

Supplemental Table 1.

Hepatic expression of 1wk and 18wks aLivPPAR γ kd mice fed a chow-diet (A) and 14 wk aLivPPAR γ kd mice fed a LF or HF-diet (B).

Selected genes of the metabolic pathways involved in the control of hepatic TAG levels: FA acid oxidation, TAG hydrolysis, VLDL synthesis, de novo lipogenesis and TAG synthesis were measured by qPCR. Peroxisome proliferator-activated receptor α (PPAR α), acyl-CoA synthetase long-chain family member 1 (Acsl1), carnitine palmitoyltransferase 1 α (Cpt1 α), hepatic nuclear factor 4 α (Hnf4 α), PPAR γ co-activator 1 α ; (Pgc1 α), Cyp4a10, adipose triglyceride lipase (Atgl), hormone-sensitive lipase (Hsl), monoacylglycerol lipase (MglI), apolipoprotein B (ApoB), microsomal triglyceride transfer protein (Mttp), sterol response element binding protein 1c (Srebp1c), acetyl-CoA carboxilase 1 (Acc1), fatty acid synthase (Fasn), fatty acid elongase (Elovl6), stearoyl -CoA desaturase 1 (Scd1), hepatic lipase (HL), low density lipoprotein lipase receptor (Ldlr), very-low density lipoprotein receptor (Vldlr), lipoprotein related protein 1 (Lrp1), fatty acid translocase (Cd36), glycerol phosphate acyltransferase (Gpat1), monoacylglycerol acyltransferase 1 or 2 (Mogat1/2), diacylglycerol acyltransferase 1/2 (Dgat1/2). Values are shown as means of mRNA copy number adjusted by normalization factor \pm SEM. Normalization factors were determined based on the expression of three housekeeping genes (Cyclophilin A, β -actin and HPRT) by the use of geNorm software (1). n=4-6 mice/group.

2-way ANOVA followed by a Bonferroni's post-hoc analysis was performed to assess the effect of age, diet and aLivPPAR γ kd in the different groups. P-values of the effect of age (1A), diet (1B) and/or aLivPPAR γ kd (1A/B) on gene expression changes in the different groups are indicated in combination with asterisks indicating significance of fold changes in Table 1A= Change in C: 18wk C/1wk C; Change in Kd: 18wk Kd/1wk Kd; Change in 1wk: 1wk Kd/1wk C; Change in 18 wk:18wk Kd/1wk C and Table 1B= Change in C: HF C/LF C; Change in Kd: HF Kd/LF Kd; Change in LF: LF Kd/LF C; Change in HF: HF Kd/ HF C.

Fold change lower than 1 means down-regulation, shown with \downarrow when p-value is <0.05 ; and fold changes greater than 1 means upregulation, shown with \uparrow when p-value is <0.05 . *, p <0.05 ; **, p <0.01 ; ***, p <0.0001 . ns, p >0.05 .

It should be noted that 1 wk and 18 wks mice (Table 1A) were not littermates while LF and HF-fed mice were littermates. All controls were littermates of aLivPPAR γ kd mice.

Reference

1. **Vandesompele J, De Preter K, Pattyn F, Poppe B, Van Roy N, De Paepe A, Speleman F.** Accurate normalization of real-time quantitative RT-PCR data by geometric averaging of multiple internal control genes. *Genome Biol* 3: RESEARCH0034, 2002.

Supplemental Table 1B

LF 14 wk aLivPPAR γ kd					HF 14 wk aLivPPAR γ kd					Effect of Diet in gene expression				Effect of aLivPPAR γ kd in gene expression				
	Control		aLivPPAR γ kd		Control		aLivPPAR γ kd		p-value	Change in C	Change in Kd	p-value	Change in LF	Change in HF				
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	<0.0001	5.89	↑ ***	1.34	ns	<0.0001	0.09	ns	0.02	↓ ***
PPAR γ	181802.28	38964.06	158177.44	3555.60	1071381.43	110373.88	21266.01	2125.58										
FA oxidation	Control		aLivPPAR γ kd		Control		aLivPPAR γ kd		p-value	Change in C	Change in Kd	p-value	Change in LF	Change in HF				
PPAR α	171255.44	± 32079.40	207615.99	± 26710.40	209923.55	± 10179.21	216417.73	± 11120.68	0.3007	1.23	1.04	0.3486	1.21	1.03				
Acs1l	9978.53	± 1662.28	14247.65	± 2927.47	10164.22	± 1092.88	9935.71	± 705.48	0.2792	1.02	0.70	0.289	1.43	0.98				
Cpt1 α	475482.37	± 63141.60	554647.28	± 70529.14	629780.70	± 15515.54	561151.38	± 50605.05	0.1807	1.32	1.01	0.9275	1.17	0.89				
Hnf4 α	227737.24	± 9076.77	211321.93	± 20434.55	146544.77	± 5488.73	155932.67	± 7578.93	0.0001	0.64	↓ **	0.74	↓ *	0.7941	0.93	1.06		
Pgc1 α	5018.16	± 727.78	3847.50	± 391.72	3486.03	± 270.79	3837.91	± 56.37	0.3719	0.69	□	1.00		0.1036	0.77	1.10		
Cyp4a10	40766.56	± 9244.92	40281.65	± 7287.39	67839.11	± 1155.53	45725.48	± 2272.02	0.0163	1.66	↑ *	1.14	ns	0.0786	0.99	0.67	□	
TAG hydrolysis	Control		aLivPPAR γ kd		Control		aLivPPAR γ kd		p-value	Change in C	Change in Kd	p-value	Change in LF	Change in HF				
Atgl	33844.86	± 2345.99	26596.63	± 2048.51	27704.90	± 1086.83	23916.41	± 1476.67	0.0218	0.82	ns	0.90	ns	0.0059	0.79	↓ *	0.86	ns
Hsl	12376.39	± 1141.76	12359.86	± 252.73	12983.06	± 890.36	13209.61	± 838.68	0.4199	1.05	1.07	0.9064	1.00	1.02				
Mgl1	2637.07	± 368.51	2122.69	± 151.00	1674.39	± 95.82	2042.24	± 47.72	0.036	0.63	↓ *	0.96	ns	0.7494	0.80	1.22		
VLDL synthesis	Control		aLivPPAR γ kd		Control		aLivPPAR γ kd		p-value	Change in C	Change in Kd	p-value	Change in LF	Change in HF				
Apob	1584510.28	± 117227.09	1808800.78	± 89961.67	1749719.16	± 126744.39	2118832.62	± 45883.75	0.035	1.10	ns	1.17	ns	0.0118	1.14	ns	1.21	↑ *
Mttp	90297.88	± 7281.48	93074.76	± 5350.36	94692.81	± 6454.95	74411.78	± 4922.04	0.2597	1.05	0.80	0.1712	1.03	0.79				
de novo lipogenesis	Control		aLivPPAR γ kd		Control		aLivPPAR γ kd		p-value	Change in C	Change in Kd	p-value	Change in LF	Change in HF				
Srebp1c	33706.63	± 1870.28	30792.95	± 3431.32	46836.32	± 5539.74	53114.55	± 2202.37	<0.0001	1.39	↑ *	1.72	↑ ***	0.626	0.91	1.13		
Acc1	115177.71	± 27376.25	84017.22	± 14382.14	37102.66	± 2477.76	38547.08	± 2146.70	0.0025	0.32	↓ *	0.46	ns	0.3924	0.73	1.04		
Fasn	3999506.83	± 1383384.28	3839248.23	± 508344.08	1861680.18	± 202295.06	1865612.08	± 118863.95	0.0116	0.47	ns	0.49	ns	0.9128	0.96	1.00		
Elovl6	33138.12	± 8708.33	26855.07	± 3766.65	11272.81	± 2215.54	9748.98	± 1201.84	0.0026	0.34	↓ *	0.36	ns	0.4769	0.81	0.86		
Scd1	2609454.68	± 432975.41	2033378.84	± 62652.91	513802.13	± 97101.36	391618.35	± 47638.73	<0.0001	0.20	↓ ***	0.19	↓ ***	0.1646	0.78	0.76		
Lipid uptake	Control		aLivPPAR γ kd		Control		aLivPPAR γ kd		p-value	Change in C	Change in Kd	p-value	Change in LF	Change in HF				
Hl	63946.58	± 2758.29	70966.81	± 11239.20	41982.97	± 5973.80	53717.65	± 5776.60	0.0179	0.66	ns	0.76	ns	0.2253	1.11	1.28		
Ldlr	24820.28	± 1041.31	33125.06	± 1869.27	37480.72	± 8962.48	29382.24	± 2356.43	0.3992	1.51	0.89	0.9842	1.33	0.78				
Vldlr	2968.16	± 942.07	1506.11	± 561.13	13273.85	± 1752.96	3580.22	± 523.40	<0.0001	4.47	↑ ***	2.38	ns	<0.0001	0.51	ns	0.27	↓ ***
Lrp1	52927.95	± 10577.96	62613.83	± 5007.27	45596.14	± 3987.68	61784.81	± 3141.77	0.5491	0.86	0.99	0.0709	1.18	1.36				
Cd36	305433.09	± 57843.61	205183.61	± 11563.38	2051094.04	± 116361.95	987986.01	± 228687.01	<0.0001	6.72	↑ ***	4.82	↑ **	0.003	0.67	ns	0.48	↓ ***
TAG synthesis	Control		aLivPPAR γ kd		Control		aLivPPAR γ kd		p-value	Change in C	Change in Kd	p-value	Change in LF	Change in HF				
Gpat1	3707416.96	± 1296912.44	3666002.58	± 1247913.85	3577411.16	± 437574.20	2550055.16	± 49527.29	0.5401	0.96	0.70	0.5985	0.99	0.71				
Mogat1	130.38	± 56.53	37.09	± 5.14	2882.92	± 145.94	252.75	± 54.78	<0.0001	22.11	↑ ***	6.81	ns	<0.0001	0.28	ns	0.09	↓ ***
Mogat2	103930.18	± 4449.32	98215.41	± 3894.80	80556.64	± 3776.55	88021.04	± 3973.08	0.001	0.78	↓ **	0.90	ns	0.8354	0.95	1.09		
Dgat1	9895.17	± 517.84	9408.28	± 293.21	9359.86	± 537.43	9472.29	± 95.68	0.6041	0.95	1.01	0.6798	0.95	1.01				
Dgat2	49958.29	± 3405.42	47583.45	± 3365.34	60305.72	± 1856.79	67214.13	± 1830.30	<0.0001	1.21	↑ *	1.41	↑ ***	0.4362	0.95	1.11		

Supplemental Table 1B

LF 14 wk aLivPPAR γ kd					HF 14 wk aLivPPAR γ kd					Effect of Diet in gene expression				Effect of aLivPPAR γ kd in gene expression								
		Control		aLivPPAR γ kd		Control		aLivPPAR γ kd		p-value	Change in C		Change in Kd		p-value	Change in LF		Change in HF				
PPAR γ	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	<0.0001	5.89	↑	***	1.34	ns	<0.0001	0.09	ns	0.02	↓	***
		Control		aLivPPAR γ kd		Control		aLivPPAR γ kd														
FA oxidation	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	p-value	Change in C		Change in Kd		p-value	Change in LF		Change in HF			
PPAR α	171255.44	± 32079.40	207615.99	± 26710.40	209923.55	± 10179.21	216417.73	± 11120.68	0.3007	1.23		1.04		0.3486	1.21		1.03					
Acs1	9978.53	± 1662.28	14247.65	± 2927.47	10164.22	± 1092.88	9935.71	± 705.48	0.2792	1.02		0.70		0.289	1.43		0.98					
Cpt1 α	475482.37	± 63141.60	554647.28	± 70529.14	629780.70	± 15515.54	561151.38	± 50605.05	0.1807	1.32		1.01		0.9275	1.17		0.89					
Hnf4 α	227737.24	± 9076.77	211321.93	± 20434.55	146544.77	± 5488.73	155932.67	± 7578.93	0.0001	0.64	↓	**	0.74	↓	*	0.7941	0.93		1.06			
Pgc1 α	5018.16	± 727.78	3847.50	± 391.72	3486.03	± 270.79	3837.91	± 56.37	0.3719	0.69	□		1.00		0.1036	0.77		1.10				
Cyp4a10	40766.56	± 9244.92	40281.65	± 7287.39	67839.11	± 1155.53	45725.48	± 2272.02	0.0163	1.66	↑	*	1.14	ns	0.0786	0.99		0.67		□		
		Control		aLivPPAR γ kd		Control		aLivPPAR γ kd														
TAG hydrolysis	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	p-value	Change in C		Change in Kd		p-value	Change in LF		Change in HF			
Atgl	33844.86	± 2345.99	26596.63	± 2048.51	27704.90	± 1086.83	23916.41	± 1476.67	0.0218	0.82	ns	0.90		ns	0.0059	0.79	↓	*	0.86	ns		
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VLDL synthesis	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	p-value	Change in C		Change in Kd		p-value	Change in LF		Change in HF			
Apob	1584510.28	± 117227.09	1808800.78	± 89961.67	1749719.16	± 126744.39	2118832.62	± 45883.75	0.035	1.10	ns	1.17		ns	0.0118	1.14	ns	1.21	↑	*		
Mttp	90297.88	± 7281.48	93074.76	± 5350.36	94692.81	± 6454.95	74411.78	± 4922.04	0.2597	1.05		0.80		0.1712	1.03		0.79					
		Control		aLivPPAR γ kd		Control		aLivPPAR γ kd														
de novo lipogenesis	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	p-value	Change in C		Change in Kd		p-value	Change in LF		Change in HF			
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		Control		aLivPPAR γ kd		Control		aLivPPAR γ kd														
Lipid uptake	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	p-value	Change in C		Change in Kd		p-value	Change in LF		Change in HF			
HI	63946.58	± 2758.29	70966.81	± 11239.20	41982.97	± 5973.80	53717.65	± 5776.60	0.0179	0.66	ns	0.76		ns	0.2253	1.11		1.28				
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		Control		aLivPPAR γ kd		Control		aLivPPAR γ kd														
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Dgat2	49958.29	± 3405.42	47583.45	± 3365.34	60305.72	± 1856.79	67214.13	± 1830.30	<0.0001	1.21	↑	*	1.41	↑	***	0.4362	0.95		1.11			