S2. 7,8-DHF stimulation does not inhibit adipogenesis, related to Fig 1.

Adipogenesis of 3T3-L1 preadipocytes were induced by isobutylmethylxanthine-dexamethasone-insulin and various concentrations of 7,8-DHF as stated in the "Methods". Cellular lipid accumulation was determined by oil-red O staining and isopropanol extraction (n=3).

Fig S3. Chronic consumption of 7,8-DHF does not alter the gastrointestinal absorption of lipid, related to Fig 3.

Free fatty acid (A), triglyceride (B) and cholesterol (C) content of feces from female mice treated with 7,8-DHF for 20 weeks were determined (n=6-7).

Fig S4. Chronic 7,8-DHF treatment activates hypothalamic TrkB receptors, related to Fig 5.

Female wild-type and MTKO mice were fed with HFD and 7,8-DHF for 20 weeks. The hypothalamus was collected and phosphorylation of and expression of TrkB were then determined using immunoblotting.

Fig S5. 7,8-DHF does not directly activate AMPK *in vitro*, related to Fig 7.

AMPKa was immunoprecipitated from HEK293 cells and incubated with its specific activator A769662 (1 mM) or various concentrations of 7,8-DHF for 30 min. The kinase activity on SAMS peptide phosphorylation was then determined (***: $P<0.05$, one-way ANOVA, n=3).

Supplemental Tables

Table S1 Complete blood count of mice after chronic 78DHF treatment , related to Fig 1.

	H_2O	78DHF	Normal value
White blood cell (10^6/ml)	3.89 ± 0.38	3.60 ± 0.36	1.8 - 10.7
Neutrophil (10^6/ml)	1.06 ± 0.13	0.84 ± 0.10	0.1 - 2.4
(%)	25.76 ± 1.79	23.27 ± 1.07	
Lymphocyte (10^6/ml)	2.54 ± 0.23	2.37 ± 0.21	0.9 - 9.3
(%)	65.70 ± 1.75	66.37 ± 1.90	
Monocyte (10^6/ml)	0.29 ± 0.04	0.29 ± 0.04	0 - 0.4
(%)	7.20 ± 0.57	7.92 ± 0.55	
Eosinophil (10^6/ml)	0.04 ± 0.02	0.07 ± 0.03	0 - 0.2
(%)	0.92 ± 0.32	1.66 ± 0.65	
Basophil (10^6/ml)	0.02 ± 0.01	0.03 ± 0.01	0 - 0.2
(%)	0.42 ± 0.19	0.78 ± 0.30	
Hematocrit (%)	40.13 ± 0.72	44.36 ± 5.12	35.1 - 45.4
Red blood cell (10^9/ml)	9.58 ± 0.13	10.63 ± 1.24	6.36 - 9.42
Hemoglobin (g/dL)	13.62 ± 0.27	13.05 ± 0.28	11.0 - 15.1
Mean corpuscular volume (fL)	41.89 ± 0.26	41.76 ± 0.18	45.4 - 60.3
Mean corpuscular hemoglobin (pg)	14.20 ± 0.14	13.13 ± 1.03	14.1 - 19.3
Mean corpuscular hemoglobin concentration (g/dL)	33.95 ± 0.23	31.4 ± 2.47	30.2 - 34.2
Red cell distribution width (%)	13.61 ± 0.12	14.06 ± 0.18	12.4 - 27.0
Reticulocyte (10^6/ml)	31.60 ± 5.97	15.33 ± 4.02	
(%)	0.37 ± 0.07	0.16 ± 0.04	
Platelet (10^6/ml)	846.50 ± 17.33	914.88 ± 115.68	592.0 - 2972.0
Mean platelet volume (fL)	5.34 ± 0.03	5.49 ± 0.09	5.0 - 20.0
Plate distribution width (%)	42.64 ± 0.47	42.55 ± 0.53	39 - 49
Plateletcrit (%)	0.45 ± 0.01	0.51 ± 0.07	

Female C57/BL6 mice (n = 8) that have been fed with chow diet ± 78DHF (1.6 mg/L in drinking water) for 20 weeks.

Table S2 Hepatic gene expression change after 7,8-DHF treatment, related to Fig 4.

Function	Gene	NCBI Accession	Gene expression (Arbitrary unit)					
			H_2O			7,8-DHF		
Proteolysis /catabolism	Usp18	NM_011909	454.9	420.7	484.5	250.9	239.1	210.7
	Sumo1	NM_009460	1211.3	930.9	1215.9	1973.6	1655.6	1478.4
	Cpb1	NM_029706	150.7	106.1	161.8	33.1	36.9	38.9
	Try4	NM_011646	345.1	263.9	270.3	152.3	139.4	120.1
	Try10	NM_001038996	518.5	494.9	491.0	145.2	167.1	117.2
	Cpa1	NM_025350	1672.3	1691.2	1601.8	136.9	127.4	129.2
	Ctrb1	NM_025583	2081.6	1997.4	2018.0	287.8	234.9	252.7
Glucose/fatty acid metabolism	Lipo1	NM_001013770	119.6	100.0	162.1	230.8	245.2	224.9
Detoxification	Sult3a1	NM_020565	794.0	1047.3	1173.9	2383.2	2126.6	1931.1
	Cyp2c54	NM_206537	1176.4	1470.1	1453.6	2585.1	2317.1	2315.5
	Cyp2c67	NM_001024719	3670.3	5652.2	5245.3	7673.1	6745.0	6499.4
	Cyp3a16	NM_007820	1102.8	1133.1	1221.8	2511.8	2433.6	2348.0
	Sult2a1	NM_001111296	860.4	1076.7	1459.5	914.1	737.1	631.1
	Sult2a3	NM_001101586	375.4	337.2	382.6	235.9	205.9	174.9
DNA/RNA processing	Egr1	NM_007913	91.1	86.9	91.4	218.9	193.8	189.0
	Snora44	NM_034050	279.7	310.7	283.6	121.7	134.2	131.4
	Snora73b	NM_028513	641.6	452.4	439.4	303.4	355.7	379.1
Carrier protein	Fabp5	NM_010634	183.1	175.5	190.8	384.9	414.4	411.6
	Fabp7	NM_021272	601.8	627.0	637.8	1173.3	1171.7	1224.0
	Orm3	NM_013623	461.3	513.2	515.7	235.0	242.4	241.3
Energy expenditure /metabolism	ND6	ENSMUST00000082419	564.2	783.2	243.2	312.0	288.4	370.7
Protein synthesis/sorting	Dnajc13	NM_001163026	190.3	126.1	175.4	296.1	287.7	243.0
	Uxt	NM_013840	177.1	64.8	148.1	83.0	116.7	138.0
Hormone /growth factor	Bmp2	NM_007553	244.8	217.3	217.9	416.6	435.9	408.6
Inflammation	Il1a	NM_010554	127.7	119.2	142.7	247.8	265.3	263.4
	Ifi44	NM_133871	326.8	265.0	280.4	588.8	568.5	526.4
	Gbp4	NM_008620	121.6	85.1	112.5	152.1	189.2	158.7
	Gbp9	NM_172777	103.7	78.1	90.1	158.3	179.8	160.6
Unknown	Vmn1r125	NM_001166740	41.7	44.4	41.8	134.3	128.6	142.4
	Ly6a	NM_010738	401.0	456.8	502.7	946.8	952.3	899.2
	Slco1a1	NM_013797	65.7	59.0	76.6	161.3	176.0	158.3
	Olfr767	NM_146318	83.4	173.3	116.5	133.4	75.5	68.9
	Amy2a5	NM_001042711	505.6	562.2	623.8	187.7	183.1	195.4
	Amy2b	NM_001190403	394.2	390.5	440.5	121.8	129.4	150.6
	Dmbt1	NM_007769	762.8	774.6	852.2	37.1	41.4	34.3

Liver total RNA was isolated from female mice that have been treated with HFD ± 78DHF for 20 weeks. Expression of the genes was determined by microarray analysis. Only those genes with expression change >2 fold and $P<0.05$ were presented.

Table S3 Skeletal muscle gene expression change after 7,8-DHF treatment, related to Fig 4.

			Gene expression (Arbitrary unit)					
Function	Gene	NCBI Accession	H_2O			7,8-DHF		
Proteolysis /catabolism	Ublcp1	NM_024475	310.4	374.7	422.2	518.0	563.8	625.5
	Scpep1	NM_029023	118.6	100.2	112.5	202.6	193.1	204.7
	Ggh	NM_010281	201.0	161.4	209.5	313.5	316.0	323.7
	Rbbp6	NM_011247	106.2	110.1	146.7	232.2	196.4	202.7
	Htra4	NM_001081187	121.7	147.6	156.6	414.6	414.8	410.9
	Cdo1	NM_033037	252.5	261.7	274.7	705.5	750.2	690.2
	Cfd	NM_0134598	268.0	223.8	225.0	440.8	421.0	457.0
Glucose/fatty acid metabolism	Mgat2	NM_146035	174.0	146.9	190.7	275.4	267.7	301.0
	Pde3b	NM_011055	103.2	70.7	105.5	198.7	187.7	192.4
	Pnpla3	NM_054088	98.6	97.4	98.5	199.6	215.7	190.4
	Scd1	NM_009127	2849.5	2701.0	2700.3	5540.5	5688.0	5906.6
	Scd2	NM_009128	274.7	223.3	227.2	549.5	569.7	590.1
	Acly	NM_134037	108.5	107.4	113.7	353.3	352.1	356.3
	Fasn	NM_007988	184.6	170.9	172.5	1120.6	1105.6	1149.4
	Elovl6	NM_130450	58.8	57.0	52.9	240.9	234.0	248.7
	Plin1	NM_175640	315.7	309.5	310.8	607.6	598.4	638.1
	Thrsp	NM_009381	121.6	114.3	97.6	382.2	382.0	410.7
	Pepck1	NM_011044	114.8	118.3	134.2	241.5	253.6	245.3
	Acaca	NM_133360	100.8	143.0	123.2	344.1	356.4	377.3
	Slc25a1	NM_153150	169.5	148.8	174.7	518.2	531.4	511.2
	Slc25a10	NM_013770	177.3	107.1	103.8	256.4	237.3	250.2
	Fads1	NM_146094	131.2	132.7	131.3	262.7	266.1	254.6
	Tkt	NM_009388	74.8	64.9	77.5	203.9	182.7	186.3
	Insig1	NM_153526	241.5	196.6	225.7	483.1	451.9	456.3
	Nsdhl	NM_010941	180.6	190.0	163.1	327.0	298.9	312.0
	Agpat2	NM_026212	167.2	159.0	170.3	459.7	436.3	275.1
Detoxification	Aldh1a7	NM_011921	107.4	88.7	111.9	195.0	183.2	203.4
	Cyp4f39	NM_177307	138.3	135.8	146.4	276.9	283.4	298.8
	Car5b	NM_181315	124.7	124.0	126.9	327.9	341.7	325.0
	Cyp3a41a	NM_017396	207.5	212.3	200.5	104.3	113.9	101.7
	Cyp3a41b	NM_001105159	212.0	216.2	200.2	102.3	119.5	104.7
DNA/RNA processing	Rpp40	NM_145938	105.9	83.1	98.4	185.5	173.0	160.6
	Rpa3	NM_026632	120.7	87.9	107.7	188.4	212.0	186.5
	Ankrd1	NR_030779	110.3	130.1	126.5	164.3	145.9	162.0
	Mir297b	NR_30474	191.5	191.1	249.3	96.9	128.3	91.6
	Mir680-1	NR_030447	439.9	432.4	458.2	78.9	92.1	96.0
	Mir680-2	NR_030448	853.8	863.1	805.1	181.0	175.2	171.6
	Snord115	AF357427	750.2	735.8	725.9	83.6	105.0	78.4
	Snord116	NR_002895	1089.4	1014.8	1048.1	332.0	351.2	343.8
	Rnu2	NR_004414	1746.7	1606.3	1846.7	940.2	913.0	862.0
	Tsen15	NM_025677	213.4	163.3	168.9	324.8	328.4	297.8
Cell adhesion /structural protein	Krt10	NM_010660	56.6	55.0	44.7	239.8	265.2	230.1
	Krt77	NM_001003667	52.6	49.3	53.6	190.2	184.9	190.5
	Myoc	NM_010865	137.6	118.9	131.6	285.8	328.8	297.6
	Chad	NM_007689	70.8	58.7	63.0	166.7	174.2	189.8
	Prg4	NM_021400	117.4	120.2	130.5	335.1	342.6	329.0
	Fmod	NM_021355	251.2	237.8	240.5	588.3	623.6	608.7
	Myo9a	NM_173018	145.7	146.2	147.9	267.6	237.4	235.3
	Lgals12	NM_019516	77.4	86.4	86.9	273.5	285.2	296.7
	Sprr2a1	NM_011468	214.1	200.9	207.9	92.2	85.3	94.5
	Krtap16-8	ENSMUST0000	445.0	411.0	418.3	111.7	109.6	121.0

		0074637						
	Krtap20-2	NM_001163615	220.6	219.3	219.1	48.6	55.5	53.0
	Krtap5-1	NM_015808	222.5	224.4	188.2	107.9	115.7	122.6
	Krtap5-2	NM_027844	287.1	296.8	243.9	167.8	141.5	153.8
Carrier protein	Orm1	NM_008768	131.0	120.2	128.6	260.9	289.6	299.7
	Hp	NM_017370	317.8	281.6	279.3	159.5	151.1	166.3
Energy expenditure /metabolism	Mup1	NM_001163011	1507.3	1398.3	1412.4	3158.0	3390.1	3037.1
	Ucp1	NM_009463	23.7	25.5	26.0	254.3	265.1	245.4
	Prkar2b	NM_011158	226.4	244.3	232.7	485.3	451.0	445.0
	ND6	ENSMUST00000082419	1537.2	1353.1	1206.7	225.2	183.0	197.1
Protein synthesis/sorting	Vps33b	NM_178070	103.6	90.1	94.9	163.0	191.1	168.7
Hormone /growth factor	Retn	NM_022984	659.2	670.3	634.2	1344.9	1331.4	1291.1
	Bmp5	NM_007555	107.3	104.9	102.0	287.6	245.0	263.9
Cell cycle control	Lgals3bp	NM_011150	148.7	164.6	151.2	297.6	266.5	284.85
Unknown	Tusc5	NM-177709	150.4	134.4	131.6	266.7	282.6	261.2
	Lrrn4cl	NM_001013019	113.5	85.0	98.3	187.8	182.7	173.2
	Cenpq	NM_031863	125.5	87.4	105.1	186.1	203.6	179.8
	Sfxn1	NM_027324	87.3	77.4	77.3	167.9	180.5	191.0
	Mup2	NM_001045550	1562.0	1529.9	1451.8	3216.8	3502.6	3077.8
	Mup7	NM_001134675	2111.1	2060.1	2021.1	4433.1	4676.8	4332.0
	Mup11	NM_001164256	1810.8	1778.6	1752.3	3980.4	4149.8	3849.9
	Mup19	NM_001135127	1553.0	1570.9	1495.1	3225.7	3366.4	3215.7
	Tmem45b	NM_144936	250.3	261.6	250.4	719.8	748.7	704.5
	Ighv1-72	ENSMUST00000103541	135.8	148.1	166.4	62.0	64.1	68.6
	Slfn3	AF099974	1355.6	1295.1	1415.8	600.8	637.0	620.0
	V1rg10	NM_001166835	184.0	174.5	192.9	37.5	40.1	38.1
	Amy2a5	NM_001042711	255.3	254.9	242.2	81.6	85.6	79.6
	Amy2b	NM_001190403	187.6	168.5	175.6	59.0	64.9	60.3
	Nlrp4f	ENSMUST00000081507	186.1	177.0	181.8	39.6	37.6	39.0
	Speer4d	NM_025759	608.3	574.6	543.4	90.5	98.2	84.8
	Speer4e	NM_001122661	593.3	575.3	581.0	89.1	88.4	86.3
	Speer8-ps1	NR_001584	375.7	381.1	353.6	75.9	75.3	69.9
	Ssxb1	NM_199064	86.5	85.6	92.5	47.6	43.6	34.0
	Slxl1	NM_029181	437.9	416.8	369.8	54.3	50.6	45.9
	Rex2	NM_009051	404.7	397.3	342.6	98.9	112.7	101.6
	Zfp600	NM_009051	129.5	122.0	110.3	30.2	25.5	33.3

Hind limb skeletal muscle (mixed muscle type) total RNA was isolated from female mice that have been treated with HFD ± 78DHF for 20 weeks. Expression of the genes was determined by microarray analysis. Only those genes with expression change >2 fold and P<0.05 were presented.

Figure S1

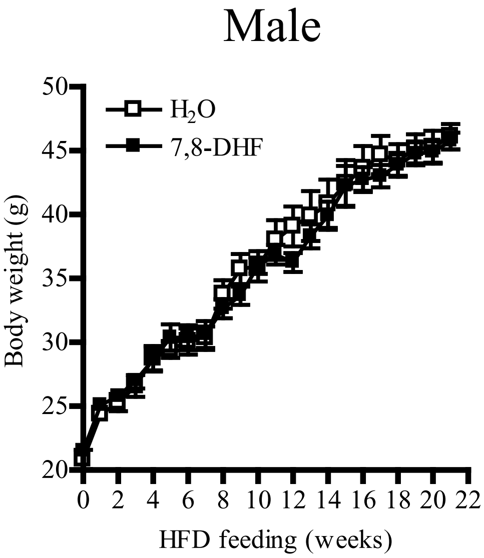
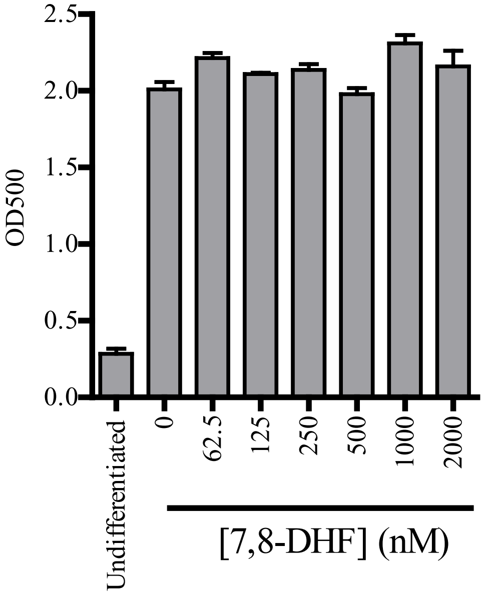

Male
H2O
7,8-DHF
Body weight (g)
50
45
40
35
30
25
20
0
2
4
6
8
10
12
14
16
18
20
22
HFD feeding (weeks)

Figure S2



OD500
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2.0
1.5
1.0
0.5
0.0
Undifferentiated
0
62.5
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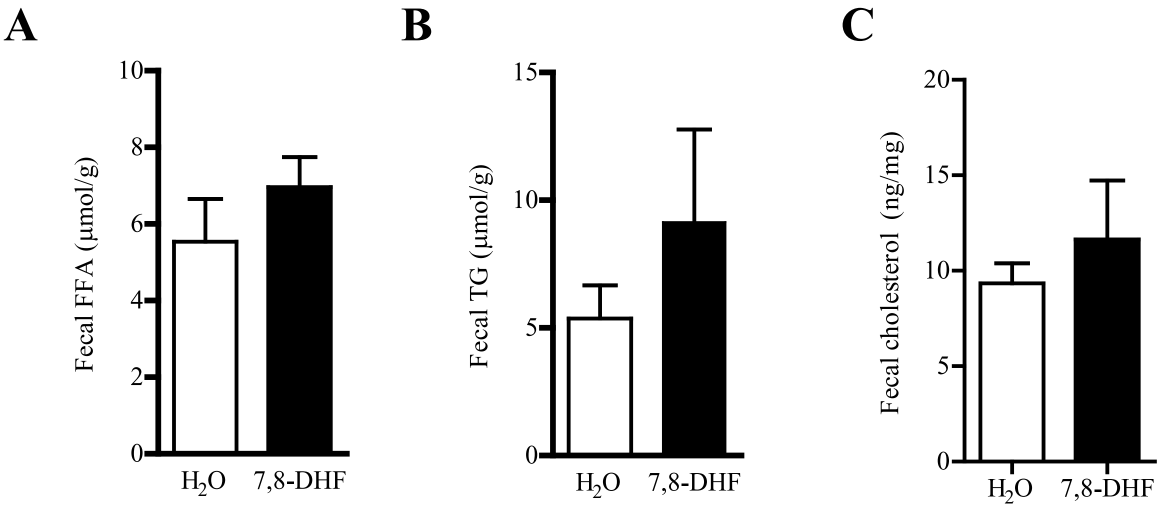
250
500
1000
2000
[7,8-DHF] (nM)

Figure S3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B
C
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2
4
6
8
10
Fecal TG (µmol/g)
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5
10
15
Fecal cholesterol (ng/mg)
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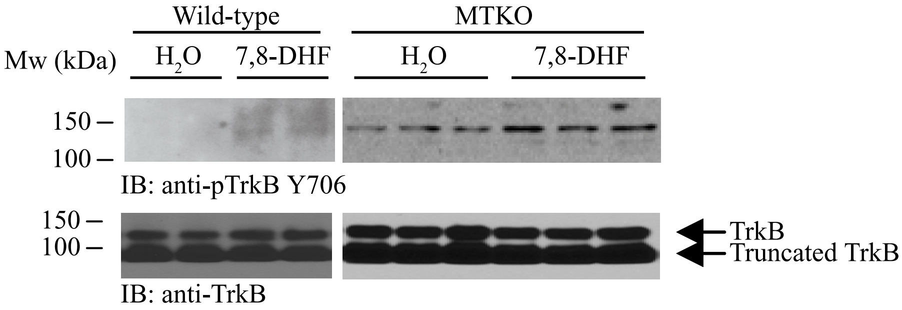
5
10
15
20
H_2O
7,8-DHF

Figure S4


Wild-type
MTKO
Mw (kDa)
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7,8-DHF
H_2O
7,8-DHF
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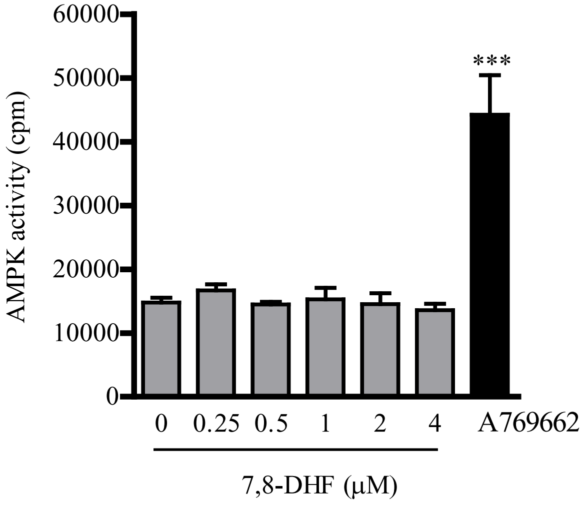
100
IB: anti-pTrkB Y706
150
100
IB: anti-TrkB
TrkB
Truncated TrkB

Figure S5


AMPK activity (cpm)
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40000
30000
20000
10000
0
***
0
0.25
0.5
1
2
4
A769662
7,8-DHF (μM)