Supporting Information

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Fig. S1. Adipocytes express peroxisome proliferator-activated receptor delta (PPARô). Immunohistochemical (*Left*) and immunofluorescent (*Right*) staining for PPARô in adipose tissue.



Fig. S2. Effect of KD3010 on Kupffer cells. (*A*) The morphology of cultured Kupffer cells treated with KD3010 for 1 d did not change compared with DMSOincubated cells. (*B*) LPS-stimulated expression of M1 markers (*TNF* α , *IL*-6, and *IL*-1 β) and IL-4–induced expression of M2 makers, arginase1 and macrophage galactose-type Ic-type lectin 1 (*MgI-1*) in Kupffer cells cultured with KD3010 was analyzed by quantitative PCR and normalized to 18S.



Fig. S3. Effect of KD3010 on hepatic stellate cells. (A) Images of cultured hepatic stellate cells treated with KD3010 or DMSO for 3 d are shown. (B) The expression of fibrosis associated genes [α -smooth muscle actin (α SMA), collagen α 1(l), and tissue inhibitor of matrix metalloproteinases (*TIMP-1*)], proliferation marker (*cyclin D1*), and hepatocyte growth factor (*HGF*) in hepatic stellate cells incubated with KD3010 was analyzed by qPCR and normalized to 18S. Results shown are the mean of four independent experiments. *P < 0.05.



Fig. 54. PPAR& agonists induced gene-expression patterns. (*A*) Hepatocytes were isolated and cultured in Waymouth's medium for 12 h in the presence of DMSO, KD3010 (5 μ M), or GW501516 (100 nM). Clustergram of genes whose expression pattern is altered by PPAR& agonist treatment. Gene expression was normalized to DMSO in each group, data imported into the cluster, and the genes were subjected to hierarchical clustering. Red indicates induction relative to DMSO treatment, green indicates repression, and black indicates no change. (*B* and C) Venn diagrams comparing GW501516 and KD3010 target genes identified in microarray analysis of hepatocytes (*n* = 3). The selection criteria used a *P* < 0.05 on Bonferroni's multiple comparison test. (*D*) Hepatic gene expression for connective tissue growth factor (*CTGF*) was assessed by quantitative PCR in mice subjected to oil (*n* = 4) and CCl₄ treatment (*n* = 7–12) for a total of 12 injections and gavaged daily with vehicle, KD3010, or GW501516. **P* < 0.05.



Fig. S5. Structure of KD3010.

Table S1. Up-regulated genes in cultured hepatocytes incubated with GW501516

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	Gene symbol	Control (DMSO) signal	GW501616 signal	Fold change	Gene annotation
1	Pdk4	631	3110	4.93	Pyruvate dehydrogenase kinase, isoenzyme 4 (Pdk4), mRNA
2	Adfp	1721	5410	3.14	Adipose differentiation related protein (Adfp), mRNA
3	Creb3l3	706	2129	3.02	cAMP responsive element binding protein 3-like 3 (Creb3l3), mRNA
4	2310016C08Rik	2264	5712	2.52	RIKEN cDNA 2310016C08 gene (2310016C08Rik), mRNA
5	Hmgcs2	1685	3529	2.09	3-Hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (Hmgcs2), nuclear gene encoding mitochondrial protein, mRNA
6	Aadacl1	1008	2080	2.06	Arylacetamide deacetylase-like 1 (Aadacl1), mRNA
7	Ehhadh	393	669	1.70	Enoyl-Coenzyme A, hydratase/3-hydroxyacyl Coenzyme A dehydrogenase (Ehhadh), mRNA
8	Cpt2	1399	2290	1.64	Carnitine palmitoyltransferase 2 (Cpt2), mRNA
9	Acaa1b	4060	6543	1.61	Acetyl-Coenzyme A acyltransferase 1B (Acaa1b), mRNA
11	E130016E03Rik	454	713	1.57	RIKEN cDNA E130016E03 gene (E130016E03Rik), mRNA
12	Ctgf	12460	18879	1.52	Connective tissue growth factor (Ctgf), mRNA
13	Gm2a	1594	2412	1.51	GM2 ganglioside activator protein (Gm2a), mRNA

Comparative DNA microarray data of hepatocytes cultured with DMSO or GW501516 (100nM), showing the top 13 genes whose expression were upregulated in hepatocytes cultured with GW501516 compared with control.

Table S2. Up-regulated genes in cultured hepatocytes incubated with KD3010

	Gene symbol	Control (DMSO) signal	KD3010 signal	Fold change	Gene annotation
1	Adfp	1721	6577	3.82	Adipose differentiation related protein (Adfp), mRNA
2	Creb3l3	706	2215	3.14	cAMP responsive element binding protein 3-like 3 (Creb3l3), mRNA
3	2310016C08Rik	2264	6431	2.84	RIKEN cDNA 2310016C08 gene (2310016C08Rik), mRNA
4	Pdk4	631	1732	2.74	Pyruvate dehydrogenase kinase, isoenzyme 4 (Pdk4), mRNA
5	E130016E03Rik	454	934	2.06	RIKEN cDNA E130016E03 gene (E130016E03Rik), mRNA
6	Aadacl1	1008	1925	1.91	Arylacetamide deacetylase-like 1 (Aadacl1), mRNA
7	Adora2b	1136	2026	1.78	Adenosine A2b receptor (Adora2b), mRNA
8	4632417N05Rik	1212	2026	1.67	RIKEN cDNA 4632417N05 gene (4632417N05Rik), mRNA
9	Cpt2	1399	2270	1.62	Carnitine palmitoyltransferase 2 (Cpt2), mRNA
10	Hist1h1c	2231	3540	1.59	Histone cluster 1, H1c (Hist1h1c), mRNA
11	Nol5a	1803	2827	1.57	Nucleolar protein 5A (Nol5a), mRNA
12	Fcgrt	1245	1946	1.56	Fc receptor, IgG, alpha chain transporter (Fcgrt), mRNA
13	Vim	975	1523	1.56	Vimentin (Vim), mRNA

Comparative DNA microarray data of hepatocytes cultured with DMSO or KD3010 (5µM), showing the top 13 genes whose expression were up-regulated in hepatocytes cultured with KD3010 compared with control.