Supplemental Table 1. Primer and probe sequences used for qPCR.

Gene	Sense	Antisense	Probe	Accession number
Aox	GCC ACG GAA CTC ATC TTC GA	CCA GGC CAC CAC TTA ATG GA	CCA CTG CCA CAT ATG ACC CCA AGA CCC	NM_015729
Elovl5	TGG CTG TTC TTC CAG ATT GGA	CCC TTT CTT GTT GTA AGT CTG AAT GTA	CAT GAT TTC CCT GAT TGC TCT CTT CAC AAA C	NM_134255.2
Elovl6	ACA CGT AGC GAC TCC GAA GAT	AGC GCA GAA AAC AGG AAA GAC T	TTT CCT GCA TCC ATT GGA TGG CTT C	NM_130450.2
Fads1	CCT TCG CGG ACA TTG TTT ACT C	TAT GGA GGT CTG CTG CTG CTA T	CTC TGG TTG GAC GCT TAC CTT CAC CA	NM_013402.3
Fads2	CCC TGA TCG ACA TTG TGA GTT C	GAC GGC AGC TTC ATT TAT GGA	CCA GCC ACA GCT CCC CAG ACT TCT	NM_019699.1
Fgf-21	CCG CAG TCC AGA AAG TCT CC	TGA CAC CCA GGA TTT GAA TGA C	CCT GGC TTC AAG GCT TTG AGC TCC A	NM_020013.4
G6pdh	GCA ACA GAT ACA AGA ATG TGA AGC T	AGG CTT CCC TGA GTT CAT CAC T	CCT ATG AAC GCC TCA TCC TGG ATG TCT T	NM_008062
Gyk	GGG TTG GTG TGT GGA GTC TTG	GAT TTC GCT TTC TTC AGC ATT GA	ACC GCT CCA TTG TGA CAG CTG ACA	NM_008194.3
Lcad	TAC GGC ACA AAA GAA CAG ATC G	CAG GCT CTG TCA TGG CTA TGG	CAC TTG CCC GCC GTC ATC TGG	NM_007381
Me1	AGG CAG CGT CTT CCA AAT ATG	TCG ATA CTT GTT CAG GAG ACG AA	TGG CAA AAT CTT CAA ACT GAA TAA GGC AAT TC	NM_008615.1
6Pdgh	GGA CAT CCG TAA GGC CCT CTA T	ATT GAG GGT CCA GCC AAA CTC	CTT TAT GCT GCT CAG ACA GGC AGC CAC	NM_025801
Taldo1	CAG AAG TTG ATG CAA GGC TTT C	CCA GCT TCT TTG TAA AGC TCG A	CTC GGG CCA CCA TGG CAT CC	NM_011528
Tkt	GCA TCC TGT CCC GAA ACA AG	CAA TAG ACT CGG TAG CTG GCT TT	CCC TGG CCC AGG GAG CCA GT	NM_009388

Aox, acyl-CoA oxidase; *Elovl*, fatty acid elongase; *Fads*, fatty acid desaturase; *Fgf-21*, fibroblast growth factor 21; *G6pdh*, glucose-6-phosphate dehydrogenase; *Gyk*, glycerol kinase; *Lcad*, long-chain acyl-CoA dehydrogenase; *Me*, malic enzyme; *Pdgh*, 6-phosphogluconate dehydrogenase; *Taldo*, transaldolase; *Tkt*, transketolase.

Supplemental Table 2. Hepatic gene expression levels.

	Srebp-1c $^{+/+}$ control	**Srebp-1c $^{+/+}$ fenofibrate**	**Srebp-1c $^{-/-}$ control**	**Srebp-1c $^{-/-}$ fenofibrate**
Fatty acid esterification				
Dgat1	1.0±0.1	2.4±0.1*	1.0±0.0	1.3±0.1
Dgat2	1.0±0.0	0.8±0.0	1.0±0.0	0.6±0.0*
Gpat	1.0±0.0	1.8±0.0*	1.0±0.0	1.2±0.1
PPP/NADPH synthesis				
G6pdh	1.0±0.1	2.0±0.5	1.0±0.2	0.7±0.1
6Pdgh	1.0±0.1	3.2±0.2*	1.0±0.0	1.5±0.2*
Taldo1	1.0±0.1	1.5±0.1*	1.0±0.1	1.1±0.0
Me1	1.0±0.1	6.0±0.4*	1.0±0.1	2.8±0.3*
	Chrebp $^{+}/_{+}$ control	**Chrebp $^{+}/_{+}$ fenofibrate**	**Chrebp $^{-}/_{-}$ control**	**Chrebp $^{-}/_{-}$ fenofibrate**
Fatty acid esterification				
Dgat1	1.0±0.1	2.6±0.3*	1.0±0.0	3.0±0.1*
Dgat2	1.0±0.1	0.6±0.1*	1.0±0.0	0.8±0.0
Gpat	1.0±0.1	1.3±0.1	1.0±0.0	2.0±0.1*
PPP/NADPH synthesis				
G6pdh	1.0±0.1	0.9±0.2	1.0±0.1	1.2±0.1
6Pdgh	1.0±0.0	2.4±0.3*	1.0±0.1	3.3±0.3*
Taldo1	1.0±0.1	1.8±0.3*	1.0±0.1	1.8±0.3*
Me1	1.0±0.1	4.9±0.4*	1.0±0.1	10.8±1.2*

Expression levels were normalized to 18S expression. Values of untreated mice of each genotype were set to 1. Values are given as means ± SEM for n=4; * $p<0.05$ fenofibrate vs. control (Mann-Whitney U-test). *Dgat*, diacylglycerol acyltransferase; *Gpat*, glycerol-3-phosphate acyltransferase; *G6pdh*, glucose-6-phosphate dehydrogenase; *6Pdgh*, 6-phosphogluconate dehydrogenase; *Taldo*, transaldolase; *Me*, malic enzyme.

Supplemental Table 3. Hepatic gene expression levels.

	Control	**Fenofibrate**
Lxrα	1.0±0.0	0.9±0.1
Abca1	1.0±0.2	1.1±0.1
Abcg5	1.0±0.2	0.8±0.2
Abcg1	1.0±0.2	0.9±0.1

Values are given as means ± SEM for *n*=6. *Lxrα*, Liver X Receptor α; *Abca1/g1/g5*, ATP binding cassette a1/g1/g5.

Supplemental Table 4. Blood glucose concentrations and primary isotopic parameters.

	Control	**Fenofibrate**
Blood glucose (mM)	8.2±0.2	8.5±0.6
Isotope dilution		
d(glc)	0.018±0.001	0.018±0.002
d(UDPglc)	0.196±0.010	0.166±0.009*
Isotope exchange		
c(glc)	0.176±0.011	0.079±0.005*
c(UDPglc)	0.137±0.008	0.157±0.008
MIDA analysis		
f(glc)	0.55±0.02	0.59±0.02
f(UDPglc)	0.46±0.02	0.53±0.01*

Values are given as means ± SEM for n=5-6; * p<0.05 fenofibrate *vs.* control (Mann-Whitney U-test). d(glc), fractional contribution of infused glucose to blood glucose; d(UDPglc), fractional contribution of infused galactose to uridine diphosphate-glucose; c(glc), fractional contribution of blood glucose to UDP-glucose formation; c(UDPglc), fractional contribution of UDPglucose to blood glucose formation; MIDA, mass isotopomer distribution analysis; f(glc), fractional contribution of newly synthesized glucose to blood glucose; f(UDPglc), fractional contribution of newly synthesized glucose to UDPglc pool.

Supplemental Figure 1

Schematic model of hepatic carbohydrate metabolism. Major metabolic pathways and enzymatic reactions are depicted, sharing glucose-6-phosphate (G6P) as a central metabolite. The pathways included are: (1) Gluconeogenic flux toward G6P, (2) Glycogen phosphorylase flux, (3) Glucose-6-phosphatase flux, (4) Glucokinase flux and (5) Glycogen synthase flux. Mice received an infusion containing [U-^{13}C]glucose, [2-^{13}C]glycerol, [1-^{2}H]galactose and paracetamol for six hours. Mass isotopomer distribution analysis (MIDA) was applied on blood glucose and urinary paracetamol glucuronide samples.