Gadd45β is an inducible coactivator of transcription that facilitates rapid liver growth in mice

Jianmin Tian, Haiyan Huang, Barbara Hoffman, Daniel Liebermann, Giovanna Ledda-Columbano, Amedeo Columbano, and Joseph Locker

Supplemental Data

Table S1. Profile of altered expression of liver genes in the Gadd45β-null mouse

N	Probe[1]	Unigene	Symbol	Gene	Function	Ratio[2]	TCPOBOP effect[3]
1	M200013880	Mm.42101	Cyp2c39	Cytochrome P450 2c39	Detoxification	**6.5**	–
2	M300007093	Mm.103665	Slco1a1	Solute carrier organic anion transporter family, member 1a1	Transport	**6.9**	–
3	M300020438 M300020605	Mm.741	Fabp5	Fatty acid binding protein 5, epidermal	Lipid metabolism	**5.8**	–
4	M200001797	Mm.4533	Apoa4	Apolipoprotein A-IV	Serum protein; Lipid metabolism	**4.6**	↑↑
5	M300010447	Mm.1491	Fxyd1	FXYD domain-containing ion transport regulator 1	Transport	**4.0**	–
6	M200002386	Mm.6562	Sult5a1	Sulfotransferase family 5A, member 1	Detoxification	**4.0**	↑
7	M300000564	Mm.230249	Ctse	Cathepsin E	Protein catabolism	**3.5**	–
8	M200002163	Mm.5121	Pam	Peptidylglycine α-amidating monooxygenase	Protein modification	**3.4**	–
9	M300008067	Mm.49611	Mpzl3	Myelin protein zero-like 3	Cell membrane	**2.9**	↑
10	M200000822	Mm.2161	Apom	Apolipoprotein M	Lipid metabolism	**2.9**	–
11	M200005828	Mm.28088	Mvk	Mevalonate kinase	Sterol synthesis	**2.9**	–
12	M300005862	Mm.34242	Pmvk	Phosphomevalonate kinase	Sterol synthesis	**2.8**	–
13	M200005433	Mm.27136	Insig2	Insulin induced gene 2	Sterol metabolism	**2.7**	↑↑↑
14	M200007778	Mm.35605	Cdh1	Cadherin 1	Cell adhesion	**2.6**	–
15	M300011464 M300011465 M300021731	Mm.469917	Tubb2a	Tubulin β2a	Cytoskeleton	**2.5**	–
16	M200000279	Mm.788	Ly6e	Lymphocyte antigen 6 complex, locus E	Cell surface; Signal transduction	**2.3**	–
17	M200006403	Mm.29254	Igfbp3	Insulin-like growth factor binding protein 3	Regulation of cell growth; Apoptosis	**2.3**	–
18	M300009371 M300020143	Mm.38002	Rarres1	Retinoic acid receptor responder (tazarotene induced) 1	Membrane protein	**2.3**	↑↑↑
19	M300021915	Mm.319660	Hmgn2	High mobility group nucleosomal binding domain 2	Transcriptional coregulator	**2.2**	–
20	M300020421	Mm.102312	Cyp2g1	Cytochrome P450 2g1	Detoxification	**2.2**	–
21	M300001129 M300009512 M300013500	Mm.34102	Odc1	Ornithine decarboxylase, structural 1	Polyamine biosynthesis; Amino acid metabolism	**2.2**	–
22	M300003868 M300010092	Mm.261984	Glo1	Glyoxalase 1	Detoxification; carbohydrate metabolism	**2.2**	–
23	M300012822	Mm.27955	Wbscr1	Williams-Beuren syndrome chromosome region 1 homolog	Protein synthesis	**2.1**	↑
24	M200006651	Mm.29778	Armet	Arginine-rich, mutated in early stage tumors	Unknown	**2.1**	↑↑
25	M300018787 M300018788	Mm.21965	Stbd1	Starch binding domain 1	Carbohydrate metabolism	**2.1**	↑↑
26	M300021114	Mm.332336	Mrfap1	Morf4 family associated protein 1	Unknown	**2.1**	–
27	M300006584	Mm.160362	Ugt2b37	UDP glucuronosyltransferase 2 family, polypeptide B37	Detoxification	**2.1**	–
28	M300020770	Mm.24724	Ppp1rc3	Protein phosphatase 1, regulatory (inhibitor) subunit 3C	Signal transduction	**2.1**	↓
29	M300001030	Mm.458125	Ube2g2	Ubiquitin-conjugating enzyme E2G 2	Protein catabolism	**2.0**	–
30	M200002749	Mm.276466	Hsd17b2	Hydroxysteroid (17β) dehydrogenase 2	Sterol metabolism	**2.1**	–
31	M200008682	Mm.273251	Sdh1	Sorbitol dehydrogenase 1	Carbohydrate metabolism	**0.5**	–
32	M300002385	Mm.356689	Acox1	Acyl-Coenzyme A oxidase 1, palmitoyl	Lipid metabolism	**0.5**	–
33	M200005441	Mm.27154	Vnn1	Vanin 1	Detoxification	**0.5**	↑
34	M300011992	Mm.4065	Fam102A	Family with sequence similarity 102, member A	Unknown	**0.5**	–
35	M200005141	Mm.25549	Zc3h14	Zinc finger CCCH type containing 14	mRNA processing	**0.5**	–
36	M300007817	Mm.4676	Slc7a2	Solute carrier family 7 member 2	Transport	**0.5**	–
37	M300003246	Mm.212789	Ppara	Peroxisome proliferator activated receptor α	Transcription factor	**0.5**	–
38	M300000210	Mm.112	Tcea3	Transcription elongation factor A (SII) 3	Transcription	**0.5**	↓↓
39	M300021668	Mm.16898	Phgdh	3-phosphoglycerate dehydrogenase	Carbohydrate metabolism	**0.4**	–
40	M300001672	Mm.260627	Dhx40	DEAH (Asp-Glu-Ala-His) box polypeptide 40	RNA processing	**0.4**	–
41	M300001060	Mm.3283	G0s2	G0/G1 switch gene 2	Cell cycle	**0.4**	–
42	M300008442	Mm.290578	Alas1	Aminolevulinic acid synthase 1	Iron metabolism	**0.4**	↑
43	M300008204 M300008205	Mm.197422	Gsta2	Glutathione S-transferase, alpha 2 (Yc2)	Detoxification	**0.4**	–
44	M300008991	Mm.299916	Pcsk4	Proprotein convertase subtilisin/kexin type 4	Protein processing	**0.4**	↓↓
45	M300006180	Mm.25181	Zcchc11	Zinc finger, CCHC domain containing 11	Signal transduction	**0.3**	–
46	M300011856	Mm.335309	Gsta1	Glutathione S-transferase, α1 (Ya)	Detoxification	**0.3**	–
47	M300004296	Mm.329814	Lipl3	Lipase-like ab-hydrolase domain containing 3	Lipid metabolism	**0.3**	–
48	M200008142	Mm.296022	Mme	Membrane metallo endopeptidase	Protein catabolism	**0.3**	–
49	M200003652 M300000348 M300000349	Mm.18628	Cd36	CD36 antigen	Lipid metabolism	**0.3**	–
50	M300007885	Mm.192991	Mt1	Metallothionein 1	Detoxification	**0.3**	↓
51	M200009417	Mm.147226	Mt2	Metallothionein 2	Detoxification	**0.2**	↓
52	M300002172	Mm.6856	Pttg1	Pituitary tumor-transforming 1	Cell cycle	**0.2**	–
53	M300018596	Mm.329462	Gm4841	Predicted gene 4841 (Gm4841)	Stress/damage response	**0.2**	↓↓
54	M200000532	Mm.1360	Gadd45b	Growth arrest and DNA-damage-inducible 45β	Transcriptional coactivator; Stress/damage response	**-**	↑↑↑

[1] Operon oligonucleotide accession number.

[2] Ratio of expression in untreated Gadd45β-null to untreated C57Bl/6 mouse liver. Average of two microarrays.

[3] Comparison to data in Tables S2 and S3.

Table S2. Genes upregulated by TCPOBOP treatment

N	Probe[1]	Unigene	Symbol	Gene	Function	Baseline[2]	Max[3]	Confirm[4]	WT[5]			Gadd45β-null[6]			
									3 hr	6 hr	12 hr	3 hr	6 hr	12 hr	-
1	M200009401	Mm.142581	Cyp2c55	Cytochrome P450 2c55	Detoxification	0.4	52.8		**2.1**	**12.0**	**52.8**	1.5	**6.2**	**22.1**	0.8
2	M200003009	Mm.272632	Xlkd1	Extracellular link domain-containing 1	Transport; Hyaluronic acid binding	0.5	16.2		**6.4**	**16.2**	-	**8.3**	**12.6**	**20.6**	1.3
3	M300007265 M300007266	Mm.218749	Cyp2b10	Cytochrome P450 2b10	Detoxification	3.0	14.0	M, P	**9.5**	**15.1**	**9.9**	**6.1**	**11.0**	**28.1**	1.1
4	M300012751 M300012791	Mm.294678	Cyp2b13	Cytochrome P450 2b13	Detoxification	0.6	12.2		**7.5**	**12.2**	**2.0**	**5.4**	**10.4**	**4.5**	0.9
5	M200002065	Mm.262106	Itgam	Integrin αM	Cell adhesion	0.2	10.9		**3.2**	**10.9**	-	**2.3**	**11.4**	**7.6**	0.7
6	M300006850 M300006851	Mm.70371	Akr1b7	Aldo-keto reductase family 1B7	Detoxification	0.4	12.3	M	**2.0**	**5.4**	**12.3**	1.1	**3.0**	**9.5**	1.1
7	M200005433	Mm.27136	Insig2	Insulin induced gene 2	Sterol metabolism	1.3	9.8	N	**3.1**	**6.5**	**9.7**	**2.2**	**2.5**	**4.1**	3.0
8	M200000532	Mm.1360	Gadd45b	Growth arrest and DNA-damage-inducible 45β	Transcriptional coactivator; Stress/damage response	0.4	6.6	M, P, N	**4.5**	**6.6**	**4.2**	-	-	-	-
9	M200007081	Mm.31325	Gdf15	Growth differentiation factor 15	Signal transduction: Growth factor	1.1	6.2		**3.4**	**6.2**	**5.4**	**3.7**	**4.4**	**3.9**	1.0
10	M300019560	Mm.83037	Insc	Inscuteable homolog (Drosophila)	Cell cycle; Cytoskeleton	0.4	6.6		**3.2**	**5.0**	**6.6**	**3.0**	**3.8**	**3.4**	1.3
11	M300012787	Mm.14413	Cyp2b9	Cytochrome P450 2b9	Detoxification	7.7	4.4		**4.1**	**2.4**	**4.4**	**4.7**	**1.3**	**0.9**	0.9
12	M200008547	Mm.103581	Slc23a2	Solute carrier family 23 member 2	Transport	0.6	3.4		**2.9**	**5.2**	**6.2**	**2.2**	**3.4**	**4.2**	0.8
13	M200004544	Mm.282978	2010003K11Rik	2010003K11Rik	Unknown	0.7	9.7		**2.5**	**1.4**	**9.7**	**3.0**	**4.0**	**7.1**	**0.5**
14	M200004688	Mm.23780	1810055G02Rik	Aldo-keto reductase	Detoxification	0.8	7.5		**3.6**	**2.4**	**7.5**	**3.9**	**5.4**	**4.7**	0.8
15	M200003934	Mm.20764	Cyp2c29	Cytochrome P450 2c29	Detoxification	12.1	6.1		**2.5**	**6.1**	**3.4**	1.3	**3.1**	**5.6**	1.4
16	M200004351	Mm.313181	Gna14	Guanine nucleotide binding protein α14	Signal transduction	0.3	6.2		**2.9**	**4.5**	**3.9**	0.9	**2.5**	**2.7**	1.6
17	M300006480	Mm.6250	Prom1	Prominin 1	Membrane protein	0.4	7.4		**1.3**	**2.4**	**7.4**	0.8	**0.9**	**3.5**	1.3
18	M200005479 M300006735	Mm.27250	Mad1l1	Mitotic arrest deficient 1-like 1	Cell cycle	0.4	3.9	M	**3.1**	**3.8**	**3.9**	**3.7**	**3.5**	**7.1**	1.2
19	M300011396	Mm.4079	Vps37b	Vacuolar protein sorting 37B	Vesicular transport	0.5	4.6		**2.0**	**4.3**	**4.6**	1.7	**2.7**	**1.9**	1.2
20	M300005831	Mm.347436	Gstm3	Glutathione S-transferase µ3	Detoxification	3.0	8.2		**0.9**	**1.3**	**8.1**	0.6	**1.2**	**7.3**	1.0
21	M300009540	Mm.148342	Dio1	Deiodinase iodothyronine type I	Detoxification	2.8	5.8		**2.3**	**2.1**	**5.7**	**1.7**	**1.5**	**1.9**	1.6
22	M300017614	Mm.65181	1700024P16Rik	1700024P16Rik	Unknown	0.3	5.1		**1.7**	**5.1**	**3.3**	1.6	**3.5**	**2.2**	0.9
23	M200012975 M300011391 M300011482	Mm.213128	Pik3cb	Phosphatidylinositol 3-kinase catalytic β	Signal transduction	0.5	3.0	M	**2.6**	**4.4**	**2.9**	1.6	**3.4**	**3.0**	0.753
24	M300009371 M300020143	Mm.38002	Rarres1	Retinoic acid receptor responder 1	Membrane protein	1.0	6.1	M	**1.9**	**1.8**	**6.1**	**2.3**	**1.7**	**2.9**	**2.5**
25	M200012066	Mm.261842	4931406C07Rik	Ester hydrolase C11orf54 homolog	Detoxification; lipid metabolism	4.2	5.8		**2.0**	**2.0**	**5.8**	1.9	**3.1**	**4.1**	0.6
26	M200000453	Mm.1236	Gadd45a	Growth arrest and DNA-damage-inducible 45α	Transcriptional coactivator; Stress/damage response	0.5	4.4	P	**3.0**	**2.6**	**4.1**	**3.9**	**4.3**	**5.4**	0.7
27	M300006512 M300006513	Mm.24684	Fosl2	Fos-like antigen 2	Transcription factor	0.6	6.0	M, P	**1.7**	**1.8**	**6.0**	0.7	**2.1**	**2.7**	1.2
28	M200000925	Mm.2444	Myc	Myelocytomatosis oncogene	Transcription factor; Cell cycle	0.3	3.2	P	**2.8**	**3.0**	**3.4**	**2.0**	**2.6**	**2.2**	1.0
29	M200009831 M300013801	Mm.155620	Pla2g6	Phospholipase A2 group VI	Signal transduction	0.4	4.4	M	1.9	**2.7**	**4.4**	1.6	**2.5**	**4.6**	1.0
30	M200000873	Mm.2312	Tnfaip8l1	Tumor necrosis factor α-induced protein 8-like 1	Signal transduction?	0.8	4.6		1.9	**2.6**	**4.6**	1.4	**2.5**	**2.8**	1.1
31	M200001695	Mm.255332	Tnfaip2	Tumor necrosis factor α-induced protein 2	Secreted protein	1.0	2.9		1.7	**2.9**	**4.3**	1.2	**1.5**	**1.2**	1.2
32	M300008363	Mm.23782	Glt25d2	Glycosyltransferase 25 domain containing 2	Protein modification	0.2	2.9		1.3	**2.9**	**4.7**	**3.3**	**1.9**	**3.3**	1.1
33	M300016594	Mm.3741	Plekha7	Pleckstrin homology domain containing family A member 7	Unknown	0.3	4.5		**2.1**	**2.2**	**4.5**	1.5	**2.1**	**1.4**	1.4
34	M200001797	Mm.4533	Apoa4	Apolipoprotein A-IV	Sterol metabolism; Serum protein	3.2	3.7		1.6	**3.7**	**3.3**	1.7	**2.1**	**2.8**	**4.3**
35	M200000354	Mm.10628	Setd4	SET domain containing 4	Transcriptional coregulator?	0.7	3.0	P	**2.6**	**4.0**	**2.0**	1.5	**2.3**	**2.0**	0.6
36	M200007345	Mm.335370	Ssb4	SPRY domain-containing SOCS box 4	Signal transduction	0.3	5.0		1.5	**2.0**	**5.0**	1.5	1.6	**2.5**	1.3
37	M300008454 M300022008	Mm.42100	Cyp2c38	Cytochrome P450 2c38	Detoxification	4.0	2.6	M	**2.8**	**2.4**	**3.2**	0.7	**2.2**	**2.1**	1.2
38	M200005849	Mm.28130	Pctk3	PCTAIRE-motif protein kinase 3	Signal transduction; Vitamin metabolism	0.7	3.4		**2.4**	**3.4**	**2.6**	**4.1**	**4.7**	**2.1**	0.7
39	M200007964 M300013643	Mm.271824	Ikbke	Inhibitor of κB kinase ε	Transcriptional corepressor	0.4	4.3	M	1.6	**2.4**	**4.3**	1.4	1.8	**2.7**	1.2
40	M300003757 M300003758	Mm.236068	Synj2	Synaptojanin 2	Signal transduction	0.3	3.9	M	1.9	**3.9**	**2.5**	**3.9**	**3.5**	**4.3**	0.9

Table 2 continued

	Probe[1]	Unigene	Symbol	Gene	Function	Baseline[2]	Max[3]	Confirm[4]	WT[5]			Gadd45β-null[6]			
									3 hr	6 hr	12 hr	3 hr	6 hr	12 hr	-
41	M300007953 M300007960	Mm.212983	Ces6	Carboxylesterase 6	Detoxification; Lipid metabolism	1.7	3.2	M	2.1	**3.2**	**2.4**	**1.1**	**3.2**	**3.5**	1.4
42	M300004159	Mm.34281	Mal2	T-cell differentiation protein 2	Transport	0.8	3.5		**2.1**	**3.5**	**2.4**	**2.2**	**2.6**	**3.4**	1.1
43	M300013667 M300013595	Mm.379575	Cyp2c54	Cytochrome P450 2c54	Detoxification	18.4	4.3	M	1.9	**1.8**	**4.3**	**0.9**	**2.0**	**3.5**	0.9
44	M300007634 M300018833	Mm.214504	Timm8a	Translocase of inner mitochondrial membrane 8a	Mitochondrial transport	1.3		M	1.8	**2.3**	**3.9**	**2.0**	**2.3**	**3.7**	0.9
45	M300013594 M300013596	Mm.38963	Cyp2c50	Cytochrome P450 2c37	Detoxification	17.8	4.4	M	1.8	**1.6**	**4.4**	**0.9**	**1.9**	**2.5**	0.9
46	M300018270	Mm.385009	Spryd3	SPRY domain containing 3	Signal transduction: Receptor	0.4	4.3		1.5	1.9	**4.3**	0.6	1.0	1.1	1.8
47	M200005103	Mm.5731	Gstt3	Glutathione S-transferase θ3	Detoxification	3.5	4.0		1.7	**2.1**	**4.0**	1.5	**2.1**	**3.4**	1.0
48	M300012114	Mm.235175	Picalm	Phosphatidylinositol binding clathrin assembly protein	Vesicular transport	1.1	4.4		1.5	**4.4**	**1.9**	1.1	**2.3**	1.7	0.8
49	M200014547	Mm.46561	Lect1	Leukocyte cell derived chemotaxin 1	Signal transduction; Secreted protein	0.4	2.8		1.8	**2.8**	**3.0**	**2.2**	**2.6**	1.2	1.5
50	M300019596	Mm.275071	Jun	Jun oncogene	Transcription factor	0.6	3.3	P	**3.3**	**2.9**	1.5	**2.2**	**2.3**	**3.0**	0.6
51	M200013352	Mm.215122	Caskin2	Cask-interacting protein 2	Unknown	0.6	3.2		1.9	**2.6**	**3.2**	1.4	**2.6**	1.2	0.8
52	M300022178 M300022179	Mm.332152	Pusl1	Pseudouridylate synthase-like 1	Protein synthesis; tRNA synthesis	0.4	3.7	M	1.7	**2.3**	**3.7**	**1.6**	**2.5**	**1.5**	0.9
53	M200013731	Mm.335252	Dapk2	Death-associated kinase 2	Apoptosis	0.5	3.2		1.7	**3.3**	**2.6**	1.2	**2.1**	1.7	1.1
54	M300007005 M300007006	Mm.227912	Itpr1	Inositol 1 4 5-triphosphate receptor 1	Signal transduction	0.8	2.8	M	1.8	**3.2**	**2.5**	**1.6**	**2.0**	**1.6**	0.9
55	M300011526 M300011527 M300019387	Mm.286753	Rgs3	Regulator of G-protein signaling 3s	Signal transduction	0.6	4.4	M	**2.6**	**2.6**	**2.3**	1.3	**2.4**	0.8	1.3
56	M300001668	Mm.274370	Shroom1	Shroom family member 1	Cytoskeleton	1.3	3.5		1.8	**2.1**	**3.5**	1.2	1.9	**2.3**	0.9
57	M300013609	Mm.27120	Sestd1	SEC14 and spectrin domains 1	Unknown	1.3	3.3		1.8	**2.3**	**3.3**	**2.6**	**2.8**	**0.5**	1.0
58	M200003769	Mm.33716	BC013529	BC013529	Membrane protein	0.8	3.2		1.5	**2.8**	**3.2**	1.1	1.7	1.8	1.3
59	M300005480	Mm.196153	Rapgef4	Rap guanine nucleotide exchange factor (GEF) 4	Signal transduction	1.6	2.5		1.8	**2.5**	**3.1**	0.8	1.2	1.8	1.5
60	M300011752	Mm.261208	Nup205	Nucleoporin 205	Nuclear pore complex	0.4	3.7		1.5	**2.2**	**3.7**	0.7	1.4	**2.4**	0.9
61	M200001453	Mm.284891	Slc34a2	Solute carrier family 34 (sodium phosphate) member 2	Ion transport	0.3	3.1		1.5	**2.6**	**3.1**	1.4	1.7	**3.1**	1.1
62	M200004392	Mm.22455	Mrap	Melanocortin 2 receptor accessory protein	Signal transduction	1.4	3.8		1.5	**1.7**	**3.8**	**2.0**	1.1	1.7	1.3
63	M200004708 M300008259	Mm.172346	Tgfbr2	Transforming growth factor beta receptor II	Signal transduction: Receptor	0.4	2.8	M	1.6	**2.6**	**2.8**	**1.3**	**1.4**	**1.3**	1.1
64	M300004003	Mm.99400	Gm749	Gm749	Unknown	0.9	3.1		1.8	**2.1**	**3.0**	1.1	**2.3**	**3.3**	0.8
65	M200012027	Mm.292567	Creld2	Cysteine-rich with EGF-like domains 2	Secreted protein	0.7	3.4		1.5	**2.1**	**3.3**	0.8	1.0	1.9	1.9
66	M200001478	Mm.3863	Por	P450 (cytochrome) oxidoreductase	Detoxification	10.8	2.7	P	1.8	**2.6**	**2.5**	**3.6**	**3.4**	**4.9**	0.5
67	M200002258 M300018472	Mm.5540	Ttc39b	Tetratricopeptide repeat domain 39B	Unknown	0.5	3.0	M	1.4	**2.8**	**2.7**	**1.2**	**1.7**	**2.0**	0.9
68	M200001827	Mm.4593	Slc35b1	Solute carrier 35B1	Transport	0.8	3.4		1.9	1.6	**3.5**	1.1	1.3	1.6	1.7
69	M200004975 M300003910 M300010144	Mm.175403	Arl6ip2	ADP-ribosylation factor-like 6 interacting protein 2	Unknown	1.5	3.4	M	**1.8**	**3.4**	**1.7**	1.4	**1.4**	0.8	0.8
70	M300006589 M300006590	Mm.6824	Sult1d1	Sulfotransferase 1D1	Detoxification	2.2	3.5	M, P	1.8	**3.5**	**1.6**	**1.6**	**2.0**	**3.2**	0.6
71	M300007355	Mm.103319	Pde3b	Phosphodiesterase 3B cGMP-inhibited	Signal transduction	0.8	3.1	P	1.8	**2.9**	**2.2**	0.8	1.4	1.7	0.8
72	M200012889	Mm.26088	Tmem56	Transmembrane protein 56	Membrane protein	1.0	3.6		1.3	1.9	**3.6**	**0.2**	0.9	**0.5**	1.5
73	M300007971	Mm.46749	Slc7a6	Solute carrier family 7 member 6	Amino acid transport	0.4	2.5		2.0	**2.4**	**2.5**	1.1	**2.3**	**2.9**	1.4
74	M200004483	Mm.22701	Gas1	Growth arrest specific 1	Cell cycle arrest	1.3	3.9		1.3	1.6	**3.9**	1.1	**2.2**	**2.0**	0.7
75	M300019635	Mm.202653	Slc25a47	Solute carrier family 25, member 47	Mitochondrial transport	9.9	2.4		2.4	**2.0**	**2.4**	**7.7**	**4.2**	**4.0**	0.7
76	M200001752	Mm.341377	Ahr	Aryl-hydrocarbon receptor	Transcription factor; Detoxification	0.8	2.0		2.0	**2.0**	**2.7**	1.9	1.5	**2.5**	0.9
77	M200015880	Mm.258545	Fam114a1	Family with sequence similarity 114, member A1	Unknown	0.5	3.5		1.3	**2.0**	**3.5**	0.9	1.4	1.1	1.3
78	M300020322	Mm.25317	Tsku	Tsukushin	Secreted protein	#REF!	2.8		2.0	**2.8**	**2.0**	1.5	**4.4**	1.8	0.7

Table 2 continued

	Probe[1]	Unigene	Symbol	Gene	Function	Baseline[2]	Max[3]	Confirm[4]	WT[5]			Gadd45β-null[6]			
									3 hr	6 hr	12 hr	3 hr	6 hr	12 hr	-
79	M300017417 M300020021 M300020366 M300021388	Mm.374437	Ptp4a1	Protein tyrosine phosphatase 4a1	Signal transduction; Cell cycle	2.9	3.2	M	**2.5**	**3.1**	1.0	1.2	**2.1**	1.0	0.6
80	M200004856	Mm.24283	Leap2	Liver-expressed antimicrobial peptide 2	Secreted protein	3.0	4.1		1.3	1.2	**4.1**	1.6	1.9	**3.5**	1.1
81	M300002156	Mm.196592	Sara2	SAR1a gene homolog 2	Endoplasmic reticulum	5.5	3.0		1.9	1.7	**3.0**	1.5	1.9	**2.7**	0.7
82	M200015567	Mm.81022	1700063H04Rik	1700063H04Rik	Unknown	0.4	2.5		**2.4**	**2.5**	1.7	1.6	**2.5**	0.8	1.2
83	M200008446	Mm.255586	Slco1a4	Solute carrier organic anion transporter 1a4	Transport	1.9	2.7		1.8	**2.1**	**2.7**	1.4	1.9	**2.2**	0.9
84	M300009238	Mm.293635	Mscp	Mitochondrial solute carrier protein	Mitochondrial transport	0.7	2.7		1.7	**2.2**	**2.7**	**1.9**	**2.2**	**2.4**	0.8
85	M300011679	Mm.41261	Fam65a	Family with sequence similarity 65a	Unknown	0.8	3.3		1.8	**3.3**	1.4	1.6	1.8	**2.6**	**0.4**
86	M200000004	Mm.10	Srm	Spermidine synthase	Polyamine synthesis	0.7	4.7		1.6	**2.9**	**2.1**	**2.4**	**2.4**	**3.9**	1.0
87	M200004316	Mm.440269	Stk40	Serine/threonine kinase 40	Signal transduction?	0.9	2.9		1.6	**2.1**	**2.9**	**0.4**	1.3	1.4	1.3
88	M300006580	Mm.281844	Ugt2b34	UDP glucuronosyltransferase 2 family, polypeptide B34	Detoxification	8.1	2.5		1.8	**2.3**	**2.5**	1.2	1.5	1.8	0.8
89	M200011953	Mm.180546	Ormdl3	ORM1-like 3	Membrane protein	1.6	3.0		1.4	**2.1**	**3.0**	**2.6**	**2.2**	**2.4**	1.0
90	M300008559	Mm.23951	Gmppa	GDP-mannose pyrophosphorylase A	Carbohydrate metabolism	0.6	3.3		1.5	1.6	**3.3**	**0.3**	1.0	1.3	1.5
91	M200004484	Mm.22702	Slc23a1	Solute carrier family 23 member 1	Transport	1.6	3.8		1.2	1.4	**3.8**	0.7	1.2	0.8	1.3
92	M200009603	Mm.199223	Dhx32	DEAH (Asp-Glu-Ala-His) box polypeptide 32	RNA processing	0.6	2.6		1.5	**2.4**	**2.6**	1.0	1.0	1.2	1.1
93	M300014373	Mm.438136	Map3k13	Mitogen-activated protein kinase kinase kinase 13	Signal transduction	0.4	2.7		1.9	**2.6**	**1.8**	1.1	1.6	0.8	1.3
94	M300000291	Mm.7952	Peg3	Paternally expressed 3	Transcription factor	0.4	2.6		1.8	**2.0**	**2.6**	1.5	**2.2**	**2.7**	1.3
95	M200007664	Mm.270681	Hsp105	Heat shock protein 105	Stress/damage response	1.1	3.0		1.2	**2.2**	**3.0**	0.8	0.9	1.5	1.2
96	M200004731 M300002429	Mm.23942	Abcc3	ATP-binding cassette C3	Ion transport	3.4	3.1	M	1.3	**1.9**	**3.2**	**0.8**	**1.8**	**1.9**	0.9
97	M300015013	Mm.76757	Fam47e	Family with sequence similarity 47, member E	Unknown	0.5	2.3		**2.3**	**2.1**	**1.9**	**3.0**	**2.5**	**2.2**	0.8
98	M300002217	Mm.22718	Xbp1	X-box binding protein processed isoform	Transcription factor	0.4	2.9		1.6	**2.9**	**1.8**	**2.0**	**2.1**	1.4	1.1
99	M200000033	Mm.110	Idb3	Inhibitor of DNA binding 3	Transcriptional corepressor	1.9	3.0		1.5	1.7	**3.1**	1.9	1.4	**2.4**	0.9
100	M300004169	Mm.30649	Prelid2	PRELI domain containing 2	Unknown	0.4	2.2		1.9	**2.1**	**2.2**	1.9	**2.5**	**3.0**	0.8
101	M200004898	Mm.24446	1110018G07Rik	1110018G07Rik	Protein catabolism	0.7	2.4		1.4	**2.4**	**2.4**	1.7	1.8	1.9	0.9
102	M200004085	Mm.136223	Nrbf2	Nuclear receptor binding factor 2	Transcriptional coactivator	0.8	2.2	P	**2.2**	1.9	**2.1**	**2.5**	1.7	1.1	1.0
103	M300004222	Mm.29889	Prrc1	Proline-rich coiled-coil 1	Unknown	0.9	3.2		1.4	1.6	**3.2**	1.3	1.2	1.6	1.1
104	M300011852 M300011854	Mm.168854	Seli	Selenoprotein I	Phospholipid synthesis	0.6	2.8		1.4	**1.9**	**2.8**	**0.4**	**1.1**	**0.7**	1.5
105	M200012586	Mm.143167	Ncaph2	Non-SMC condensin II complex, subunit H2	Unknown	1.1	3.8		1.3	1.0	**3.8**	1.6	1.4	**2.1**	1.7
106	M300007063	Mm.299604	Csda	Cold shock domain protein A	Transcription factor; RNA binding	0.7	2.8		1.5	1.9	**2.8**	**2.0**	1.8	**2.7**	1.2
107	M200003403	Mm.15868	Vdp	Vesicle docking protein	Vesicular transport	1.3	2.3		1.7	**2.1**	**2.3**	1.6	1.4	**2.0**	0.8
108	M200006420	Mm.29293	Sec24d	SEC24 related gene family member D	Golgi protein sorting	1.0	2.4		1.9	1.8	**2.4**	1.7	1.4	0.9	1.1
109	M200005745	Mm.27897	Dnaja1	DnaJ (Hsp40) homolog A1	Stress/damage response; DNA repair	1.6	2.3		1.8	**2.3**	**2.0**	**2.1**	1.5	**2.5**	1.0
110	M300002002	Mm.200373	Sgpl1	Sphingosine phosphate lyase 1	Signal transduction; Lipid metabolism	1.6	2.5		1.4	**2.5**	**2.2**	1.3	1.9	**3.1**	0.9
111	M200006651	Mm.29778	Armet	Arginine-rich mutated in early stage tumors	Unknown	2.4	2.7		1.4	1.9	**2.7**	0.7	0.8	1.4	**2.3**
112	M300018787 M300018788	Mm.21965	Stbd1	Starch binding domain 1	Carbohydrate metabolism	1.2	2.8	M	1.2	**2.8**	**2.0**	**0.7**	**1.0**	**2.0**	2.0
113	M300008759	Mm.237099	Agl	Amylo-16-glucosidase 4α-glucanotransferase	Carbohydrate metabolism	1.1	2.8		1.5	1.7	**2.8**	0.7	1.2	1.0	0.9
114	M200006772	Mm.293605	Trp53inp2	Tumor protein p53 inducible nuclear protein 2	Stress/damage response?	1.7	2.3		**2.3**	1.7	**2.1**	1.5	1.4	1.3	1.1
115	M300018218	Mm.23031	Zfp768	Zinc finger protein 768	Transcription factor	1.0	2.5		1.7	1.8	**2.5**	1.4	**2.0**	**2.2**	0.8
116	M300004064	Mm.18556	Slc39a7	Solute carrier family 39 member 7	Transport	1.3	3.1		1.3	1.5	**3.1**	0.7	0.9	1.0	1.7
117	M200001079	Mm.244549	Slc6a9	Solute carrier family 6 member 9	Amino acid transport	1.5	2.4		1.3	**2.3**	**2.4**	1.7	1.8	**2.3**	1.1
118	M200014327	Mm.45815	Bcar3	Breast cancer anti-estrogen resistance 3	Signal transduction	0.8	2.1		**2.1**	1.9	**1.9**	1.4	1.6	1.8	1.1
119	M200005621	Mm.27606	Tmed3	Transmembrane emp24 domain containing 3	Endoplasmic reticulum; Golgi	0.8	2.9	M	1.4	1.6	**2.9**	1.0	1.0	1.5	1.6
120	M200004417 M300005889	Mm.151951	Pla2g12a	Phospholipase A2 group XIIA	Signal transduction	0.5	2.2	M	1.7	**2.0**	**2.2**	**2.8**	**2.2**	**5.0**	1.6
121	M200004368	Mm.22362	H47	Selenoprotein S	Protein catabolism	1.4	2.1		1.2	2.1	**2.5**	0.7	0.9	1.5	**1.2**
122	M200007599	Mm.275332	Apg7l1	Autophagy 7-like	Autophagy	1.2	3.5		1.0	1.3	**3.5**	1.1	1.4	1.6	**0.9**
123	M200006133	Mm.211211	Prei4	Preimplantation protein 4	Carbohydrate metabolism	1.7	2.5		1.9	2.5	**1.4**	**2.9**	1.7	1.2	**0.7**
124	M300004168	Mm.270382	Yipf5	Yip1 domain family member 5	Vesicular transport	0.9	2.3		1.7	1.8	**2.4**	1.5	1.3	1.9	1.2
125	M200006774	Mm.30003	Lamtor1	Late endosomal/lysosomal adaptor, MAPK and MTOR activator 1	Catabolism; signal transduction	1.2	2.9		1.4	1.5	**2.9**	1.5	1.3	0.7	1.8

Table 2 continued

	Probe[1]	Unigene	Symbol	Gene	Function	Baseline[2]	Max[3]	Confirm[4]	WT[5]			Gadd45β-null[6]			
									3 hr	6 hr	12 hr	3 hr	6 hr	12 hr	-
126	M300019854	Mm.147052	Zadh2	Zinc binding alcohol dehydrogenase domain containing 2	Detoxification	1.9	2.2		1.8	**2.2**	**1.8**	1.5	**2.4**	**2.2**	0.6
127	M300011758 M300011759	Mm.355174	Degs2	Sphingolipid Delta4-desaturase	Lipid metabolism	0.6	3.2	M	1.3	**1.2**	**3.2**	**0.5**	**1.6**	**2.5**	0.8
128	M200000606	Mm.251115	Tnk2	Tyrosine kinase non-receptor 2	Signal transduction	0.5	2.5		**2.5**	1.4	**1.9**	**3.2**	1.8	**2.7**	1.4
129	M300006581	Mm.312095	Ugt2b35	UDP glucuronosyltransferase 2B35	Detoxification; Sulfur metabolism	2.7	2.6		1.3	**2.6**	**1.8**	1.0	1.1	1.6	0.9
130	M200006094	Mm.28622	Txndc5	Thioredoxin domain containing 5	Protein stabilization; Endoplasmic reticulum	2.3	2.7		1.4	1.6	**2.7**	1.1	1.3	1.4	0.8
131	M200013414	Mm.21912	Fbxo21	F-box only protein 21	Cell cycle; Ubiquitinylation	0.8	2.3		1.2	**2.1**	**2.3**	0.5	0.6	0.6	**2.0**
132	M200005972	Mm.28375	Sec61a1	Sec61 α1 subunit	Protein transport; Endoplasmic reticulum	2.2	2.8		1.4	1.5	**2.8**	1.1	1.1	1.4	1.4
133	M300021248	Mm.280784	Ppp1cc	Protein phosphatase 1 catalytic subunit γ isoform	Signal transduction	1.8	2.5		1.4	1.7	**2.5**	1.4	1.3	1.0	1.3
134	M200012032 M300019130	Mm.181852	Ob1	Odd homeobox 1 protein	Transcriptional coregulator	2.0	2.4	M	1.5	**1.7**	**2.4**	**1.2**	**0.9**	**0.5**	1.7
135	M300010521 M300014672	Mm.227260	Tubb2c	Tubulin β2c	Cytoskeleton	3.0	2.8		1.4	**1.4**	**2.8**	**0.9**	**1.1**	**3.7**	1.1
136	M200008157	Mm.39054	Abcc2	ATP-binding cassette C2	Ion transport	5.4	2.2		1.3	**2.0**	**2.3**	0.6	1.4	0.9	0.7
137	M300005024	Mm.300095	Ugt1a1	UDP-glucuronosyltransferase 1a1	Detoxification	8.2	2.5	P	1.3	**2.5**	**1.8**	**0.5**	1.1	1.4	0.9
138	M300008520	Mm.26704	Stch	Stress 70 protein chaperone microsome-associated	Stress/damage response	0.9	2.2		1.1	**2.2**	**2.2**	0.6	0.9	0.9	1.8
139	M300007957	Mm.28191	Ces2	Carboxylesterase 2	Detoxification; Lipid metabolism	0.7	2.3		1.2	**2.3**	**2.0**	0.6	1.1	0.9	1.5
140	M200001707	Mm.4364	Il6st	Interleukin 6 signal transducer	Signal transduction	1.0	2.5		1.3	**2.5**	**1.7**	0.7	1.1	0.7	0.9
141	M200003007	Mm.10812	Pde9a	Phosphodiesterase 9A	Signal transduction	0.5	2.7		1.2	1.6	**2.7**	1.0	1.3	0.6	1.9
142	M300006785	Mm.358586	Cyp3a11	Cytochrome P450 3a11	Detoxification	26.1	3.2		1.2	0.9	**3.3**	1.2	1.3	**3.1**	1.1
143	M300007767	Mm.348038	Lsm6	LSM6 homolog U6 small nuclear RNA associated	RNA processing	1.5	2.5		1.5	1.4	**2.5**	1.4	1.3	**2.1**	1.1
144	M200002837	Mm.9925	Idh1	Isocitrate dehydrogenase 1 (NADP+) soluble	Carbohydrate metabolism	3.9	2.4		1.5	**2.4**	1.5	0.7	1.2	1.0	1.0
145	M300011733	Mm.279287	Fam63a	Family with sequence similarity 63, member A	Unknown	1.5	2.5		1.3	1.6	**2.5**	1.1	1.4	**2.0**	0.8
146	M300004099	Mm.282335	Ercc3	Excision repair cross-complementing group 3	DNA repair; Transcription	0.4	2.3		1.6	**2.2**	**1.7**	1.3	0.9	0.9	1.5
147	M300004432	Mm.222266	Pik3ap1	Phosphoinositide-3-kinase adaptor protein 1	Signal transduction	0.4	2.1		1.7	1.6	**2.1**	1.3	1.1	0.8	1.7
148	M200005726	Mm.27842	Slc9a3r1	Solute carrier family 9 isoform 3 regulator 1	Transport	5.1	2.4		1.5	1.5	**2.4**	1.5	**2.1**	**2.2**	0.7
149	M300003882 M300003890	Mm.26539	Cyp4f15	Cytochrome P450 4f15	Detoxification	2.3	2.6	M	1.2	**2.6**	**1.6**	**1.3**	**2.1**	**2.9**	0.8
150	M200001235	Mm.3200	Gly1	L-threonine aldolase	Amino acid metabolism	0.4	1.8		1.9	1.8	**1.7**	**3.3**	**2.3**	**2.7**	1.2
151	M300005153	Mm.303071	Srp9	Signal recognition particle 9	Protein transport; Endoplasmic reticulum	0.8	2.4		1.3	1.7	**2.4**	**0.5**	0.8	0.6	**2.1**
152	M200009492	Mm.143818	Nek6	NIMA (never in mitosis gene a)-related expressed kinase 6	Cell cycle	0.8	2.5		1.3	**2.5**	1.6	1.1	1.1	1.5	1.0
153	M300001006	Mm.323358	Tmem184b	Transmembrane protein 184b	Signal transduction?	0.6	2.5		1.4	**2.5**	1.4	0.7	1.5	1.2	1.3
154	M300017670	Mm.247126	Ppp1r3b	Protein phosphatase 1 regulatory subunit 3B	Signal transduction	1.6	2.3		1.8	**2.3**	1.2	0.8	1.3	0.7	1.1
155	M300021562	Mm.3941	Eif4e	Eukaryotic translation initiation factor 4E	Protein synthesis	1.2	2.3		1.8	**2.3**	1.2	1.3	1.0	1.2	0.9
156	M300016117	Mm.301881	Gstm1	Glutathione S-transferase µ1	Detoxification	22.8	3.2		1.0	1.1	**3.2**	0.7	1.0	1.5	1.1
157	M300005085	Mm.332693	Cdk2ap1	CDK2 (cyclin-dependent kinase 2)-associated protein 1	Cell cycle	0.5	2.1		1.5	1.6	**2.1**	1.6	1.1	0.8	1.8
158	M300014178 M300014179	Mm.88212	Tuba6	Tubulin α6	Cytoskeleton	3.2	2.2	M	1.4	**1.7**	**2.2**	**0.7**	**1.0**	**1.2**	1.4
159	M300011071	Mm.250193	Inf2	Inverted formin, FH2 and WH2 domain containing	Cytoskeleton	1.0	2.5		1.2	1.5	**2.5**	1.8	1.8	**2.3**	0.9
160	M300002125 M300002439	Mm.344779	Cdc34	Cell division cycle 34 homolog	Cell cycle	1.8	3.0	M	1.1	**1.1**	**3.0**	**1.3**	**1.1**	**1.4**	1.4
161	M200006673	Mm.29820	Bnip3l	BCL2/adenovirus E1B 19kDa-interacting protein 3-like	Apoptosis	1.1	2.2		1.9	**2.2**	1.1	1.7	1.4	1.3	0.7
162	M300006787	Mm.302599	Cyp3a25	Cytochrome P450 3a25	Detoxification	8.3	2.6		1.3	1.3	**2.6**	0.9	1.2	1.5	0.7
163	M300019551	Mm.331805	Tmem53	Transmembrane protein 53	Membrane protein	1.6	2.6		1.1	1.5	**2.6**	0.7	1.2	0.9	1.4
164	M200001120	Mm.2941	Mttp	Microsomal triglyceride transfer protein	Lipid metabolism	2.2	2.2		1.5	**2.2**	1.4	1.2	1.1	0.3	1.1
165	M300003485	Mm.10174	Thap7	THAP domain containing 7	Transcriptional corepressor	0.4	2.3		1.1	1.7	**2.3**	1.7	1.0	1.1	1.6
166	M300018457	Mm.31178	Rraga	Ras-related GTP binding A	Signal transduction	0.8	2.0		1.2	1.9	**2.0**	1.5	1.0	0.7	1.5
167	M200003380	Mm.15537	Cyp1a2	Cytochrome P450 1a2	Detoxification	13.1	2.7		1.2	1.2	**2.7**	1.0	1.1	**2.0**	0.8
168	M200015400	Mm.75101	1700067K01Rik	1700067K01Rik	Unknown	0.3	2.5		1.2	**2.5**	1.3	**2.9**	**4.1**	**4.3**	0.8
169	M200014019	Mm.275963	Cach	Cytosolic acetyl-CoA hydrolase	Carbohydrate metabolism	0.8	2.4		1.7	**2.4**	1.0	1.5	1.1	0.8	0.7
170	M300021054	Mm.27286	Ptplb	Protein tyrosine phosphatase-like member b	Signal transduction	2.0	2.7		1.1	1.2	**2.7**	1.0	0.9	0.6	1.6
171	M200003071	Mm.313303	Smarca2	SWI/SNF related a2	Transcriptional coregulator	1.1	3.9		1.5	**2.3**	1.1	**2.4**	**2.2**	1.8	0.6
172	M200012792	Mm.23296	E2f6	E2F transcription factor 6	Transcription factor; Cell cycle	0.4	2.1		1.4	1.4	**2.1**	1.2	0.9	1.0	1.8

Table 2 continued

	Probe[1]	Unigene	Symbol	Gene[2]	Function	Baseline[2]	Max[3]	Confirm[4]	WT[5]			Gadd45β-null[6]			
									3 hr	6 hr	12 hr	3 hr	6 hr	12 hr	-
173	M200005892	Mm.28219	Cdipt	CDP-diacylglycerol-inositol 3-phosphatidyltransferase	Signal transduction	0.7	2.5		1.0	1.3	**2.5**	1.6	1.0	1.0	1.6
174	M300009211 M300009212	Mm.44591	Gas2l1	Growth arrest-specific 2 like 1	Cell cycle	0.5	2.1	M	1.2	**1.5**	**2.1**	**1.1**	**1.3**	**1.2**	1.3
175	M200002386	Mm.6562	Sult5a1	Sulfotransferase 5A 1	Detoxification	0.6	2.1		1.2	1.5	**2.1**	0.7	0.6	0.4	**4.5**
176	M200005724	Mm.27839	Ubxn1	UBX domain protein 1	Unknown	2.4	2.9		1.0	0.9	**3.0**	1.3	0.9	**2.1**	0.9
177	M300005167	Mm.330510	Apcs	Serum amyloid P-component	Serum protein; Stress/damage response	5.2	2.1		1.2	1.4	**2.1**	0.6	0.9	1.9	1.9
178	M200000418	Mm.1155	Tuba4	Tubulin α4	Cytoskeleton	4.1	2.4		1.2	1.1	**2.4**	0.6	0.8	1.7	1.4
179	M300007624	Mm.336205	Pgk1	Phosphoglycerate kinase 1	Carbohydrate metabolism	4.3	2.1		1.3	**2.1**	1.1	1.2	1.1	1.3	0.9
180	M300019641	Mm.335639	Copg2	Coatomer protein complex subunit γ2	Golgi protein sorting	0.6	2.0		1.8	1.9	0.8	**2.7**	**2.1**	1.0	0.9
181	M200003602 M300008090	Mm.18353	Dpagt1	Dolichyl-phosphateacetyl-glucosaminephosphotransferase 1	Glycosylation	0.6	2.0	M	1.1	**1.4**	**2.0**	**1.2**	**1.1**	**1.2**	1.5
182	M300000848	Mm.12239	Gmnn	Geminin	Cell cycle arrest	0.4	2.0		1.3	**2.0**	1.1	**3.5**	**2.2**	**2.9**	0.8
183	M200000634	Mm.1566	Atf5	Activating transcription factor 5	Transcription factor	7.0	2.8		0.9	0.7	**2.8**	0.9	0.9	1.8	1.2
184	M300000027	Mm.271740	Slc22a18	Solute carrier family 22 member 18	Transport	1.1	2.0		0.7	1.5	**2.0**	1.5	0.8	0.8	1.8
185	M200005251	Mm.314113	Elovl6	ELOVL family member 6 elongation of long chain fatty acids	Lipid synthesis	2.0	2.1		1.4	**2.1**	**0.3**	0.8	0.8	**0.5**	**0.5**
186	M300000797	Mm.193212	Hyi	Hydroxypyruvate isomerase homolog	Carbohydrate metabolism	0.5	1.5		1.0	1.0	1.5	**3.8**	**2.0**	**2.6**	1.3
187	M300013375	Mm.344148	Abca8a	ATP-binding cassette, sub-family A (ABC1) member 8a	Transport	1.0	2.2		1.0	**2.2**	**0.2**	1.0	**0.4**	0.6	1.4

[1] Operon oligonucleotide accession number.

[2] Level of gene expression in the untreated wild type. The maximal fully saturated signal on the array is 100%.

[3] Confirmatory studies. M, mutiple oligonucleotide probes on array; P, quantitative RT-PCR; N, Northern blot

[4] Maximum induction in wild-type.

[5] Wild-type C57Bl/6 mice were treated with TCPOBOP in corn oil for 3, 6, or 12 hr, compared to RNA from untreated C57Bl/6 livers. Values are the means of ratios from 2 – 4 arrays.

[6] Gadd45β–null mice, untreated (-) or treated with TCPOBOP for 3, 6 or 12 hr. Values for WT mice are the ratios to untreated C57Bl/6. Values for mutant mice are the ratios to untreated Gadd45β-null.

Table S3. Genes downregulated by TCPOBOP treatment

N	Probe[1]	Unigene	Symbol	Gene	Function	Baseline[2]	Min[3]	Confirm[4]	WT[5]			Gadd45β-null[6]			
									3 hr	6 hr	12 hr	3 hr	6 hr	12 hr	-
1	M300019285	Mm.38231	8430408G22Rik	8430408G22Rik	Unknown	1.7	0.3		0.4	0.3	0.3	0.6	0.2	0.3	1.0
2	M300018596	Mm.329462	Gm4841	Rel. interferon-inducible GTPase	Stress/damage response	1.3	0.3		0.5	0.3	0.5	3.3	1.4	1.4	0.1
3	M200008967	Mm.125110	Sucnr1	Succinate receptor 1	Signal transduction: Receptor	1.1	0.2		0.5	0.7	0.2	0.7	0.4	0.5	0.6
4	M200013654	Mm.296918	Aacs	Acetoacetyl-CoA synthetase (Aacs)	Lipid synthesis	2.2	0.3		0.6	0.5	0.3	0.4	0.4	0.2	0.8
5	M200001342	Mm.3459	Dbp	D site albumin promoter binding protein	Transcription factor	3.4	0.3		0.6	0.5	0.3	1.5	1.7	1.3	0.6
6	M300001082	Mm.296560	Slc38a3	Solute carrier family 38, member 3	Transport	20	0.2		0.9	0.4	0.2	1.4	1.0	0.5	0.7
7	M200007744	Mm.270003	Gpr146	G protein-coupled receptor 146	Signal transduction: Receptor	1.6	0.4		0.6	0.4	0.4	0.8	0.8	0.4	0.8
8	M300005128	Mm.210745	Glul	Glutamate-ammonia ligase (glutamine synthase)	Amino acid metabolism	3.2	0.2		0.5	0.4	0.6	0.6	0.9	0.4	1.1
9	M300007047	Mm.291826	Adipor2	Adiponectin receptor 2	Lipid metabolism	7.1	0.3		0.7	0.6	0.3	0.8	0.6	0.3	0.7
10	M300000210	Mm.112	Tcea3	Transcription elongation factor A (SII) 3	Transcription	2.3	0.3		0.8	0.5	0.3	1.7	1.0	1.0	0.4
11	M300009854	Mm.35802	9030607L17Rik	9030607L17Rik	Unknown	0.7	0.3		0.7	0.3	0.6	0.5	0.5	0.7	0.8
12	M200000134	Mm.234090	Htr2c	5-hydroxytryptamine (serotonin) receptor 2C	Signal transduction	0.6	0.6		0.5	0.6	0.6	0.6	0.4	0.5	0.4
13	M300004511	Mm.264894	Scd3	Stearoyl-coenzyme A desaturase 3	Lipid synthesis	2.3	0.5		1.1	0.2	0.4	0.3	0.3	0.4	0.8
14	M300017967	Mm.313583	Scd4	Stearoyl-coenzyme A desaturase 4	Lipid synthesis	1.4	0.3		0.8	0.3	0.7	0.4	0.2	0.6	1.1
15	M300004950	Mm.336625	Dst	Dystonin	Cytoskeleton	0.6	1.0		0.9	0.4	0.5	0.7	0.6	0.4	0.6
16	M300016263	Mm.30221	Insig1	Insulin induced gene 1	Sterol metabolism	2.9	0.5		0.7	0.7	0.5	0.3	0.6	0.2	1.0
17	M300004404 M300004405	Mm.210196	Gpam	Glycerol-3-phosphate acyltransferase mitochondrial	Phospholipid synthesis	4.5	0.4	M	1.0	0.6	0.4	0.5	0.4	0.3	0.9
18	M200009317	Mm.267377	Scd1	Stearoyl-Coenzyme A desaturase 1	Lipid synthesis	62	0.4		0.6	0.9	0.4	0.4	0.6	0.2	0.8
19	M300021139	Mm.333763	Hamp2	Hepcidin antimicrobial peptide 2	Secreted protein	41	0.3		0.9	0.8	0.3	0.6	0.5	0.3	0.7
20	M200013808	Mm.41964	Tgm1	Transglutaminase 1	Protein modification	1.1	0.6		0.6	0.7	0.7	0.8	0.4	0.3	0.8
21	M300003246	Mm.212789	Ppara	Peroxisome proliferator activated receptor α	Transcription factor	7.4	0.4		1.0	0.6	0.4	1.1	1.0	0.5	0.5
22	M200009662	Mm.153218	Slc46a3	Solute carrier family 46 member 3	Transport	2.2	0.4		0.9	0.7	0.4	1.8	1.1	0.6	0.9
23	M200008687	Mm.311696	M6prbp1	Mannose-6-phosphate receptor binding protein 1	Vesicular transport	1.3	1.0		0.9	0.5	0.6	0.6	1.0	0.4	0.7
24	M300013463 M300013468	Mm.81793	Acacb	Acetyl-Coenzyme A carboxylase β	Lipid synthesis	1.2	0.3	M	1.1	0.8	0.3	0.9	0.3	0.2	1.0
25	M200013299	Mm.274540	Camkv	CaM kinase-like vesicle-associated	Vesicular transport	0.7	0.7		0.7	0.8	0.7	0.6	0.6	0.5	0.3
26	M300003727	Mm.27908	Nfatc4	Nuclear factor of activated T-cells calcineurin-dependent 4	Transcription factor	0.7	0.6		0.8	0.6	0.7	0.7	0.5	0.4	0.7
27	M300002981	Mm.202665	Rnase4	Ribonuclease family 4	RNA catabolism	19	0.4		1.1	0.8	0.4	1.0	0.7	0.4	0.9
28	M300004506	Mm.329866	Cyp2c44	Cytochrome P450 2c44	Detoxification	6.3	0.1		0.8	1.1	0.3	0.9	0.6	0.4	0.7
29	M200006335	Mm.348326	Ppap2b	Phosphatidic acid phosphatase type 2B	Lipid metabolism	3.0	0.7		0.8	0.7	0.7	0.5	0.6	0.3	0.8
30	M200005275	Mm.26462	Sgk2	Serum/glucocorticoid regulated kinase 2	Ion transport	1.0	0.4		0.8	0.4	1.1	0.7	0.3	0.5	1.2
31	M200002675	Mm.250719	Bche	Butyrylcholinesterase	Detoxification	0.8	0.5		0.8	0.9	0.5	0.4	0.4	0.2	0.9
32	M200006801	Mm.30045	Mbl2	Mannose binding lectin, serum C	Serum protein	9.9	0.4		0.8	1.0	0.4	0.8	0.8	0.6	0.9
33	M200001441	Mm.236443	Fasn	Fatty acid synthase	Lipid synthesis	10	0.4		1.3	0.6	0.4	0.6	0.4	0.2	1.2
34	M200001709 M300008206	Mm.89888	Gclc	Glutamate-cysteine ligase catalytic subunit	Glutathione synthesis; Amino acid metabolism	2.5	0.6	M	0.6	0.7	1.0	0.5	0.4	0.5	1.0
35	M200004762	Mm.24030	Slc17a2	Solute carrier family 17 (sodium phosphate) member 2	Transport	3.0	0.3		1.0	1.1	0.3	1.6	0.8	0.4	0.7
36	M300005464	Mm.124316	Tfpi	Tissue factor pathway inhibitor	Secreted protein	0.6	0.6		0.6	0.9	0.9	0.6	0.4	0.3	0.5
37	M300002615 M300002616	Mm.37605	Akr1c20	Aldo-keto reductase family 1 member C20	Unknown	7.5	0.5	M	1.0	0.9	0.5	0.5	0.7	0.7	1.2
38	M200007310	Mm.33062	Slc44a3	Solute carrier family 44 member 3	Transport	0.5	0.8		0.9	0.8	0.8	0.4	0.4	0.3	1.2
39	M200003013	Mm.10865	Uox	Urate oxidase	Purine metabolism	24	0.4		1.3	0.9	0.4	0.6	0.7	0.2	0.7
40	M200012003	Mm.41044	Slc4a4	Solute carrier family 4 (anion exchanger) member 4	Transport	1.4	0.8		1.1	0.6	0.8	0.4	0.6	0.4	0.8
41	M300000435	Mm.28456	Prodh	Proline dehydrogenase	Amino acid metabolism	4.1	0.4		1.3	0.8	0.4	1.4	0.9	0.7	0.9
42	M300000820	Mm.28146	Mvd	Mevalonate (diphospho) decarboxylase	Sterol biosynthesis	1.0	0.4		0.7	0.4	1.4	0.6	0.4	0.4	1.5
43	M300002260 M300002261	Mm.153625	Lpin1	Lipin 1	Lipid metabolism	1.1	0.4	M	1.7	0.4	0.5	2.5	0.4	0.2	1.3
44	M300010233	Mm.314378	Arl5	ADP-ribosylation factor-like 5	Transcriptional coregulator?	1.1	0.7		0.8	0.7	1.0	0.5	0.5	0.3	0.8
45	M200001102	Mm.2900	Fmo3	Flavin containing monooxygenase 3	Detoxification	4.9	0.5		1.4	1.1	0.1	1.0	0.6	0.1	0.6
46	M300004619	Mm.26719	Hsd17b9	Hydroxysteroid (17β) dehydrogenase 9	Sterol metabolism	5.7	0.4		0.9	1.2	0.5	0.8	0.7	0.4	0.9
47	M300014520	Mm.329582	Bhmt	Betaine-homocysteine methyltransferase	Amino acid metabolism; Protein modification	29	0.5		1.5	0.5	0.5	0.9	0.9	0.4	0.9
48	M200004926	Mm.24547	Aadac	Arylacetamide deacetylase (esterase)	Lipid metabolism	7.4	0.5		1.0	1.1	0.5	0.8	0.7	0.6	0.6
49	M300012697	Mm.127014	Zfp28	Zinc finger protein 28	Transcription factor	1.2	0.7		1.1	0.8	0.7	0.4	0.6	0.3	0.8
50	M200007836 M300001095	Mm.237103	2610507B11Rik	2610507B11Rik	Carbohydrate metabolism?	1.0	0.6	M	1.0	1.0	0.6	0.4	0.6	0.5	1.1
51	M200013329	Mm.214923	BC089597	Cis-retinol/3alpha hydroxysterol short-chain dehydrogenase-like	Retinoid metabolism	12	0.5		1.2	1.0	0.5	0.9	0.9	0.5	0.9
52	M300012160 M300012161 M300012162	Mm.193099	Fn1	Fibronectin 1	Extracellular matrix	6.2	0.9	M	0.9	0.9	0.9	0.2	0.7	0.3	0.9
53	M300012062	Mm.262184	Zfp67	Zinc finger protein 67	Transcription factor	0.7	0.7		0.8	0.7	1.2	0.3	0.5	0.3	1.6
54	M300022269	Mm.39472	Fdps	Farnesyl diphosphate synthetase	Sterol biosynthesis	4.9	0.4		1.5	0.8	0.4	0.4	0.3	0.3	2.0
55	M200004493	Mm.255026	Acas2	Acetyl-Coenzyme A synthetase 2 (ADP forming)	Carbohydrate metabolism	4.6	0.2		1.5	1.0	0.2	0.4	0.2	0.2	1.4
56	M300022236	Mm.193116	Krt1-9	Keratin complex 1 acidic gene 9	Cytoskeleton	1.8	0.7		0.9	0.7	1.2	0.6	0.6	0.5	0.8
57	M300005056	Mm.25788	Ccdc93	Coiled-coil domain containing 93	Unknown	1.0	0.8		0.9	0.8	1.1	0.4	0.6	0.3	0.8

Table 3 continued

	Probe[1]	Unigene	Symbol	Gene	Function	Baseline[3]	Min[4]	Confirm[5]	WT[6]			Gadd45β-null[7]			
									3 hr	6 hr	12 hr	3 hr	6 hr	12 hr	-
58	M200004397 M300008117	Mm.335570	Aqp9	Aquaporin 9	Transport	4.2	0.9	M	1.0	0.9	0.9	**0.3**	**0.5**	**0.3**	1.3
59	M300013123	Mm.333594	Zc3h4	Zinc finger CCCH-type containing 4	Transcription factor?	0.4	0.6		0.9	0.9	1.0	0.6	0.6	**0.4**	0.9
60	M300008273	Mm.85410	Smarcc1	SWI/SNF related matrix associatedregulator of chromatin c1	Transcriptional coregulator	14	0.7		1.0	0.7	1.2	**0.4**	**0.5**	**0.3**	1.2
61	M200005104	Mm.282039	Acly	ATP citrate lyase	Lipid synthesis	2.9	0.1		1.6	1.0	**0.1**	1.3	0.7	**0.5**	0.5
62	M300019855	Mm.20294	Sephs2	Selenophosphate synthetase 2	Selenium metabolism	5.5	0.6		1.0	1.2	0.6	**0.2**	0.7	**0.2**	1.0
63	M200003608	Mm.18443	Slc2a2	Solute carrier family 2 (facilitated glucose transporter) member 2	Transport	3.2	0.4		1.3	1.2	**0.4**	1.3	**0.6**	**0.4**	0.9
64	M200008136	Mm.38901	Fads2	Fatty acid desaturase 2	Lipid synthesis	5.7	0.4		1.3	1.2	**0.4**	0.7	**0.5**	**0.3**	1.1
65	M300013078	Mm.8359	Pklr	Pyruvate kinase liver and red blood cell	Carbohydrate metabolism	5.3	0.4		1.2	1.3	**0.4**	0.7	1.0	**0.3**	0.8
66	M200014102	Mm.278805	Trmt12	TRNA methyltranferase 12 homolog	tRNA synthesis	4.6	0.3		**2.0**	**0.3**	0.7	**0.4**	**0.3**	**0.1**	0.7
67	M300015378	Mm.29023	Erbb3	v-erb-b2 erythroblastic leukemia viral oncogene homolog 3	Signal transduction: Receptor	0.9	0.8		0.8	0.9	1.4	**0.3**	**0.4**	**0.2**	1.3
68	M300006933	Mm.33401	Mgam	Maltase-glucoamylase	Carbohydrate metabolism	1.1	0.9		0.9	1.3	0.9	**0.3**	**0.5**	**0.2**	1.1
69	M200000642	Mm.245395	Pten	Phosphatase and tensin homolog	Signal transduction	2.6	0.8		1.1	1.2	0.8	**0.3**	0.7	**0.4**	0.9
70	M200005356	Mm.260054	Chst10	Carbohydrate sulfotransferase 10	Protein modification	0.7	0.8		0.8	0.9	1.4	**0.6**	0.6	**0.3**	**0.5**
71	M300016572	Mm.149438	Mtus1	Mitochondrial tumor suppressor 1	Signal transduction	1.1	1.0		1.0	1.1	1.1	**0.4**	0.6	**0.3**	0.8
72	M300015261 M300021326	Mm.29847	Idi1	Isopentenyl-diphosphate delta isomerase	Sterol biosynthesis	1.4	0.7	M	1.2	0.7	1.3	**0.2**	**0.4**	**0.5**	1.9
73	M300005063	Mm.8655	Cfh	Complement component factor h	Serum protein	8.0	0.9		1.1	0.9	1.1	**0.4**	0.7	**0.4**	0.9
74	M300008028	Mm.32700	Sc5d	Sterol-C5-desaturase homolog	Sterol metabolism	7.4	0.6		1.3	1.2	0.6	**0.4**	0.6	**0.4**	1.1
75	M200012584	Mm.276155	Ihpk1	Inositol hexaphosphate kinase 1	Vesicular transport	0.6	0.4		0.8	1.1	1.4	**0.5**	**0.4**	**0.3**	1.2
76	M300013222	Mm.277634	Gltscr2	Small nucleolar RNA, C/D box 23	Unknown	3.0	0.6		0.9	0.6	1.9	**0.4**	1.1	**0.3**	1.1
77	M300011072 M300002272 M300002273	Mm.221239	Apob	Apolipoprotein B	Lipid metabolism; Serum protein	9.3	1.0	M	1.0	1.2	1.2	**0.2**	0.6	**0.2**	1.0
78	M300003351	Mm.8924	Atp13a3	ATPase type 13A3	Ion transport	0.8	0.9		0.9	1.4	1.0	**0.4**	**0.4**	**0.3**	1.2
79	M300003111	Mm.149720	Lifr	Leukemia inhibitory factor receptor	Signal transduction: Receptor	1.6	1.0		1.0	1.4	1.1	**0.3**	0.6	**0.3**	1.5
80	M300005021 M300005025	Mm.300095	Ugt1a5	UDP glycosyltransferase 1 family polypeptide A5	Detoxification	1.8	0.8	M	1.0	1.7	0.8	**0.2**	**0.3**	**0.2**	0.8
81	M300006904	Mm.182746	Mtpn	Myotrophin	Transcription factor; Transcriptional coregulator	1.8	0.7		1.0	1.2	1.3	**0.4**	0.7	**0.3**	1.2
82	M300004875 M300004877	Mm.343942	Cps1	Carbamoyl-phosphate synthetase 1	Urea cycle	19	0.9	M	1.2	1.7	0.9	**0.3**	0.7	**0.2**	1.0
83	M200001280	Mm.253403	Slc38a10	Solute carrier family 38, member 10	Unknown	0.9	1.0		1.0	1.5	1.4	**0.4**	**0.4**	**0.3**	1.3
84	M300016143	Mm.314576	Zfp650	Zinc finger protein 650	Membrane protein	0.8	0.4		1.0	1.7	1.4	0.6	0.6	**0.3**	0.9
85	M300004553	Mm.218851	Eif2s3x	Eukaryotic translation initiation factor 2 subunit 3 X-linked	Protein synthesis	1.6	1.3		1.3	1.6	1.4	**0.2**	**0.5**	**0.3**	1.5
86	M300012510	Mm.305816	Tebp	Telomerase binding protein p23	Cell cycle	2.3	1.0		1.0	1.9	1.5	**0.4**	**0.7**	**0.5**	**1.2**

[1] Operon oligonucleotide accession number.

[2] Level of gene expression in the untreated wild type. The maximal fully saturated signal on the array is 100%.

[3] Confirmatory studies. M, mutiple oligonucleotide probes on array; P, quantitative RT-PCR; N, Northern blot

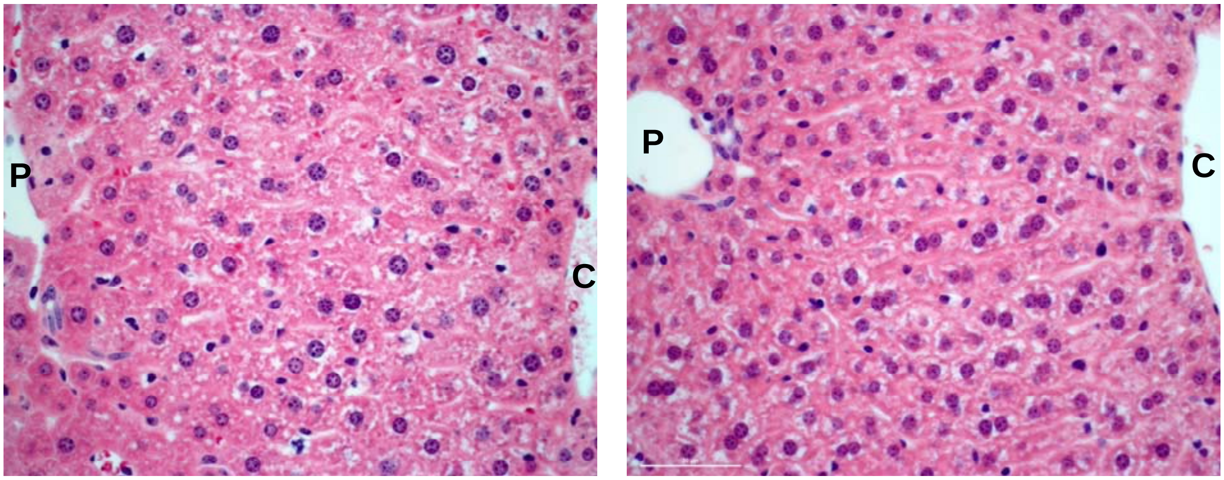
[4] Minimum level of expression induced by TCPOBOP in wild-type.

[5] Wild-type C57Bl/6 mice were treated with TCPOBOP in corn oil for 3, 6, or 12 hr, compared to pooled RNA from untreated C57 livers.

[6] Gadd45β–null mice, untreated (-) or treated with TCPOBOP for 3, 6 or 12 hr. Values for WT mice are the ratios to untreated C57Bl/6. Values for mutant mice are the ratios to untreated Gadd45β-null.

Table S4. Primers for mRNA quantification by RT-PCR

Gene	**5'**	**3'**
Ccnd1	CCTGCTACCGCACAACGCACTT	CTCCTCCTCAGTGGCCTTGGG
Cyp2b10	TCAGTTCTTGCGCCTGCTGGAG	GGCACCAGGAAAGTACTTCAGGAAG
Por	AGGCCCACAAGGTCTATGTTCAGCA	ACTCGGGAAGGGTGATGCTGG
Ugt1a1	GGCTGATGAGAAGTGACTTTGTGAAAGAT	CCCAGAGGCGTTGACATAGGCTTC
Sult1d1	CGTCTCCTCGAATAGTGAAAACACACC	GAAACAACCACATCTTTGGCATTCC
Jun	GAACTCGGACCTTCTCACGTCGC	TAGTGGTGATGTGCCCATTGCTG
Fosl2	CGTGGGCCGCAGAAGGAGA	CGACGGTTCCGACACTTGGC
Gadd45a	TGAGCTGCTGCTACTGGAGAACGAC	TCCTTCCATTGTGATGAATGTGGGT
Gadd45b	GCCCGAGACCTGCACTGCCT	CCATTGGTTATTGCCTCTGCTCTCTT
Gadd45g	GGAGACCTGCATTGCATCCTCATTT	ACTCGGGAAGGGTGATGCTGG
Ncoa1	TCCAATGATGGGCCAGATGCAAA	AGTGGACGAGAGCTGGTTGCAGTAG
Ncoa2	CCAGATGAGCATGACCTCAGTGACC	GCTTGATCATGTCCATTCCAGGC
Ncoa3	CATCCTCAGCCCACACCCATGTA	CATGTTGTAGGCTGCAGGGTTCC
Ncoa6	CCCAAAGGAAACTCCAGCCAC	TCTTCGGCTCGTCAGGGTT
Med1	GCCAACAGTGTTGATCTTCCTGCG	CTCAAACAACGGGATTCCTGTGC
Med13	CTGCTTCACAGCAAACACTCCCAC	GGAGACATGAGCGTCTGTCCTGG
Med25	AGTCATGGCCCACACAGCTTCC	AGGATGTCGTCCTCCATGACGCT
Ppargc1a	CCAAGAGCAAGTATGACTCTCTGGATTT	TCTCTCTGTCATTCCTCAGCCTGG
Ppargc1b	GTCACCAGCCACCCGGAAGAACT	AAAGGCCATCGGTGAAGGCC
Pprc1	TCTGCAAGAGGAGTTACTCTGACCTTGA	GGGTTACCTCCTGAGGTTCTTCTGG
Nrbf2	ACATATCTCTCTGAAGCCATGAAGCTG	CGCTTTGCTCTCTTCCACCTCTCC
Nrip1	ATGTATAGTTCCCCGCAGCCTG	AGTGCTCTGGGAAAGGAGGG
Carm1	CGCCGCTGTGGATGAGTACTT	CCTGTGCAAATCGCCTTCT
Kat2b	GTGTTTTCCCACCAGCTGCC	ACCACCAATGACACGGCCA
Ep300	GGGGCAATAAGAAGAAGCCTGG	AGGGAATTGGGAGCAGGACA
Crebbp	AAGCCCAGCATGCCCAAT	TGGGGGGCTGAGTGCTGATA
Trim24	ACCAAATTCATCAGTGCCATCTCC	AGCTTCCTCGACTTCCAACAC
GAPDH	GGTCATCATCTCCGCCCCTTCTGC	GAGTGGGAGTTGCTGTTGATCG

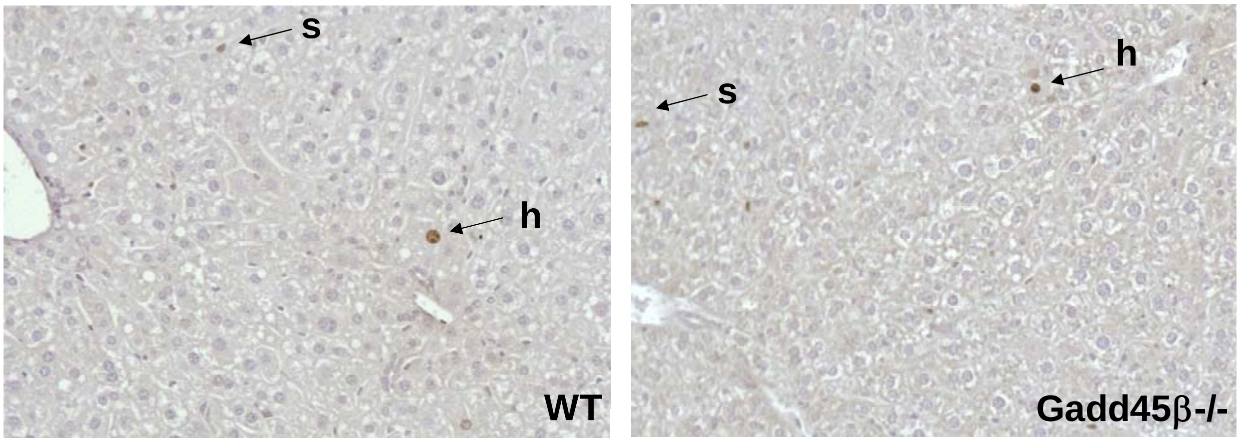


Wild Type **Gadd45β-null**

Morphometric analysis

Parameter		**Wild Type**	**Gadd45β-null**	**p**
Hepatoctye area		380 ± 36 μm^2	323 ± 33 μm^2	0.004
Hepatoctye volume		7408 ± 216 μm^3	5805 ± 190 μm^3	-
Nuclei per cell:	1	0.81 ± 0.06	0.73 ± 0.10	0.057
	2	0.19 ± 0.06	0.27 ± 0.10	-
Ploidy:	2N	0.61 ± 0.03	0.56 ± 0.03	0.144
	4N	0.36 ± 0.02	0.40 ± 0.02	0.107
	8N	0.02 ± 0.01	0.03 ± 0.01	0.700
	16N	0.002	0.001	0.511

Figure S1
Comparison of untreated wild type and Gadd45β-/- livers**.** There were no pathological changes in the mutant, which however had smaller hepatocytes, apparent in comparison of the illustrated micrographs. Three livers each from mutant and wild type were analyzed, each from three 400 X micrographs displaying the full region between portal region and central vein. Contours of all hepatocytes in the micrograph were manually traced and cross-sectional area calculated with software. Cell volume was approximated by assuming that the hepatocytes were cubic. Nuclei per cell and nuclear cross-sectional area were also measured. Values are the mean, standard deviation, and p-value determined using a two-tailed unpaired Student's T-test; P, portal; C, central. Hematoxylin and eosin, photographed at 400 X.



Untreated livers

Ki67-positive hepatocytes

WT 1.16 ± 1.66%

Null 1.10 ± 0.94%

Figure S2
Basal proliferation in untreated livers. Ki67-positive hepatocyte nuclei (h) and total hepatocyte nuclei were counted in 3 livers in each group, 5 random 200 X micrographs per liver. Stromal nuclei (s), more frequently labeled, were not quantified. Immunoperoxidase and hematoxylin, photographed at 200 X.

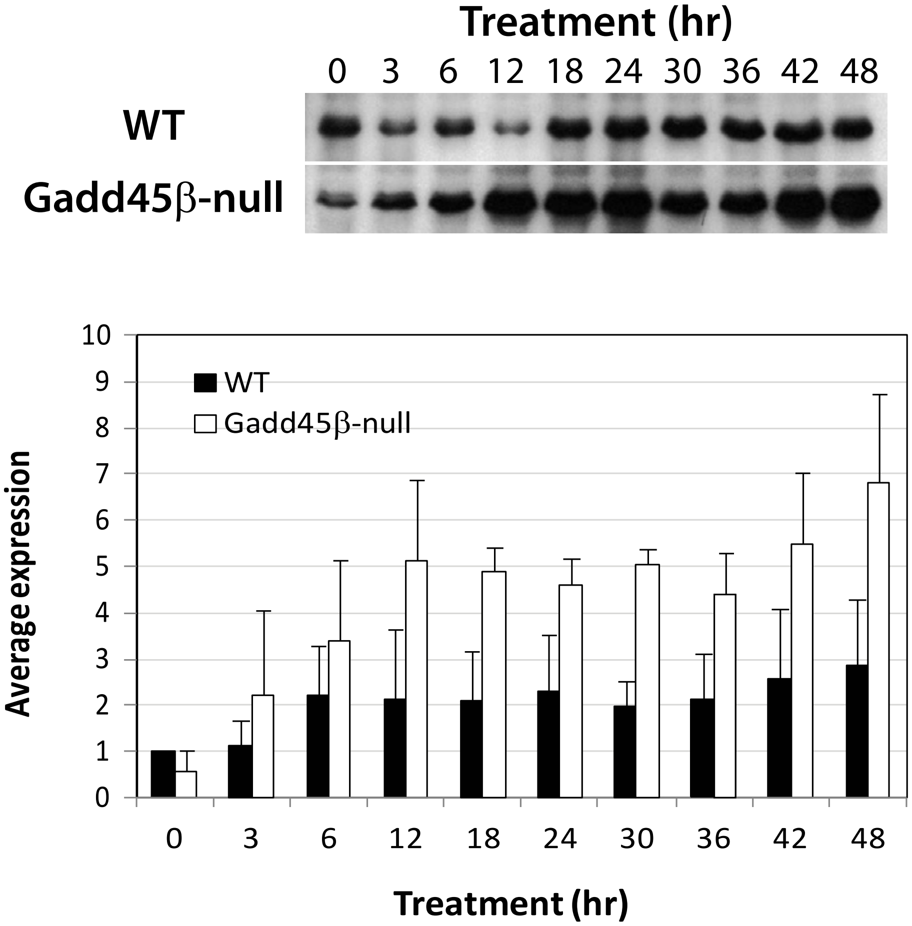


Figure S3

Cyclin D1 protein levels. Western blots of whole cell lysates demonstrate that stimulation of Cyclin D1 mRNA by TCPOBOP led to a similar increase in protein levels. The densitometric quantification at the bottom, averaged from analysis of two sets of livers, shows the mean and standard error, normalized to the level of untreated wild type liver.

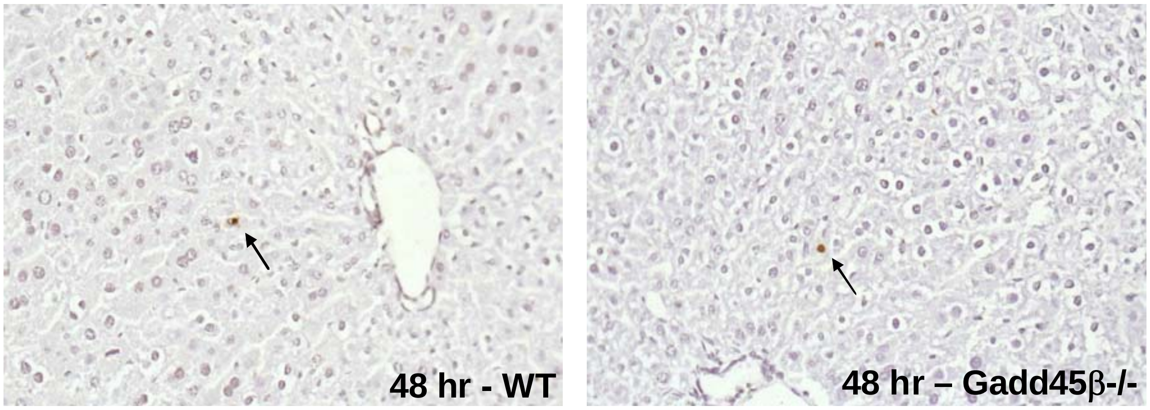


Figure S4
Representative detection of apoptosis. TUNEL staining revealed rare hepatocyte apoptosis, less than 1 per 20 intermediate power fields in both mutant and wild type. The incidence was not further quantified. Apoptosis at other treatment intervals was also minimal (not illustrated). TUNEL reaction and hematoxylin, photographed at 200 X.

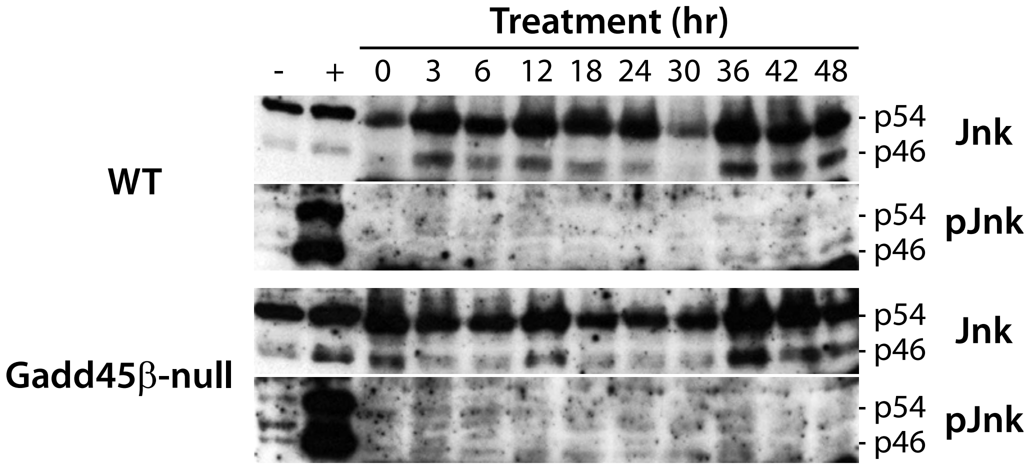


Figure S5
Absence of Jnk activation in wild type and mutant livers. Western blots of whole cell extracts were developed to maximum sensitivity to detect background levels of phosphorylation. The lanes labeled - and + are controls, HepG2 cell extracts without and with addition of anisomycin, respectively. Antibodies to Jnk and pJnk detected p54 and p46 isoforms of both Jnk1 and 2.

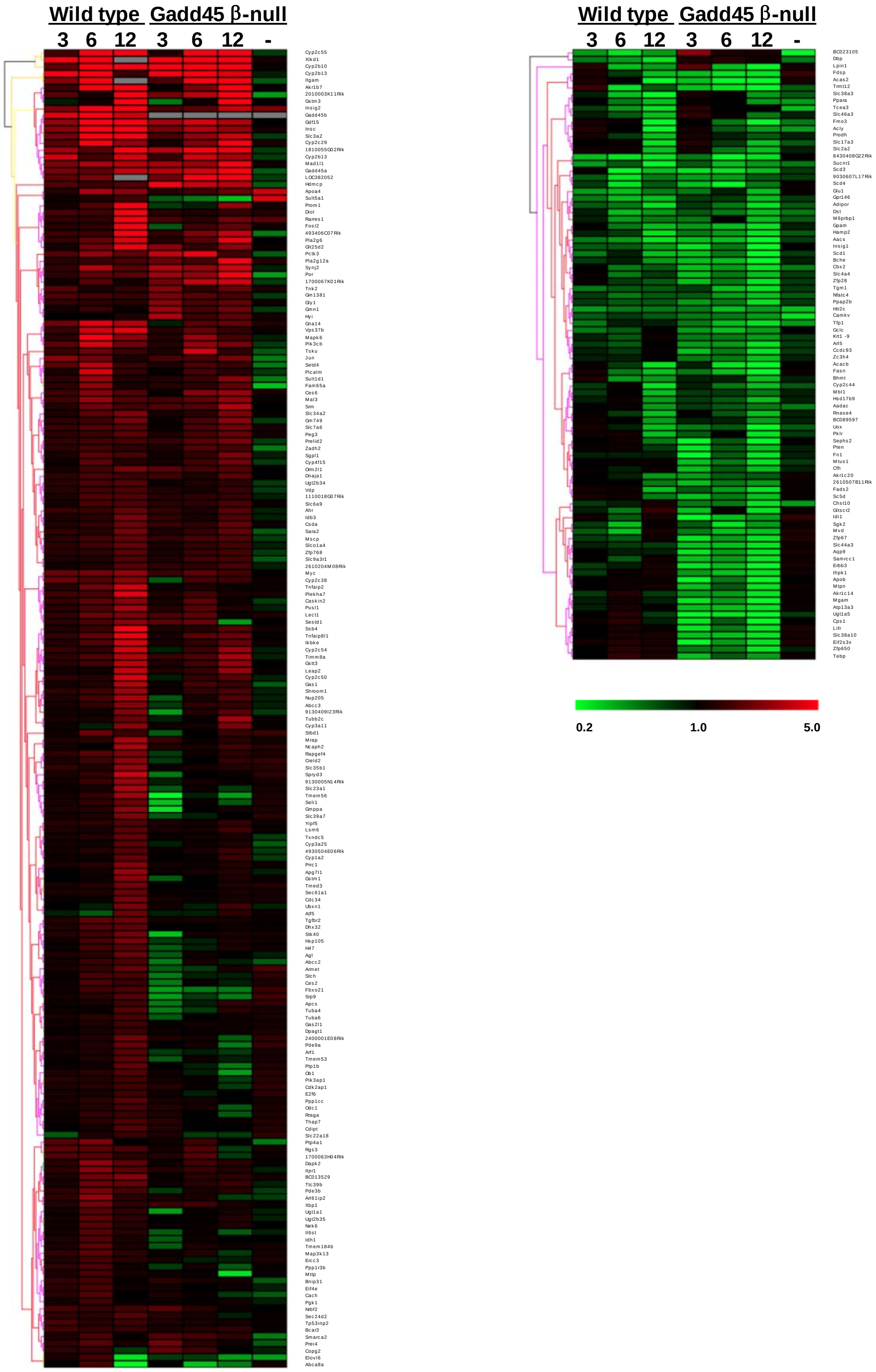


Figure S6

Heat maps of transcriptional responses to TCPOBOP. The gene expression ratios from Tables S1 - S3 are illustrated as a green-red intensity scale. Ratios compare treated (2, 6, and 12 hr) vs. untreated wild type; treated vs. untreated Gadd45β-null; and untreated Gadd45β-null (-) vs. untreated wild-type.

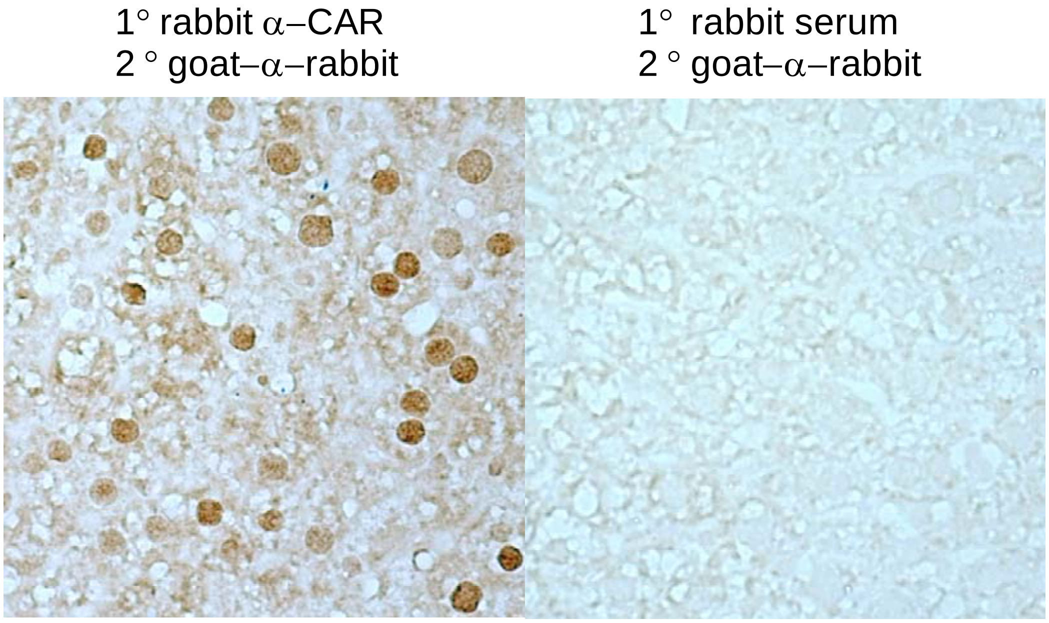


Figure S7
Immunohistochemistry control study. CAR immunodetection in paraffin sections of wild type liver, 3 hr after treatment with TCPOBOP, was compared to a rabbit serum control of a parallel tissue section. DAB incubation, photography, and image enhancement were identical for both micrographs. Photographed at 400 X.

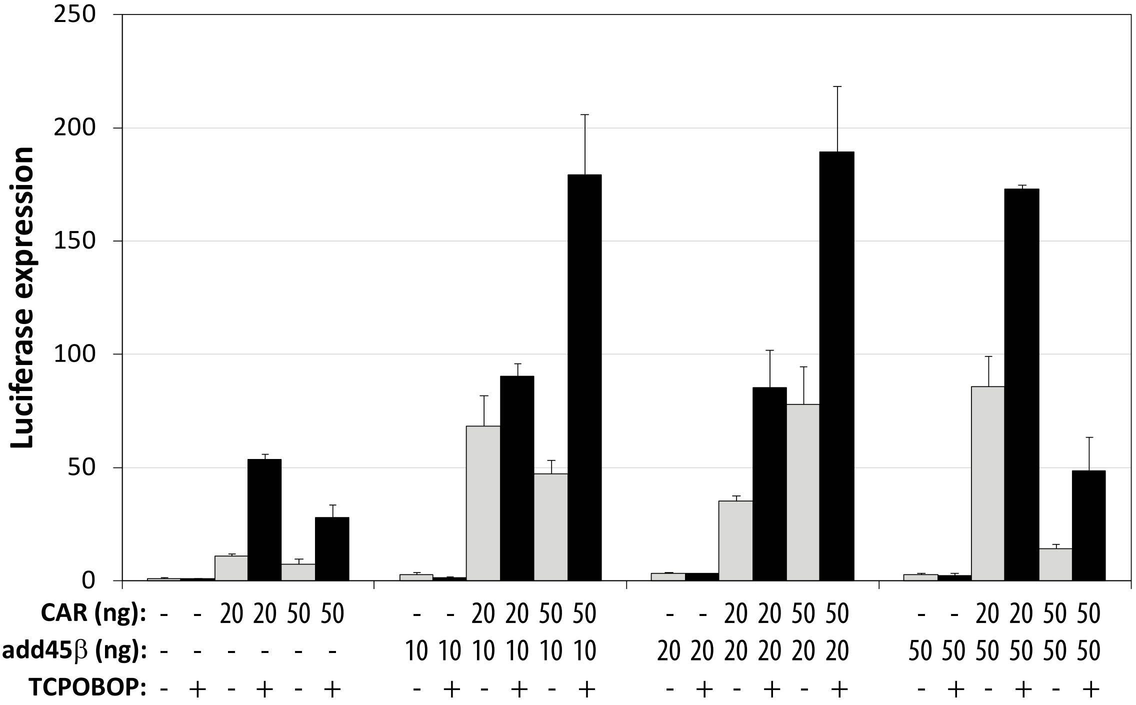


Figure S8
Coactivator titration. To establish optimum conditions for testing of coactivation, HepG2 cells were cotransfected with a constant amount of the 2b10 luciferase reporter, varied amounts of plasmids expressing CAR and Gadd45β, and TCPOBOP (125 nM, black bars) or the vehicle, DMSO (gray bars). CAR is constitutively active, but reporter activity is further stimulated by TCPOBOP. Gadd45β coactivates CAR in all combinations, with or without TCPOBOP.

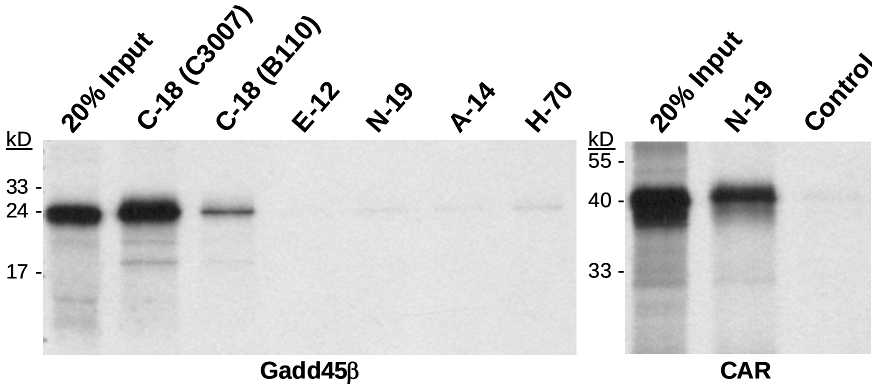


Figure S9
Characterization of Gadd45β and CAR Abs. (**Left**) Comparison of Ab to Gadd45β. 1 µg of Ab was bound to Protein G agarose and incubated with ^{35}S-labeled mouse Gadd45β prepared by in vitro translation. The panel of goat Ab generated against Gadd45β was provided by Santa Cruz Biotechnologies (Santa Cruz, CA). Only one preparation of antibody against peptide C-18 (lot #C3007) bound Gadd45β with high affinity and was suitable for ChIP (Fig. 5). (**Right**) Demonstration of an Ab with high affinity to mouse CAR. CAR Ab N-19 strongly bound ^{35}S-labeled CAR and was suitable for immunohistochemistry (Fig. 3A) and ChIP (Fig. 5).

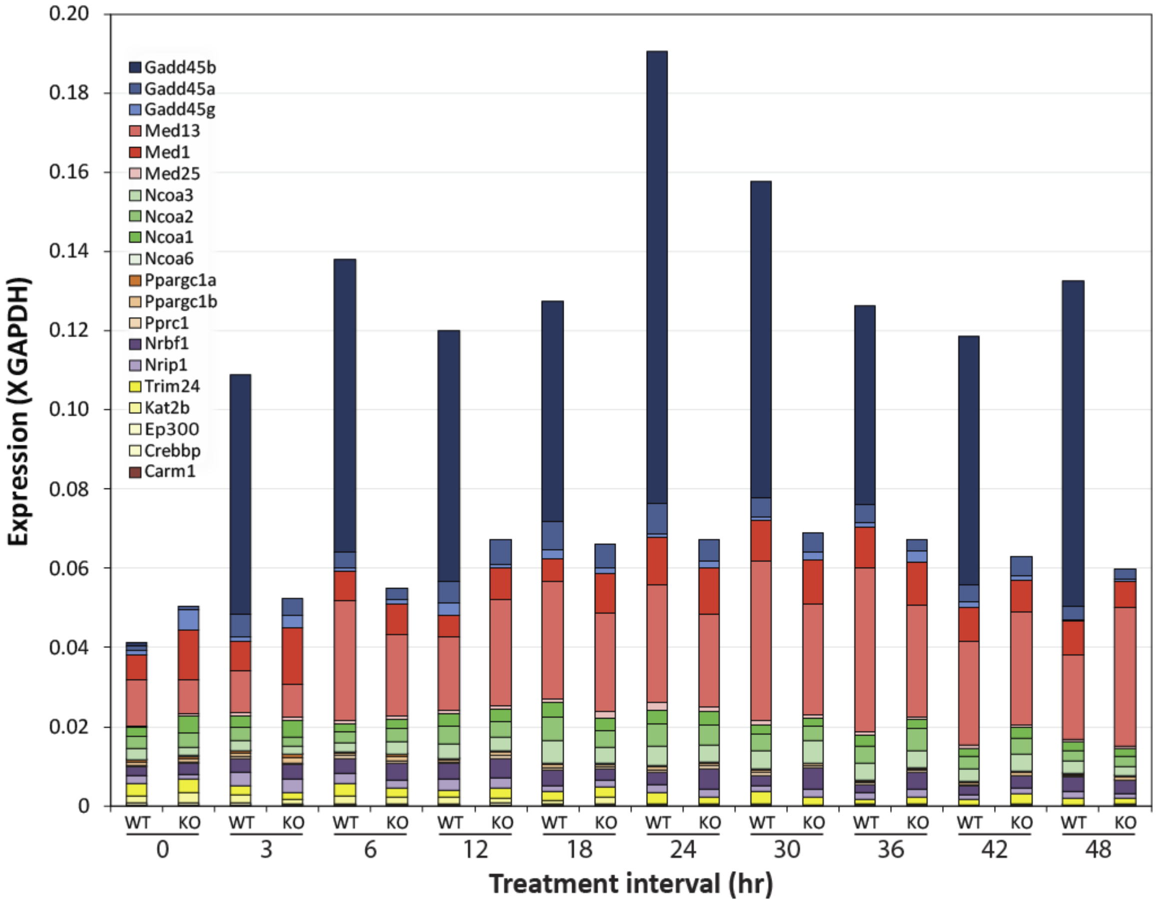


Figure S10
Coactivator mRNA levels in wild type and Gadd45β-null liver in response to TCPOBOP treatment. (**A**) Total coactivators in mutant and wild type liver.

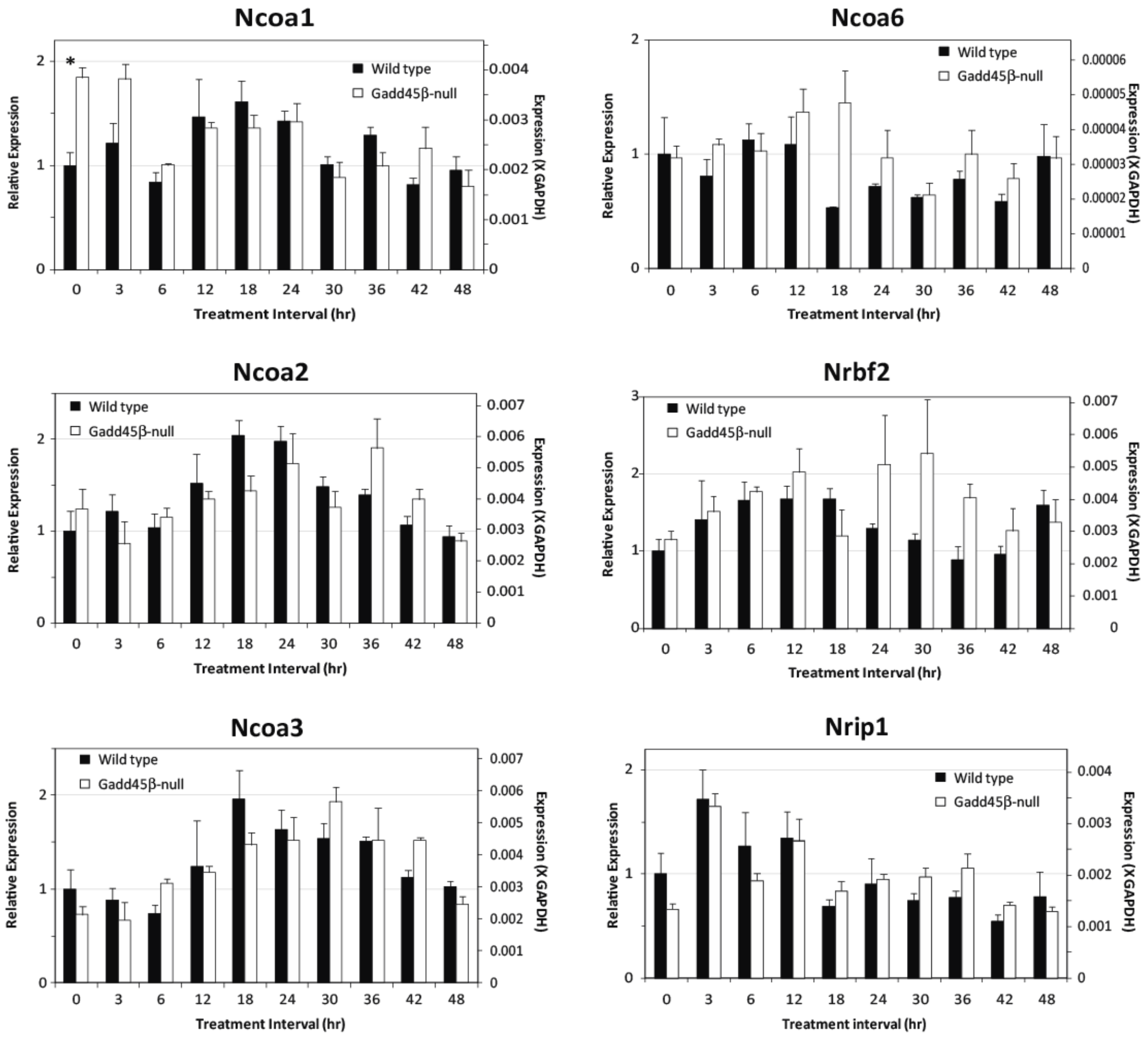


Figure S10 - continued
(**B**) Primary coactivators that directly bind nuclear receptors. Ncoa1/Src1, Ncoa2/Grip1, and Ncoa3/ACTR comprise the p160 family of primary coactivators that directly bind activated nuclear receptor transcription via LXXLL motifs. Ncoa6/Prip/Rap250, Nrbf2, and Nrip1/Rip140 are unrelated coactivators that bind nuclear receptors by a similar mechanism. Ncoa1, Ncoa2, Ncoa3, Nrbf2, and Nrip1 all have similar levels of basal expression in liver, and are moderately stimulated (1.5 - 2 fold) by TCPOBOP treatment. Ncoa6, barely detectable in liver, shows little change after treatment. T-test comparisons of wild type and mutant liver at each time interval: *, $p<0.5$.

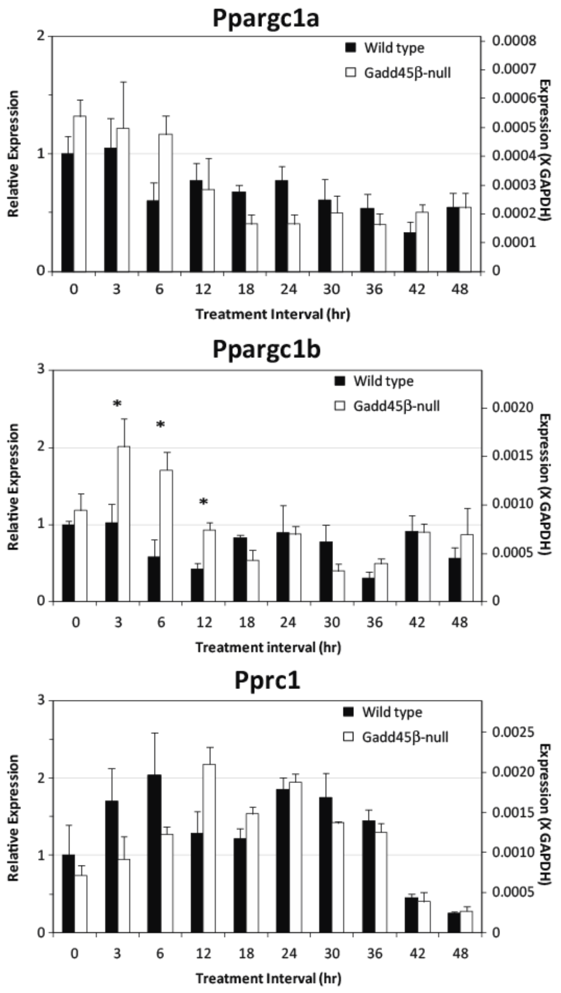


Figure S10 - continued
(**C**) PGC1 family coactivators. These inducible coactivators are primary interactors that may bind a subset of nuclear receptors, discovered via their interactions with PPAR. Ppargc1b/Pgc1b and Pprc1/Prc are moderately expressed, and the latter is induced ~2-fold by TCPOBOP. Liver expression of Ppargc1a is very low. T-test comparisons of wild type and mutant liver at each time interval: *, $p<0.5$.

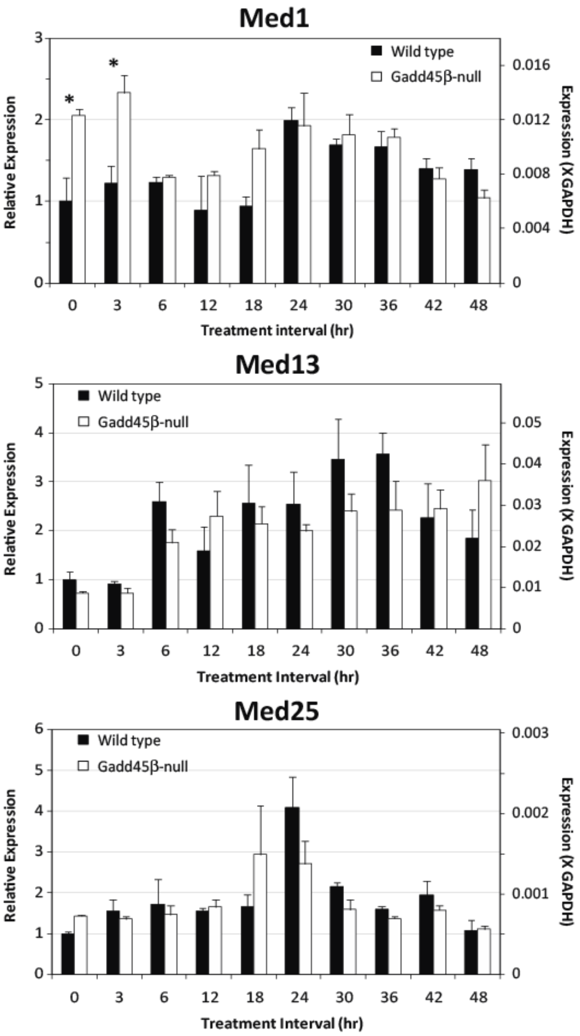


Figure S10 - continued

(**D**) Mediator complex subunits. Med1 and Med13, LXXLL-containing subunits of the mediator complex, bind nuclear receptors in a secondary interaction after primary coactivators have been displaced. Their basal levels are higher than other coactivators, and Med13 is significantly induced by TCPOBOP treatment. Med25, expressed at lower levels, is found in only a subset of mediator complexes. T-test comparisons of wild type and mutant liver at each time interval: *, $p<0.5$.

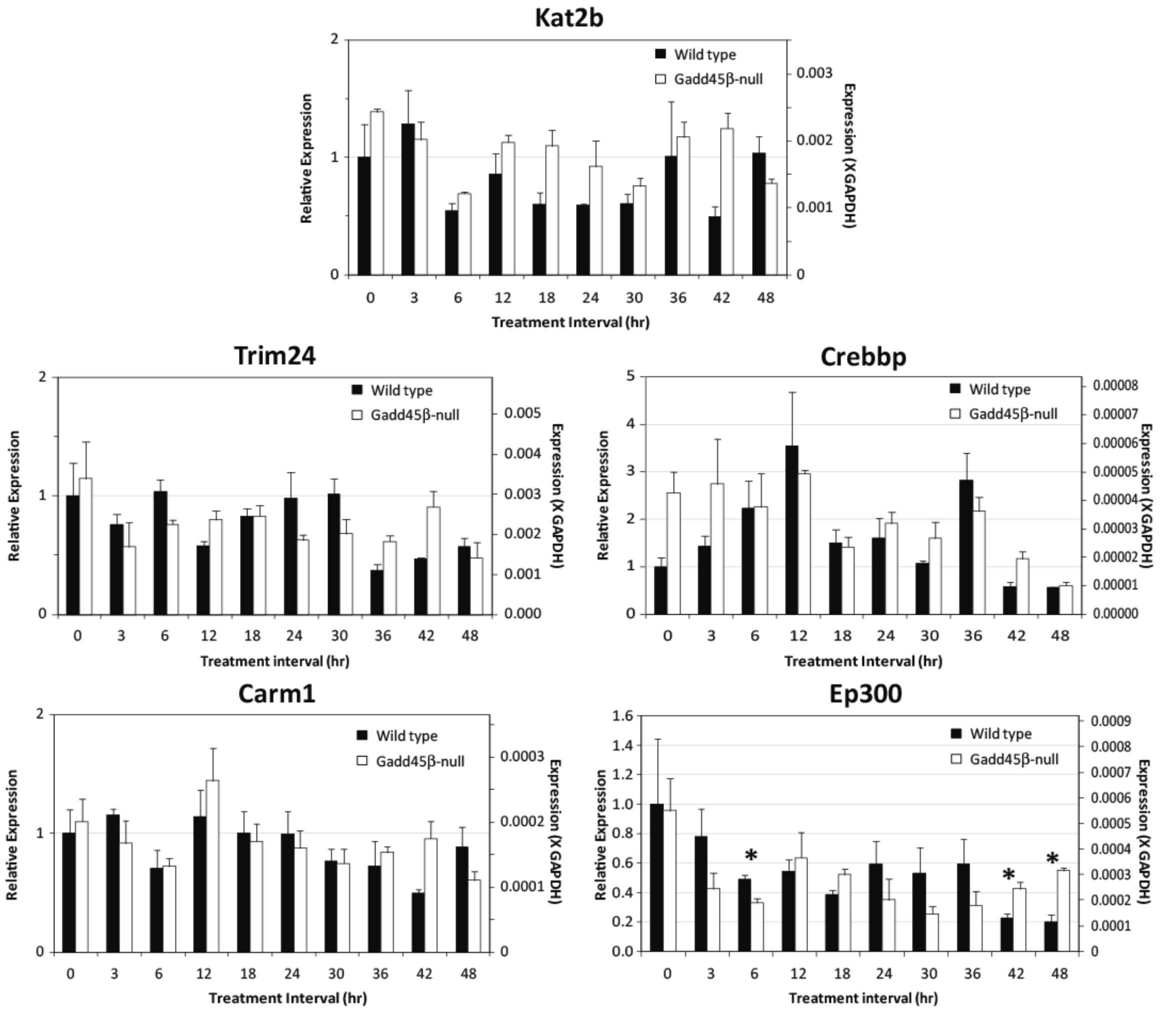


Figure S10 - continued

(**E**) Indirectly binding coactivators. Kat2b/PCAF, Crebbp/CBP, Ep300, Trim24/Tif1α, and Carm1. Although several can bind directly in vitro, these proteins are part of nuclear receptor activation complexes via binding to p160 (and other) coactivators. T-test comparisons of wild type and mutant liver at each time interval: *, p<0.5.

Plasmid cloning. CAR cDNA was synthesized from mouse liver RNA and amplified using primers that added EcoRI or SalI sites (5’AGTTCGAATTCTCTCAAGGAAAGCAGGGTCA, AGGATGTCGACCTGGGCCTCAACTGCAAATC). The 1.2 kb PCR product was cloned into the expression vector, pCI (Promega, Madison), digested with these enzymes. A CAR- and TCPOBOP-sensitive reporter plasmid contained the 53-bp phenobarbital response element from the mouse Cyp2b10 gene (5’CTCTGTACTTTCCTGACCTTGGCACAGTGCCA-CCATCAACTTGCCTGACACCC) combined with the prolactin basal promoter.

A Gadd45β expression plasmid (pCI-Gadd45β) was synthesized from mouse liver RNA as above and amplified with the Expand Long Template PCR System (Roche, Indianapolis). A 5’-primer added an EcoRI site, (5’GGGTTCGAATTCGGACTTGTACTTTGCTCTTGG) and a 3’-primer added a SalI site (5’GGACAGCAAGTCGACAGTTGCTTTAGATG). The 0.5 kb PCR product was cloned into pCI digested with these enzymes. To generate mutations M98 and M117, PCR used pCI-Gadd45β as template for Pfu DNA polymerase. For M98 (primers: 5’GTATCAGGCATGCAGAGGGCAGCGCAGGCAGCGGGGAGCCGGCGGAGACA and 3’AATTTCACAAATAAAGCATTTTTTTCAC), the PCR product was digested with SphI and XmaI and then cloned into pCI-Gadd45β digested at the same sites. For M117, separate PCR reactions amplified proximal and distal regions (proximal primers 5'CACCTATTGGTCTTACTGACATCCAC and 3’GTGCAGGTCCCGGGCTTCGGTTGTGCCCAA; distal primers 5'ACCGAAGCCCGGGACGCACACTGCGCAGCGGTCACGAACTGTCATACA and 3’AATTTCACAAATAAAGCATTTTTTTCAC). The proximal product was digested with SalI and XmaI, and the distal product with XmaI and NheI. Both inserts were cloned together into pCI digested with SalI and NheI.

To generate a Gadd45β-GST fusion protein, an 0.5 kb BspHI-SalI fragment from pCI-Gadd45β was cloned into bacterial GST expression plasmid pGEX-KG, digested with NcoI and SalI. pGST-Gadd45β was transfected into bacterial strain BL21 (Stratagene, La Jolla) for production of fusion protein. pCMV-SRC1 was kindly provided by Dr. R. Evans.

For GAL4-DBD fusion constructs, PCR was carried out with pCI-Gadd45β, wt or mutant, as template. The primers for each deletion were: Full length, aa 1 - 160 (5’CCCGGGGGATCCGGAATTCTAATGACCCTGGAAGAGCTGGT, 3’CCCGGGGTCGACTCAGCGTTCCTCTAGAGAGATATA); aa 1 - 125 (5’CCCGGGGGATCCGGAATTCTAATGACCCTGGAAGAGCTGGT, 3’CCCGGGGTCGACTCAACAGTTCGTGCCAGGAGGCA); aa 1-92 (5’CCCGGGGGATCCGGAATTCTAATGACCCTGGAAGAGCTGGT, 3’CCCGGGGTCGACTCATACCCGGACGATGTCAATGTCA); 1-68 (5’CCCGGGGGATCCGGAATTCTAATGACCCTGGAAGAGCTGGT, 3’CCCGGGGTCGACTCAATCATCCTCCTCTTCTTCGTCTAT); 69-160 (5’CCCGGGGGATCCGGAATTCTAATCGCTCTGCAGATTCACT, 3’CCCGGGGTCGACTCAGCGTTCCTCTAGAGAGATATA); aa 93-160 (5’CCCGGGGGATCCGGAATTCTATCAGGCATGCAGAGGCTGGC, 3'CCCGGGGTCGACTCAGCGTTCCTCTAGAGAGATATA); aa 126-160 (5’CCCGGGGGATCCGGAATTCTACATACAGATTCCTGGAAAA, 3’CCCGGGGTCGACTCAGCGTTCCTCTAGAGAGATATA). PCR products, digested with BamHI and SalI, were cloned into Gal4-DBD plasmid pSG424 digested with the same enzymes.

For mammalian expression of fusion proteins, PCR was carried out with pCI-mCAR as template. The 5' primer added an EcoRI site (5'ATCCGAATTCTGGGAGGAATGACAGCTATGCTAACA, 3'AATTTCACAAATAAAGCATTTTTTTCAC). To generate p6His-mCAR, the PCR product was digested with EcoRI and SalI and cloned into the mammalian His-Tag vector pRSET-A (Invitrogen) digested with EcoRI and XhoI.