

Spearman's rank correlation coefficient analysis

To determine whether there are differences between the microarray data received from T3 and GC-1 treatments, we used the Spearman's rank order correlation coefficient, r_s ,

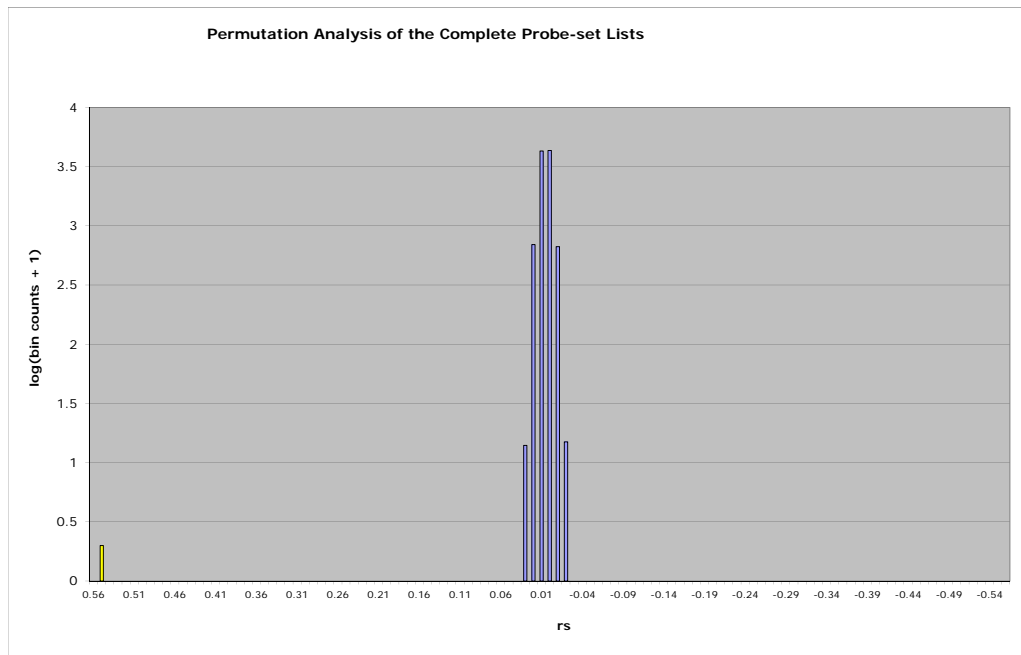
$$r_s = 1 - \frac{6\sum d_i^2}{n(n^2 - 1)}$$

where d is the difference between the probe-set rank in one dataset (T3) and that of the other (GC-1), and n is the number of probe-sets being compared. We decided to conduct the analysis with Affymetrix probe-set identifications instead of aggregating probe-sets into unified identifiers (e.g., Unigene) to eliminate the impact of splice variants.

Affymetrix probe-sets for both datasets were ordered based upon fold induction of ligand-treated versus vehicle. We analyzed both the entire Affymetrix probe-set list ("complete probe-set list"), and probe-sets receiving an adjusted p-value ≤ 0.05 in both datasets ("significant probe-sets").

To determine if the calculated correlation coefficient, r_s , is greater than would be expected by chance, we performed empirical permutation analysis, where the rank-ordering of the genes in one list is randomly shuffled, followed by r_s calculation. The permutation analysis was done 10,000 times using a custom Python script. The p-value is simply the proportion of times that the r_s value in the shuffled list is greater than or equal to the correlation coefficient calculated for the experimental dataset.

In no instance were the shuffled lists r_s greater or equal to that received for **either any** experimental datasets ([HepG2 dataset example](#) see [Figures](#) below).



Permutation Analysis of the Significant Probe-set Lists

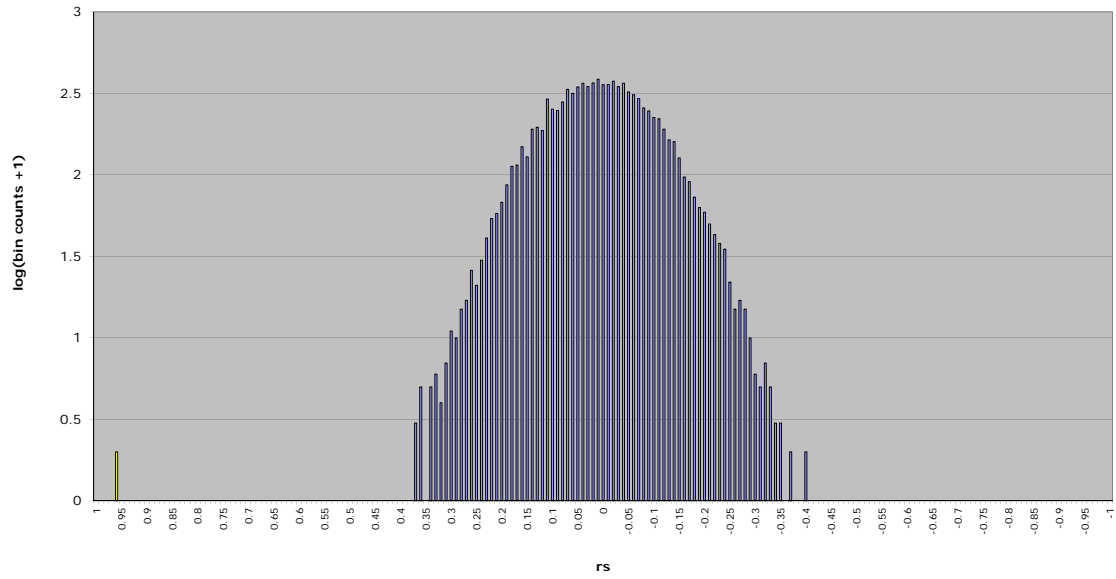


Fig. S1. Verification of hypothyroid status of mice. Induction of hypothyroidism was confirmed by decreased total thyroxine (T_4) levels in blood serum, bar graph represents T_4 levels in different conditions. The slight increase in reactivity in animals after T_3 gavage represents cross-reactivity with T_3 .

Fig. S2. HepG2 cells express TR transcripts. The figure shows RT-PCR results with $Tr\beta 1$ and $TR\alpha 1$ primers relative to GAPDH. There is a slight increase in $TR\beta 1$ expression after ligand treatment, but this did not reach statistical significance.

Fig. S3. Q-PCR analysis confirms that predicted T_3 -inducible genes are not upregulated in liver of T_3 or GC-1-treated mice (A) or HepG2 cells (B) in conditions of our experiments.

Fig. S4. Ligand dose responses with standard TRE-driven reporter gene in HepG2 cells transfected with $TR\beta$ or $TR\alpha$. There is a significant rightward shift in GC-1 dose response obtained with GC-1 in the presence of $TR\alpha$.

Table S1.

PCR primers for mouse liver Q-PCR.

Symbol	Gene Name	TaqMan Assay ID
ANGPTL4	angiopoietin-like-4	Mm00480431_m1
CPT1a	carnitine palmitoyltransferase 1a, liver	Mm00550438_m1
DIO1	deiodinase, iodothyronine, type I	Mm00839358_m1
G6PC	glucose-6-phosphatase, catalytic	Mm00839363_m1
GPD2	glycerol phosphate dehydrogenase 2, mitochondrial	Mm00439082_m1
IDH3a	isocitrate dehydrogenase 3 (NAD ⁺) alpha	Mm00499674_m1
MCAD	acyl-Coenzyme A dehydrogenase, medium chain	Mm00431611_m1
ME1	malic enzyme 1, NADP(+)-dependent, cytosolic	Mm00782380_s1
PCK1	phosphoenolpyruvate carboxykinase 1, cytosolic	Mm01247058_m1
SREBP1c	sterol regulatory element binding transcription factor 1	Mm01138344_m1
THRSP	thyroid hormone responsive	Mm01273967_m1

Sequences of primers for HepG2 QPCR*

Symbol	Accession Number	Gene Name	Sequence (forward)	Sequence (reverse)
G6PC*	NM_000151	Glucose-6-phosphatase, catalytic subunit	gctgctcatttctcatcaa	ttctgtaacagcaatgcctga
PCK1*	NM_002591	Phosphoenolpyruvate carboxykinase 1	agatggaggaagagggcatc	ggtcagtgagagccaaccag
ACSM2	NM_182617	Acyl-CoA synthetase medium-chain family member 2	gaggtggtgaaggcatttgt	ggtgagctgttctgggtcat
ACSL6	NM_001009185	acyl-CoA synthetase long-chain family member 6	atctttccgagacaggacga	cgtggcaatagacgacagac
CPT1A*	NM_001876	Carnitine palmitoyltransferase 1A (liver)	tggtgggctacaaattacgtg	atagttgctgttcacatgagc
THRSP*	NM_003251	Thyroid hormone responsive protein	tcatgcacctcaccgaga	gtcttctatcatgtgaagggatct t
FXR	NM_005123	Nuclear receptor subfamily 1, group H, member 4	gaggaagactcagtccagaatc c	ccttctacgatgtcttctacctcct
ABCB4	NM_000443	ATP-binding cassette, sub-family B (MDR/TAP), member 4	gcatcagcagcaaacacaaaa	tgatggtaccagcgacata
APOC1	NM_001645	apolipoprotein C-I	cctccagcaaggattcagag	caagacgatcgacagaacca
AGPTL4	NM_139314	Angiopoietin-like 4	gcaggatccagcaagtcttc	aaactggctttgcagatgct
DIO1*	NM_000792	deiodinase, iodothyronine, type I	cactgcctgagaggctctacat a	tgtagttcaagggccagat
CYP3A5	NM_000777	Cytochrome P450, family 3, subfamily A, polypeptide 5	aagaaaagtgcctcaacga	gagctccagatcagacagagc
ARG1	NM_000045	Arginase, liver	ggagaccacagtttgcaat	ccactgtggtgtcagtgg
SGK	NM_005627	Serum/glucocorticoid regulated kinase	acccttctctccaccaagt	cccttccgatcacttcaa
FASN	NM_004104	Fatty acid synthase	atgaaggtggtggaggtgct	ggtggccgtgtagctcag

ACACA	NM_19883 4	Acetyl-CoA Carboxylase α	gcctcttctgacaaaagcag	tgatctgtgctgcctggag
SLC2A1	NM_00651 6	solute carrier family 2 (facilitated glucose transporter), member 1	gggccaagagtgtgctaaag	tgccgactcttcttcat
PLA2G2A	NM_00030 0	phospholipase A2, group IIA (platelets, synovial fluid)	atcgctgctgtgcactcat	ttgcacaggtgattctgctc
SORBS1	NM_01538 5	sorbin and SH3 domain containing 1	cagctctgcttcactaaagat	tcatcatgacgtcttcgaataaa
SREBP1a	NM_00417 6	sterol regulatory element binding transcription factor 1	ctgaccgacatcgaagacat	caaataggccaggggaagtca
SREBP1c	NM_00100 5291	sterol regulatory element binding transcription factor 1	ctgaccgacatcgaagggtg	gcatgtcttcgaaagtgcaa
ANGPTL 3	NM_01449 5	angiopoietin-like 3	gggatcacaagcaaaaagga	accaccagcctcctgaataa

* primers were obtained from ProbeFinder for the Human Universal ProbeLibrary (<http://www.universalprobelibrary.com>) as described in Material and Methods.

Table S2. Induced genes in euthyroid mice (≥ 1.7 fold*, $p < 0.05$)

Category	GeneName	Accession No.	Fold change		Gene coded Protein
			T3	GC-1	
Fat and cholesterol metabolism	Stat5a	NM_011488	2.665	2.615	signal transducer and activator of transcription 5A
	Ptgis	NM_008968	2.257	1.537	prostaglandin I2 (prostacyclin) synthase
	Mgll	NM_011844	2.254	1.833	monoglyceride lipase
	Acot11	NM_025590	1.996	1.932	acyl-CoA thioesterase 11
	Elovl6	NM_130450	1.777	1.360	ELOVL family member 6, elongation of long chain fatty acids (yeast)
Lipid metabolism	Cyp17a1	NM_007809	12.624	10.727	cytochrome P450, family 17, subfamily a, polypeptide 1
	Hsd17b7	NM_010476	1.754	1.707	hydroxysteroid (17-beta) dehydrogenase 7
Glucose metabolism	Gpd2	NM_010274	2.606	2.501	glycerol phosphate dehydrogenase 2, mitochondrial
	Trak2	NM_172406	2.021	1.956	trafficking protein, kinesin binding 2
	Hs6st1	NM_015818	1.945	1.942	heparan sulfate 6-O-sulfotransferase 1
	Gne	NM_015828	1.885	2.183	glucosamine
Amino acid metabolism	Shmt1	NM_009171	2.059	1.846	serine hydroxymethyltransferase 1 (soluble)
	Prodh	NM_011172	1.978	1.999	proline dehydrogenase
	Gstt1	NM_008185	1.860	2.262	glutathione S-transferase, theta 1
	Slc22a4	NM_019687	1.720	1.804	solute carrier family 22 (organic cation transporter), member 4
Acetyl-CoA metabolism	Idh3a	NM_029573	2.616	2.073	isocitrate dehydrogenase 3 (NAD+) alpha
Nucleotide metabolism	Bcl3	NM_033601	2.585	3.064	B-cell leukemia/lymphoma 3
	Rab34	NM_033475	2.364	2.587	RAB34, member of RAS oncogene family
	Cebpb	NM_009883	2.141	2.131	CCAAT/enhancer binding protein (C/EBP), beta
	2310003H01Rik	NM_027980	2.058	1.847	RIKEN cDNA 2310003H01 gene
	F2r	NM_010169	2.047	1.750	coagulation factor II (thrombin) receptor
	Rcl1	NM_021525	2.008	2.131	RNA terminal phosphate cyclase-like 1
	Nt5e	NM_011851	1.983	1.164	5' nucleotidase, ecto
	Asap2	NM_001135192	1.966	1.408	RIKEN cDNA 6530401G17 gene
	Npr2	NM_173788	1.891	1.610	natriuretic peptide receptor 2
	Adarb1	NM_130895	1.869	1.837	adenosine deaminase, RNA-specific, B1

	Zfp810	NM_145612	1.828	1.909	zinc finger protein 810
Bile secretion	Slc22a7	NM_144856	3.227	3.447	solute carrier family 22 (organic anion transporter), member 7
	Atp1b1	NM_009721	1.773	1.457	ATPase, Na ⁺ /K ⁺ transporting, beta 1 polypeptide
	Abcb4	NM_008830	1.718	1.571	ATP-binding cassette, sub-family B (MDR/TAP), member 4
Cell proliferation & differentiation	Nrp1	NM_008737	2.382	2.306	neuropilin 1
	Wipf3	NM_001167861	1.821	2.089	WAS/WASL interacting protein family, member 3
	Ulk1	NM_009469	1.732	2.469	Unc-51 like kinase 1 (<i>C. elegans</i>)
	Bbs4	NM_175325	1.729	1.618	Bardet-Biedl syndrome 4 (human)
Signal transduction	Uck1	NM_011675	2.306	1.825	uridine-cytidine kinase 1
	Tns1	NM_027884	2.063	2.168	tensin 1
	Rab43	NM_133717	1.966	2.306	RAB43, member RAS oncogene family
	Gna14	NM_008137	1.877	1.646	guanine nucleotide binding protein, alpha 14
	Cblc	NM_023224	1.776	1.790	Casitas B-lineage lymphoma c
Hormone activity regulation	Thrsp	NM_009381	3.203	3.770	thyroid hormone responsive SPOT14 homolog (<i>Rattus</i>)
	Snx10	NM_028035	1.911	2.316	sorting nexin 10
	Ttr	NM_013697	1.735	1.757	transthyretin
Others	Crybb3	NM_021352	6.474	8.732	crystallin, beta B3
	Tsku	NM_001168541	5.693	4.658	tsukushin
	9030619P08Rik	NM_001039720	4.307	4.287	RIKEN cDNA 9030619P08 gene
	Mmd2	NM_175217	3.823	3.030	monocyte to macrophage differentiation-associated 2
	Wfdc16	NM_001012723	3.537	3.390	WAP four-disulfide core domain 16
	Prei4	NM_028802	3.500	3.843	glycerophosphocholine phosphodiesterase GDE1 homolog (<i>S. cerevisiae</i>)
	AK129341	NM_001045524	3.068	2.257	cDNA sequence AK129341
	Sult5a1	NM_020564	2.909	3.912	sulfotransferase family 5A, member 1
	Sbk1	NM_145587	2.905	2.317	SH3-binding kinase 1
	Sspo	NM_173428	2.855	2.625	SCO-spondin
	Aatk	NM_007377	2.762	3.062	apoptosis-associated tyrosine kinase
	Slc25a45	NM_134154	2.568	2.633	solute carrier family 25, member 45
	Gstt3	NM_133994	2.545	2.160	glutathione S-transferase, theta 3

Synpo	NM_177340	2.484	3.292	synaptopodin
Papss2	NM_011864	2.427	2.053	3'-phosphoadenosine 5'-phosphosulfate synthase 2
Pdp2	NM_001024606	2.349	2.312	pyruvate dehydrogenase phosphatase catalytic subunit 2
Anks1	NM_181413	2.336	2.337	ankyrin repeat and SAM domain containing 1
Fam107b	NM_025626	2.251	2.028	family with sequence similarity 107, member B
D230025D16Rik	NM_145604	2.210	1.704	RIKEN cDNA D230025D16 gene
Stx1a	NM_016801	2.175	1.967	syntaxin 1A (brain)
Lrrc8d	NM_178701	2.140	1.562	leucine rich repeat containing 8D
1700067K01Rik	NM_183097	2.135	1.851	RIKEN cDNA 1700067K01 gene
Lims2	NM_144862	2.103	2.303	LIM and senescent cell antigen like domains 2
Cpne2	NM_153507	2.089	1.828	copine II
Stim2	NM_001081103	2.087	2.157	stromal interaction molecule 2
Fndc5	NM_027402	2.073	2.038	fibronectin type III domain containing 5
H13	NM_010376	2.072	1.913	histocompatibility 13
Tle6	NM_053254	2.003	1.997	transducin-like enhancer of split 6, homolog of Drosophila E(spl)
Tlcd2	NM_027249	1.892	1.774	TLC domain containing 2
Letm1	NM_019694	1.886	1.906	leucine zipper-EF-hand containing transmembrane protein 1
Gorasp1	NM_028976	1.856	2.022	golgi reassembly stacking protein 1
Trp53inp2	NM_178111	1.852	1.934	transformation related protein 53 inducible nuclear protein 2
Abca3	NM_013855	1.842	1.630	ATP-binding cassette, sub-family A (ABC1), member 3
BC013529	NM_145418	1.836	1.693	cDNA sequence BC013529
Pnpla2	NM_025802	1.830	1.972	patatin-like phospholipase domain containing 2
Mapk6	NM_027418	1.811	1.648	mitogen-activated protein kinase 6
G3bp2	NM_011816	1.734	1.495	GTPase activating protein (SH3 domain) binding protein 2
Wfikkn1	NM_001100454	1.726	2.367	WAP, FS, Ig, KU, and NTR-containing protein 1
Serpina6	NM_007618	1.725	1.781	serine (or cysteine) peptidase inhibitor, clade A, member 6
Mtmr1	NM_016985	1.720	1.398	myotubularin related protein 1
Pnpla5	NM_029427	1.720	1.317	patatin-like phospholipase domain containing 5
Rtn4ip1	NM_130892	1.716	1.717	reticulon 4 interacting protein 1
Nadk	NM_138671	1.703	1.409	NAD kinase

* based on T₃ treated values

** $p \geq 0.05$

Table S3. Repressed genes in euthyroid mice (≤ 1.7 fold*, $p < 0.05$)

Category	GeneName	Accession No.	Fold change		Gene coded Protein
			T3	GC-1	
Fat and cholesterol metabolism	Adh4	NM_011996	-2.426	-2.030	alcohol dehydrogenase 4 (class II), pi polypeptide
	Adh1	NM_007409	-1.792	-1.744	alcohol dehydrogenase 1 (class I)
Lipid metabolism	Hsd17b6	NM_013786	-4.019	-5.171	hydroxysteroid (17-beta) dehydrogenase 6
Lipid transport	Abca8a	NM_153145	-4.854	-5.375	ATP-binding cassette, sub-family A (ABC1), member 8a
	Apo17a	NM_029419	-2.502	-2.662	apolipoprotein L 7a
	Abca9	NM_147220	-2.349	-2.437	ATP-binding cassette, sub-family A (ABC1), member 9
	Slco2a1	NM_033314	-1.850	-2.211	solute carrier organic anion transporter family, member 2a1
Glucose metabolism	Ppp1r3c	NM_016854	-7.602	-10.687	protein phosphatase 1, regulatory (inhibitor) subunit 3C
	Stbd1	NM_175096	-2.710	-1.906	starch binding domain 1
Amino acid metabolism	Slc17a8	NM_182959	-3.155	-3.027	solute carrier family 17 (sodium-dependent inorganic phosphate cotransporter), member 8
	Chdh	NM_175343	-1.837	-1.733	choline dehydrogenase
Bile secretion	Aqp8	NM_007474	-2.282	-2.646	aquaporin 8
Nucleotide metabolism	Nr1i3	NM_009803	-3.095	-2.265	nuclear receptor subfamily 1, group I, member 3
	Zfp707	NM_001081065	-2.240	-1.949	zinc finger protein 707
	Rhou	NM_133955	-1.995	-1.864	ras homolog gene family, member U
	Fst	NM_008046	-1.731	-1.847	follistatin
Cell proliferation & differentiation	Ppl	NM_008909	-1.811	-1.643	periplakin
Signal transduction	Sucnr1	NM_032400	-3.934	-4.274	succinate receptor 1
	Igfbp1	NM_008341	-2.062	-3.118	insulin-like growth factor binding protein 1
	Spsb4	NM_145134	-1.841	-1.726	splA/ryanodine receptor domain and SOCS box containing 4
	Arrdc4	NM_025549	-1.723	-1.660	arrestin domain containing 4

Hormone activity regulation	Serpina7	NM_177920	-4.107	-3.723	serine (or cysteine) peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 7
Others	Agxt2l1	NM_001163587	-4.817	-5.035	alanine-glyoxylate aminotransferase 2-like 1
	Gm4952	NM_001167907	-4.011	-4.257	predicted gene 4952
	AC101743.4	NM_001167907	-3.734	-3.332	predicted gene 4956
	Cyp2c44	NM_001167905	-2.972	-3.196	cytochrome P450, family 2, subfamily c, polypeptide 44
	AU018778	NM_144930	-2.628	-3.307	carboxylesterase 1F
	Susd1	NM_001163288	-2.181	-1.901	sushi domain containing 1
	1300014I06Rik	NM_025831	-2.164	-1.986	RIKEN cDNA 1300014I06 gene
	Abcc3	NM_029600	-2.089	-2.005	ATP-binding cassette, sub-family C (CFTR/MRP), member 3
	Ces1	NM_021456	-1.948	-2.337	carboxylesterase 1G
	Lrrc3	NM_145152	-1.948	-2.066	leucine rich repeat containing 3
	Cyp2c55	NM_001167905	-1.946	-2.724	cytochrome P450, family 2, subfamily c, polypeptide 55
	Upb1	NM_133995	-1.822	-1.450	ureidopropionase, beta
	Nqo2	NM_028089	-1.817	-1.738	NAD(P)H dehydrogenase, quinone 2
	Fbxo21	NM_145564	-1.811	-1.729	F-box protein 21
	Inhbc	NM_010565	-1.804	-1.604	inhibin beta-C
	Slc25a37	NM_026331	-1.775	-1.511	solute carrier family 25, member 37
	Prss8	NM_133351	-1.766	-1.807	protease, serine, 8 (prostasin)
	Fam176a	NM_145570	-1.699	-1.153	family with sequence similarity 176, member A

* based on T₃ treated values

Table S4. Induced genes in hypothyroid mice (≥ 1.7 fold*, $p < 0.05$)

Category	Gene Symbol	Accession No.	Fold Change		Gene coded Protein
			T3	GC-1	
Fat and cholesterol metabolism	Cyp17a1	NM_007809	15.802	12.367	cytochrome P450, family 17, subfamily a, polypeptide 1
	Mgll	NM_011844	3.805	4.047	monoglyceride lipase
	Acot11	NM_025590	3.276	4.329	acyl-CoA thioesterase 11
	Mup4	NM_008648	2.938	3.204	major urinary protein 4
	Cyp7b1	NM_007825	2.886	2.888	cytochrome P450, family 7, subfamily b, polypeptide 1
	Stat5a	NM_011488	2.753	2.760	signal transducer and activator of transcription 5A
	Gne	NM_015828	2.655	2.635	glucosamine
	Ang	NM_007447	2.486	2.599	angiogenin, ribonuclease, RNase A family, 5
	Pnpla2	NM_025802	2.336	2.229	patatin-like phospholipase domain containing 2
	Sqle	NM_009270	2.288	1.726	squalene epoxidase
	Ppard	NM_011145	2.257	2.011	peroxisome proliferator activator receptor delta
	Cyp27a1	NM_024264	2.254	2.465	cytochrome P450, family 27, subfamily a, polypeptide 1
	Aspg	NM_001081169	2.146	1.837	asparaginase homolog (<i>S. cerevisiae</i>)
	Daglb	NM_144915	2.030	1.901	diacylglycerol lipase, beta
	Gm4738	NM_144511	2.014	2.634	carboxylesterase 3B
	Hsd17b2	NM_008290	1.917	1.728	hydroxysteroid (17-beta) dehydrogenase 2
	Slc35c1	NM_145832	1.871	1.289	solute carrier family 35, member C1
	Bbs4	NM_175325	1.841	1.460	Bardet-Biedl syndrome 4 (human)
	Vav2	NM_009500	1.832	2.203	vav 2 oncogene
	Apof	NM_133997	1.786	1.912	apolipoprotein F
2010111I01Rik	NM_028079	1.779	1.761	RIKEN cDNA 2010111I01 gene	
Lipid metabolism	Abca3	NM_013855	2.580	3.613	ATP-binding cassette, sub-family A (ABC1), member 3
	Abcd3	NM_008991	1.992	2.418	ATP-binding cassette, sub-family D (ALD), member 3
Glucose metabolism	Gpd2	NM_010274	4.673	5.172	glycerol phosphate dehydrogenase 2, mitochondrial
	Slc3a1	NM_009205	3.129	2.070	solute carrier family 3, member 1
	Igfbp4	NM_010517	2.261	1.977	insulin-like growth factor binding protein 4
	Trak2	NM_172406	2.068	2.075	trafficking protein, kinesin binding 2
	St3gal3	NM_009176	2.001	2.018	ST3 beta-galactoside alpha-2,3-sialyltransferase 3
	Hs6st1	NM_015818	1.862	1.558	heparan sulfate 6-O-sulfotransferase 1

Acetyl-CoA metabolism	Nudt7	NM_024446	5.097	5.028	nudix (nucleoside diphosphate linked moiety X)-type motif 7
	Idh3a	NM_029573	3.327	4.333	isocitrate dehydrogenase 3 (NAD+) alpha
	Foxred1	NM_172291	1.913	1.468	FAD-dependent oxidoreductase domain containing 1
Amino acid metabolism	Slc6a12	NM_133661	3.186	3.189	solute carrier family 6 (neurotransmitter transporter, betaine/GABA), member 12
	Prodh	NM_011172	2.879	3.014	proline dehydrogenase
	Prhoxnb	NM_001039678	2.289	2.007	parahox cluster neighbor
Nucleotide metabolism	Upp2	NM_029692	3.615	7.848	uridine phosphorylase 2
	Hr	NM_021877	2.827	1.848	hairless
	Rcl1	NM_021525	2.768	2.606	RNA terminal phosphate cyclase-like 1
	Ung	NM_011677	2.581	2.069	uracil DNA glycosylase
	Adarb1	NM_130895	1.701	2.352	adenosine deaminase, RNA-specific, B1
Bile secretion	Pdp2	NM_001024606	4.072	4.834	pyruvate dehydrogenase phosphatase catalytic subunit 2
	Slc22a7	NM_144856	3.827	6.142	solute carrier family 22 (organic anion transporter), member 7
Cell proliferation & differentiation	Cebpb	NM_009883	3.757	3.596	CCAAT/enhancer binding protein (C/EBP), beta
	Nrp1	NM_008737	3.028	2.164	neuropilin 1
	Csrp3	NM_013808	2.694	2.208	cysteine and glycine-rich protein 3
	Bcl3	NM_033601	2.658	2.743	B-cell leukemia/lymphoma 3
	Hopx	NM_175606	2.527	2.154	HOP homeobox
	Mmd	NM_026178	2.513	3.248	monocyte to macrophage differentiation-associated
	Klf13	NM_021366	2.019	2.833	Kruppel-like factor 13
	Fgf21	NM_020013	2.014	1.885	fibroblast growth factor 21
	Il15ra	NM_133836	1.706	1.617	interleukin 15 receptor, alpha chain
Signal transduction	Arhgap26	NM_175164	2.237	2.881	Rho GTPase activating protein 26
	Gng10	NM_025277	2.036	2.043	guanine nucleotide binding protein (G protein), gamma 10
	Sdc4	NM_011521	1.914	1.902	syndecan 4
	Gpr97	NM_173036	1.712	1.390	G protein-coupled receptor 97

Hormone activity regulation	Dio1	NM_007860	31.720	30.805	deiodinase, iodothyronine, type I
	Thrsp	NM_009381	10.132	12.798	thyroid hormone responsive SPOT14 homolog (Rattus)
	Snx10	NM_028035	2.260	2.461	sorting nexin 10
Others	Crybb3	NM_021352	10.737	4.485	crystallin, beta B3
	Slc25a45	NM_134154	10.445	10.724	solute carrier family 25, member 45 glycerophosphocholine phosphodiesterase GDE1 homolog (S. cerevisiae)
	Prei4	NM_028802	9.126	10.016	cerevisiae)
	Sbk1	NM_145587	6.060	8.017	SH3-binding kinase 1
	Mup6	NM_001081285	5.430	5.842	major urinary protein 6
	Osgin1	NM_027950	5.397	5.872	oxidative stress induced growth inhibitor 1
	9030619P08Rik	NM_001039720	5.387	7.500	RIKEN cDNA 9030619P08 gene
	Rab34	NM_033475	5.249	4.016	RAB34, member of RAS oncogene family
	Trp53inp2	NM_178111	5.244	4.379	transformation related protein 53 inducible nuclear protein 2
	Rarres1	NM_001164763	4.980	5.011	retinoic acid receptor responder (tazarotene induced) 1
	Tlcd2	NM_027249	4.774	4.839	TLC domain containing 2
	Cela2a	NM_007919	4.642	6.771	chymotrypsin-like elastase family, member 2A
	Wfdc12	NM_138684	4.553	2.613	WAP four-disulfide core domain 12
	Ankhd1	NM_201256	4.438	2.003	ankyrin repeat and KH domain containing 1 proteoglycan 4 (megakaryocyte stimulating factor, articular superficial zone protein)
	Prg4	NM_021400	4.307	2.346	superficial zone protein)
	Aatk	NM_007377	3.526	3.807	apoptosis-associated tyrosine kinase
	Synpo	NM_177340	3.315	2.593	synaptopodin
	Slc25a30	NM_026232	3.115	3.333	solute carrier family 25, member 30
	Pfkfb4	NM_173019	3.015	1.758	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4
	Tsku	NM_001168541	2.990	4.951	tsukushin
	Ctsc	NM_009982	2.777	2.605	cathepsin C
	Lims2	NM_144862	2.763	3.308	LIM and senescent cell antigen like domains 2
	Cyp2c70	NM_145499	2.547	3.420	cytochrome P450, family 2, subfamily c, polypeptide 70
	D230025D16Rik	NM_145604	2.458	2.884	RIKEN cDNA D230025D16 gene
	Epb4.1	NM_183428	2.440	2.228	erythrocyte protein band 4.1
	Coq10a	NM_001081040	2.409	2.327	coenzyme Q10 homolog A (yeast)
	Lrrc8d	NM_178701	2.383	2.165	leucine rich repeat containing 8D
	Ostb	NM_178933	2.371	2.163	organic solute transporter beta

Nelf	NM_020276	2.352	2.807	nasal embryonic LHRH factor
Serpina3g	NM_009251	2.344	2.472	serine (or cysteine) peptidase inhibitor, clade A, member 3G
Smagp	NM_174992	2.339	2.378	small cell adhesion glycoprotein
Letm1	NM_019694	2.310	2.153	leucine zipper-EF-hand containing transmembrane protein 1
Klhl25	NM_182782	2.305	1.897	kelch-like 25 (Drosophila)
Uck1	NM_011675	2.299	3.030	uridine-cytidine kinase 1
Ulk1	NM_009469	2.220	2.378	Unc-51 like kinase 1 (C. elegans)
N4bp211	NM_133898	2.164	3.118	NEDD4 binding protein 2-like 1
Npr2	NM_173788	2.158	2.897	natriuretic peptide receptor 2
Sult1d1	NM_016771	2.137	2.319	sulfotransferase family 1D, member 1
Tomm40l	NM_001037170	2.131	2.776	translocase of outer mitochondrial membrane 40 homolog-like (yeast)
Dnaja3	NM_023646	2.109	1.659	DnaJ (Hsp40) homolog, subfamily A, member 3
Cpsf4l	NM_029794	2.099	2.150	cleavage and polyadenylation specific factor 4-like
Tlcd1	NM_026708	2.079	2.134	TLC domain containing 1
Rab43	NM_133717	2.066	2.205	RAB43, member RAS oncogene family
Slc46a3	NM_027872	2.056	2.295	solute carrier family 46, member 3
Grhpr	NM_080289	2.027	1.831	glyoxylate reductase/hydroxypyruvate reductase
1700019G17Rik	NM_029331	1.999	1.712	RIKEN cDNA 1700019G17 gene
Tapt1	NM_173764	1.957	1.789	transmembrane anterior posterior transformation 1
Ciapin1	NM_134141	1.945	1.949	cytokine induced apoptosis inhibitor 1
H13	NM_010376	1.932	2.047	histocompatibility 13
Nudt18	NM_024815	1.929	1.844	nudix (nucleoside diphosphate linked moiety X)-type motif 18
Mtap7d1	NM_144941	1.926	1.625	microtubule-associated protein 7 domain containing 1
Wipi1	NM_145940	1.914	1.690	WD repeat domain, phosphoinositide interacting 1
Decr2	NM_011933	1.882	1.744	2-4-dienoyl-Coenzyme A reductase 2, peroxisomal
Fam107b	NM_025626	1.877	2.436	family with sequence similarity 107, member B
Anks1	NM_181413	1.856	1.707	ankyrin repeat and SAM domain containing 1
Mapk6	NM_027418	1.841	1.765	mitogen-activated protein kinase 6
Dexi	NM_021428	1.800	2.231	dexamethasone-induced transcript
Tubb6	NM_026473	1.778	1.733	tubulin, beta 6
Dynlrb1	NM_025947	1.776	1.876	dynein light chain roadblock-type 1
Slc25a42	NM_001007570	1.775	1.945	solute carrier family 25, member 42
Cobl	NM_172496	1.770	1.785	cordón-bleu
Egfr	NM_207655	1.752	0.958	epidermal growth factor receptor

Tor1a

NM_144884

1.707

1.728

torsin family 1, member A (torsin A)

* based on T₃ treated values

Table S5. Repressed genes in hypothyroid mice (≤ 1.7 fold*, $p < 0.05$)

Category	Gene Symbol	Accession No.	Fold Change		Gene coded Protein
			T3	GC-1	
Fat and cholesterol metabolism	Acot1	NM_012006	-15.575	-14.603	acyl-CoA thioesterase 1
	Adh4	NM_011996	-3.921	-2.508	alcohol dehydrogenase 4 (class II), pi polypeptide
	Acot4	NM_134247	-3.072	-2.335	acyl-CoA thioesterase 4
	Pparg	NM_011146	-2.357	-2.138	peroxisome proliferator activated receptor gamma
	Cyp4a12b	NM_172306	-2.205	-2.027	cytochrome P450, family 4, subfamily a, polypeptide 12B
	Hpgd	NM_008278	-2.110	-1.376	hydroxyprostaglandin dehydrogenase 15 (NAD)
	Cyp1a2	NM_009993	-2.018	-1.963	cytochrome P450, family 1, subfamily a, polypeptide 2
	Lipa	NM_021460	-1.831	-1.342	lysosomal acid lipase A
	Acadm	NM_007382	-1.772	-1.840	acyl-Coenzyme A dehydrogenase, medium chain
Glucose metabolism	Ppp1r3c	NM_016854	-9.027	-17.838	protein phosphatase 1, regulatory (inhibitor) subunit 3C
	Entpd5	NM_007647	-3.171	-2.579	ectonucleoside triphosphate diphosphohydrolase 5
	St6gal1	NM_145933	-2.475	-2.598	beta galactoside alpha 2,6 sialyltransferase 1
Amino acid metabolism	Cth	NM_145953	-4.062	-2.252	cystathionase (cystathionine gamma-lyase)
	Htati2	NM_016865	-2.476	-2.406	HIV-1 tat interactive protein 2, homolog (human)
	Dct	NM_010024	-2.070	-1.460	dopachrome tautomerase
	Chdh	NM_175343	-1.954	-1.778	choline dehydrogenase
	Gclm	NM_008129	-1.874	-1.607	glutamate-cysteine ligase, modifier subunit
	Hagh	NM_024284	-1.858	-1.464	hydroxyacyl glutathione hydrolase
	Thns12	NM_178413	-1.757	-2.035	threonine synthase-like 2 (bacterial)
Nucleotide metabolism	Mcm10	NM_027290	-3.514	-2.648	minichromosome maintenance deficient 10 (<i>S. cerevisiae</i>)
	Cebpe	NM_207131	-2.874	-2.895	CCAAT/enhancer binding protein (C/EBP), epsilon
	Creg1	NM_011804	-2.517	-2.360	cellular repressor of E1A-stimulated genes 1
	Zfp707	NM_001081065	-2.474	-3.148	zinc finger protein 707
	Zfp1	NM_009569	-2.465	-1.949	zinc finger protein, multitype 1
	Cdkn1c	NM_009876	-2.427	-2.618	cyclin-dependent kinase inhibitor 1C (P57)
	Tcea3	NM_011542	-2.322	-1.374	transcription elongation factor A (SII), 3
	Nfyb	NM_010914	-2.212	-1.673	nuclear transcription factor-Y beta
	Tsc22d3	NM_010286	-2.153	-2.099	TSC22 domain family, member 3

	Rfx6	NM_001085374	-1.996	-1.891	regulatory factor X, 6
	Clpx	NM_011802	-1.971	-3.518	caseinolytic peptidase X (E.coli)
	Adssl1	NM_007421	-1.924	-1.963	adenylosuccinate synthetase like 1
	Zfp3611	NM_007564	-1.765	-1.643	zinc finger protein 36, C3H type-like 1
	Esrp2	NM_176838	-1.705	-1.624	epithelial splicing regulatory protein 2
Lipid transport	Apol7a	NM_029419	-4.143	-2.916	apolipoprotein L 7a
	Osbp13	NM_027881	-2.679	-2.451	oxysterol binding protein-like 3
	Slco2a1	NM_033314	-2.282	-2.303	solute carrier organic anion transporter family, member 2a1
Amino acid transport	Slc1a2	NM_001077515	-2.280	-1.646	solute carrier family 1 (glial high affinity glutamate transporter), member 2
	Slc17a8	NM_182959	-1.960	-2.071	solute carrier family 17 (sodium-dependent inorganic phosphate cotransporter), member 8
	Slc44a1	NM_133891	-1.923	-1.866	solute carrier family 44, member 1
Bile secretion	Abcc3	NM_029600	-2.297	-1.943	ATP-binding cassette, sub-family C (CFTR/MRP), member 3
	Abcc2	NM_013806	-1.892	-1.834	ATP-binding cassette, sub-family C (CFTR/MRP), member 2
	Aqp4	NM_009700	-1.768	-1.784	aquaporin 4
Cell proliferation & differentiation	Gas7	NM_008088	-5.185	-4.703	growth arrest specific 7
	Prok1	NM_029562	-2.743	-2.113	prokineticin 1
	Olig1	NM_016968	-2.626	-2.793	oligodendrocyte transcription factor 1
	Btg1	NM_007569	-2.614	-2.557	B-cell translocation gene 1, anti-proliferative
	Ildr2	NM_001164528	-2.182	-2.189	immunoglobulin-like domain containing receptor 2
	Dsp	NM_023842	-2.027	-1.726	desmoplakin
	Casp6	NM_009811	-2.011	-1.864	caspase 6
	Sdc1	NM_011519	-1.805	-1.849	syndecan 1
	Casp9	NM_015733	-1.751	-1.372	caspase 9
Signal transduction	Sucnr1	NM_032400	-4.268	-3.173	succinate receptor 1
	Plxna2	NM_008882	-2.335	-2.269	plexin A2

	Arrdc4	NM_025549	-1.811	-2.177	arrestin domain containing 4
	Rab32	NM_026405	-1.733	-1.605	RAB32, member RAS oncogene family
	Wwc1	NM_170779	-1.696	-1.426	WW, C2 and coiled-coil domain containing 1
Hormone activity regulation	Serpina7	NM_177920	-11.197	-8.046	serine (or cysteine) peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 7
Other	Cbr3	NM_173047	-9.004	-7.328	carbonyl reductase 3
	Agxt211	NM_027907	-5.337	-3.874	alanine-glyoxylate aminotransferase 2-like 1
	Gm4952	NM_001167907	-4.528	-4.218	predicted gene 4952
	Abca8a	NM_153145	-4.122	-3.426	ATP-binding cassette, sub-family A (ABC1), member 8a
	Mfsd7c	NM_145447	-3.188	-2.986	major facilitator superfamily domain containing 7C
	Car14	NM_011797	-3.064	-3.144	carbonic anhydrase 14
	Oat	NM_016978	-2.918	-2.417	ornithine aminotransferase
	Spon2	NM_133903	-2.837	-3.932	spondin 2, extracellular matrix protein
	Ndrp1	NM_008681	-2.792	-2.632	N-myc downstream regulated gene 1
	Fbxo21	NM_145564	-2.735	-2.469	F-box protein 21
	Fam129b	NM_146119	-2.689	-3.495	family with sequence similarity 129, member B
	Eps8l2	NM_133191	-2.651	-2.125	EPS8-like 2
	Susd1	NM_001163288	-2.530	-2.745	sushi domain containing 1
	Ces1b	NM_001081372	-2.499	-1.990	carboxylesterase 1B
	Fmo5	NM_010232	-2.468	-2.129	flavin containing monooxygenase 5
	Ppm1k	NM_175523	-2.389	-1.819	protein phosphatase 1K (PP2C domain containing)
	Mgst3	NM_025569	-2.348	-2.264	microsomal glutathione S-transferase 3
	Slc25a37	NM_026331	-2.341	-2.355	solute carrier family 25, member 37
	Hectd2	NM_172637	-2.292	-2.235	HECT domain containing 2
	Nqo1	NM_008706	-2.275	-2.194	NAD(P)H dehydrogenase, quinone 1
	Pcp4l1	NM_025557	-2.274	-2.173	Purkinje cell protein 4-like 1
	Cyp2c44	NM_001167905	-2.262	-2.223	cytochrome P450, family 2, subfamily c, polypeptide 44
	Cyp2d26	NM_029562	-2.262	-2.433	cytochrome P450, family 2, subfamily d, polypeptide 26
	Arsa	NM_009713	-2.259	-2.106	arylsulfatase A
	Gstm4	NM_026764	-2.170	-1.656	glutathione S-transferase, mu 4
	Syt1	NM_009306	-2.141	-1.766	synaptotagmin I
	Sgk2	NM_013731	-2.125	-1.845	serum/glucocorticoid regulated kinase 2

4933422H20Rik	NM_001033775	-2.110	-1.908	RIKEN cDNA 4933422H20 gene
Acat3	NM_153151	-2.091	-1.635	acetyl-Coenzyme A acetyltransferase 3
Krt23	NM_033373	-2.088	-1.861	keratin 23
1700037H04Rik	NM_026091	-2.074	-1.938	RIKEN cDNA 1700037H04 gene
Cpamd8	NM_008646	-2.066	-1.681	murinoglobulin 2
A230050P20Rik	NM_175687	-2.009	-2.286	RIKEN cDNA A230050P20 gene
Pnkd	NM_019999	-2.006	-2.335	paroxysmal nonkinesiogenic dyskinesia
Cmb1	NM_181588	-1.994	-1.824	carboxymethylenebutenolidase-like (<i>Pseudomonas</i>)
Lhpp	NM_029609	-1.992	-2.200	phospholysine phosphohistidine inorganic pyrophosphate phosphatase
Spag4	NM_139151	-1.976	-1.634	sperm associated antigen 4
Hyi	NM_026601	-1.966	-2.155	hydroxypyruvate isomerase homolog (<i>E. coli</i>)
Odf3b	NM_001013022	-1.952	-2.153	outer dense fiber of sperm tails 3B
Prss8	NM_133351	-1.937	-1.760	protease, serine, 8 (prostasin)
Abcb6	NM_023732	-1.933	-1.662	ATP-binding cassette, sub-family B (MDR/TAP), member 6
Comt1	NM_007744	-1.929	-2.048	catechol-O-methyltransferase
Abca9	NM_147220	-1.896	-1.742	ATP-binding cassette, sub-family A (ABC1), member 9
Trp53inp1	NM_021897	-1.885	-1.278	transformation related protein 53 inducible nuclear protein 1
Ireb2	NM_022655	-1.878	-1.753	iron responsive element binding protein 2
Daam1	NM_172464	-1.876	-1.796	dishevelled associated activator of morphogenesis 1
Pcbp4	NM_021567	-1.874	-1.679	poly(rC) binding protein 4
Il17rb	NM_019583	-1.840	-1.774	interleukin 17 receptor B
Slc35d2	NM_001001321	-1.835	-1.723	solute carrier family 35, member D2
Tm4sf4	NM_145539	-1.805	-2.202	transmembrane 4 superfamily member 4
Upb1	NM_133995	-1.801	-1.800	ureidopropionase, beta
Gstm2	NM_008183	-1.801	-1.557	glutathione S-transferase, mu 2
Blvrb	NM_144923	-1.791	-1.507	biliverdin reductase B (flavin reductase (NADPH))
Nt5dc2	NM_027289	-1.778	-1.781	5'-nucleotidase domain containing 2
Tmem51	NM_145402	-1.772	-1.828	transmembrane protein 51
Slc35d1	NM_177732	-1.748	-1.392	solute carrier family 35 (UDP-glucuronic acid/UDP-N-acetylgalactosamine dual transporter), member D1
Srxn1	NM_029688	-1.742	-1.961	sulfiredoxin 1 homolog (<i>S. cerevisiae</i>)
Fam169b	NM_001013811	-1.739	-1.423	family with sequence similarity 169, member B
Mocs1	NM_028464	-1.703	-1.559	molybdenum cofactor synthesis 1
Gstm6	NM_008184	-1.702	-1.426	glutathione S-transferase, mu 6

Lnx2

NM_080795

-1.701

-1.996

ligand of numb-protein X 2

* based on T₃ treated values

Ligand	Induced	Suppressed
T ₃	104 (42)	10 (10)
GC-1	70 (26)	5 (5)

Table S6. Number of genes regulated by T₃ and GC-1 in HepG2 (adjusted p-value ≤ 0.05). Numbers in parenthesis indicate the subset of genes regulated more than 1.7 fold.

Table S7. Induced Genes HepG2 (≥ 1.7 fold*, $p \leq 0.05$)

Category	Gene Symbol	Accession. No.	Fold Change		Gene encoded Protein
			T ₃	GC-1	
Glucose metabolism	G6PC	NM_000151	5.405	3.882	Glucose-6-phosphatase, catalytic subunit
	PCK1	NM_002591	2.723	2.073	Phosphoenolpyruvate carboxykinase 1 (PEPCK)
	GBE1	NM_000158	1.917	1.759	Glucan (1, 4-alpha-), branching enzyme 1
Fat metabolism	ACSM2	NM_001010845	3.260	2.865	Acyl-CoA synthetase medium-chain family member 2
	CPT1A	NM_001876	2.485	2.12	Carnitine palmitoyltransferase 1A (liver) (isoform 1)
	CYP4F3	NM_000896	2.081	1.808	Cytochrome P450, family 4, subfamily F, polypeptide 3
	ANGPTL4	NM_139314	2.023	1.627	Angiopoietin-like 4
Bile acid/steroid metabolism	NR1H4	NM_005123	1.883	1.781	Nuclear receptor subfamily 1, group H, member 4) (FXR)
	HSD17B2	NM_002153	1.911	1.748	Hydroxysteroid (17-beta) dehydrogenase 2
Amino acid metabolism/transport	SLC16A6	NM_004694	3.017	2.367	Solute carrier family 16, member 6 (monocarboxylic acid transporter 7)
	SLC1A2	NM_004171	1.770	1.594	Solute carrier family 1 (glial high affinity glutamate transporter), member 2
	HAL	NM_002108	1.862	1.287**	Histidine ammonia- lyase
	ARG1	NM_000045	1.701	1.443**	Arginase, liver
Apoptosis	TNFSF10	NM_003810	2.917	2.380	Tumor necrosis factor (ligand) superfamily, member 10
	GADD45B	NM_015675	1.843	1.762	Growth arrest and DNA-damage-inducible, beta
Protein phosphorylation/signal transduction	C8orf4	NM_020130	2.228	2.081	Chromosome 8 open reading frame 4
	SGK	NM_005627	2.128	2.190	Serum/glucocorticoid regulated kinase
	C10orf10	NM_007021	2.007	1.952	Chromosome 10 open reading frame 10
	TNS1	NM_022648	1.913	1.565**	Tensin 1
Blood coagulation	FGA	NM_000508	2.162	2.040	Fibrinogen alpha chain (FGA), transcript variant alpha-E
	SERPINE1	NM_000602	1.923	1.484	Serpin peptidase inhibitor, clade E(nexin, plasminogen activator inhibitor type 1), member 1
	FGB	NM_005141	1.741	1.654	Fibrinogen beta chain
Immune system /complement activation	C8B	NM_000066	2.312	2.062	Complement component 8, beta polypeptide
	CD14	NM_000591	2.251	2.071	CD14 molecule
	C8A	NM_000562	1.820	1.683	Complement component 8, alpha polypeptide
	ISG20	NM_002201	1.803	1.633	Interferon stimulated exonuclease gene 20kDa
	EBI3	NM_005755	1.709	1.546	Epstein-Barr virus induced gene 3
Xenobiotics metabolism by P450	GSTA1	NM_000846	3.112	2.632	Glutathione S-transferase A1
	UGT2B4	NM_021139	2.302	2.290	UDP glucuronosyltransferase 2 family, polypeptide B4
	CYP3A5	NM_000777	1.893	2.007	Cytochrome P450, family 3, subfamily A, polypeptide 5

Others	LOC55908	NM_018687	3.186	2.572	Hepatocellular carcinoma-associated gene TD26
	KLF9	NM_001206	3.033	3.059	Kruppel-like factor 9 (KLF9)
	SCNN1A	NM_001038	2.946	2.721	Sodium channel, nonvoltage-gated 1 alpha
	HAMP	NM_021175	2.471	2.098	Hepcidin antimicrobial peptide
	C14orf139	XR_040801	2.172	2.124	chromosome 14 open reading frame 139
	LOX	NM_002317	1.981	1.592	Lysyl oxidase
	MMP11	NM_005940	1.906	1.677	Matrix metalloproteinase 11 (stromelysin 3)
	SAA4	NM_006512	1.826	1.706	Serum amyloid A4, constitutive
	CA9	NM_001216	1.760	1.559	Carbonic anhydrase IX
	CEBPB	NM_005194	1.750	1.650	CCAAT/enhancer binding protein (C/EBP), beta
	HGFAC	NM_001528	1.713	1.495	HGF activator
	ABCC6	NM_001079528	1.712	1.461	ATP-binding cassette, sub-family C (CFTR/MRP), member 6

* based on T₃ treated values

** $p \geq 0.05$

Table S7. Induced Genes HepG2 (≥ 1.7 fold*, $p \leq 0.05$)

Category	Gene Symbol	Accession. No.	Fold Change		Gene encoded Protein
			T ₃	GC-1	
Glucose metabolism	G6PC	NM_000151	5.405	3.882	Glucose-6-phosphatase, catalytic subunit
	PCK1	NM_002591	2.723	2.073	Phosphoenolpyruvate carboxykinase 1 (PEPCK)
	GBE1	NM_000158	1.917	1.759	Glucan (1, 4-alpha-), branching enzyme 1
Fat metabolism	ACSM2	NM_001010845	3.260	2.865	Acyl-CoA synthetase medium-chain family member 2
	CPT1A	NM_001876	2.485	2.12	Carnitine palmitoyltransferase 1A (liver) (isoform 1)
	CYP4F3	NM_000896	2.081	1.808	Cytochrome P450, family 4, subfamily F, polypeptide 3
	ANGPTL4	NM_139314	2.023	1.627	Angiopoietin-like 4
Bile acid/steroid metabolism	NR1H4	NM_005123	1.883	1.781	Nuclear receptor subfamily 1, group H, member 4) (FXR)
	HSD17B2	NM_002153	1.911	1.748	Hydroxysteroid (17-beta) dehydrogenase 2
Amino acid metabolism/ transport	SLC16A6	NM_004694	3.017	2.367	Solute carrier family 16, member 6 (monocarboxylic acid transporter 7)
	SLC1A2	NM_004171	1.770	1.594	Solute carrier family 1 (glial high affinity glutamate transporter), member 2
	HAL	NM_002108	1.862	1.287**	Histidine ammonia- lyase
	ARG1	NM_000045	1.701	1.443**	Arginase, liver
Apoptosis	TNFSF10	NM_003810	2.917	2.380	Tumor necrosis factor (ligand) superfamily, member 10
	GADD45B	NM_015675	1.843	1.762	Growth arrest and DNA-damage-inducible, beta
Protein phosphorylation/ signal transduction	C8orf4	NM_020130	2.228	2.081	Chromosome 8 open reading frame 4
	SGK	NM_005627	2.128	2.190	Serum/glucocorticoid regulated kinase
	C10orf10	NM_007021	2.007	1.952	Chromosome 10 open reading frame 10
	TNS1	NM_022648	1.913	1.565**	Tensin 1
Blood coagulation	FGA	NM_000508	2.162	2.040	Fibrinogen alpha chain (FGA), transcript variant alpha-E
	SERPINE1	NM_000602	1.923	1.484	Serpin peptidase inhibitor, clade E(nexin, plasminogen activator inhibitor type 1), member 1
	FGB	NM_005141	1.741	1.654	Fibrinogen beta chain
Immune system /complement activation	C8B	NM_000066	2.312	2.062	Complement component 8, beta polypeptide
	CD14	NM_000591	2.251	2.071	CD14 molecule
	C8A	NM_000562	1.820	1.683	Complement component 8, alpha polypeptide
	ISG20	NM_002201	1.803	1.633	Interferon stimulated exonuclease gene 20kDa
	EBI3	NM_005755	1.709	1.546	Epstein-Barr virus induced gene 3
Xenobiotics metabolism by P450	GSTA1	NM_000846	3.112	2.632	Glutathione S-transferase A1
	UGT2B4	NM_021139	2.302	2.290	UDP glucuronosyltransferase 2 family, polypeptide B4
	CYP3A5	NM_000777	1.893	2.007	Cytochrome P450, family 3, subfamily A, polypeptide 5

Others	LOC55908	NM_018687	3.186	2.572	Hepatocellular carcinoma-associated gene TD26
	KLF9	NM_001206	3.033	3.059	Kruppel-like factor 9 (KLF9)
	SCNN1A	NM_001038	2.946	2.721	Sodium channel, nonvoltage-gated 1 alpha
	HAMP	NM_021175	2.471	2.098	Hepcidin antimicrobial peptide
	C14orf139	XR_040801	2.172	2.124	chromosome 14 open reading frame 139
	LOX	NM_002317	1.981	1.592	Lysyl oxidase
	MMP11	NM_005940	1.906	1.677	Matrix metalloproteinase 11 (stromelysin 3)
	SAA4	NM_006512	1.826	1.706	Serum amyloid A4, constitutive
	CA9	NM_001216	1.760	1.559	Carbonic anhydrase IX
	CEBPB	NM_005194	1.750	1.650	CCAAT/enhancer binding protein (C/EBP), beta
	HGFAC	NM_001528	1.713	1.495	HGF activator
	ABCC6	NM_001079528	1.712	1.461	ATP-binding cassette, sub-family C (CFTR/MRP), member 6

* based on T₃ treated values

** $p \geq 0.05$

Table S8. HepG2 Inhibited Genes ($p \leq 0.05$)

Gene Symbol	Accession. No.	% of Control		Gene encoded Protein	Biological process
		T ₃	GC-1		
SLC2A1	NM_006516	48.2	56.8	solute carrier family 2 (facilitated glucose transporter), member 1	A major glucose transporter in the mammalian blood-brain barrier
KIAA1199	NM_018689	52.5	63.2	KIAA1199 protein (KIAA1199)	Cell mortality
HS3ST3A1	NM_006042	56.5	69.1*	Heparan sulfate (glucosamine) 3-O-sulfotransferase 3A1	multiple biologic activities
FAM46A	NM_017633	60.2	59.5	family with sequence similarity 46, member A	(multi-function?)
SORBS1	NM_015385	61.3	69.5*	Sorbin and SH3 domain containing 1	Insulin signaling pathway
CD24	NM_013230	62.7	63.0	CD24 molecule	Signal transduction
SCGN	NM_006998	63.5	71.3*	secretagogin, EF-hand calcium binding protein	Cell proliferation
SERPINE2	NM_006216	69.8	81.7*	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2	Anti-coagulant
PLA2G2A	NM_000300	70.1	83.4*	phospholipase A2, group IIA (platelets, synovial fluid)	Lipid metabolism
SLC1A4	NM_003038	73.0	74.2	solute carrier family 1 (glutamate/neutral amino acid transporter), member 4	Amino acid transport

* $p \geq 0.05$

Supplimental links

SLC2A1

1. http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=pubmed&list_uids=3839598 (<http://links.jstor.org/sici?sici=0036-8075%2819850906%293%3A229%3A4717%3C941%3ASASOAH%3E2.0.CO%3B2-S>)
2. <http://www.ncbi.nlm.nih.gov/sites/entrez>

HS3ST3A1

<http://www.jbc.org/cgi/reprint/270/19/11267>

FAM46A

http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?val=NLM_017633.2&dopt=gb

KIAA1199

http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T54-4H3938N-3&_user=4430&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000059594&_version=1&_urlVersion=0&_userid=4430&md5=7011641dd6d664f97d08febf1b9843f

SORBS1

1. http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WG1-458NMWP-40&_user=4430&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000059594&_version=1&_urlVersion=0&_userid=4430&md5=765cc12bc1c88490e07afeb43412a616
2. <http://www.nature.com/nm/journal/v13/n4/abs/nm1550.html;jsessionid=239FFC960CE234DFFF9D0A16D3D6628E>

SCGN:

<http://www.jbc.org/cgi/content/full/275/32/24740>

SERPINE2:

<http://circres.ahajournals.org/cgi/reprint/100/8/1174>

PLA2G2A:

http://www.ncbi.nlm.nih.gov/pubmed/17892360?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

SLC1A4

1. <http://www.jbc.org/cgi/reprint/268/21/15329>
2. http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WG1-45PMRX4-BX&_user=4430&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000059594&_version=1&_urlVersion=0&_userid=4430&md5=4b1b514b9df5d3c2d1052c19ed285b2f

	T ₃	GC-1
THRSP	2.4	1.3
ANGPTL4	1.6	5.3
CPT1A	1.1	1.0
G6PC	1.7	0.8

Table S9. Average EC₅₀ values (nM) for induction of selected TR-regulated genes derived from dose response curves obtained with T₃ and GC-1 (n=4).

Table S10. Possible TREs near ANGPTL4 gene, only the 3' DR-4 element was verified as functional.

Number	Location/Type	Sequence (5'->3')
1	-12kbp IR-1	TGACCTgAGGTCA
2	-11kbp IR-1	TGACCTgAGGTCA
3	-5kbp IR-1	TGACCTgAGGTCA
4	-4kbp IR-1	TGACCTgAGGTCA
5	-2Kb IR-1	TGACCTgAGGTCA
6	+ 136bp DR-4	AGGTCActtgAGGTCA

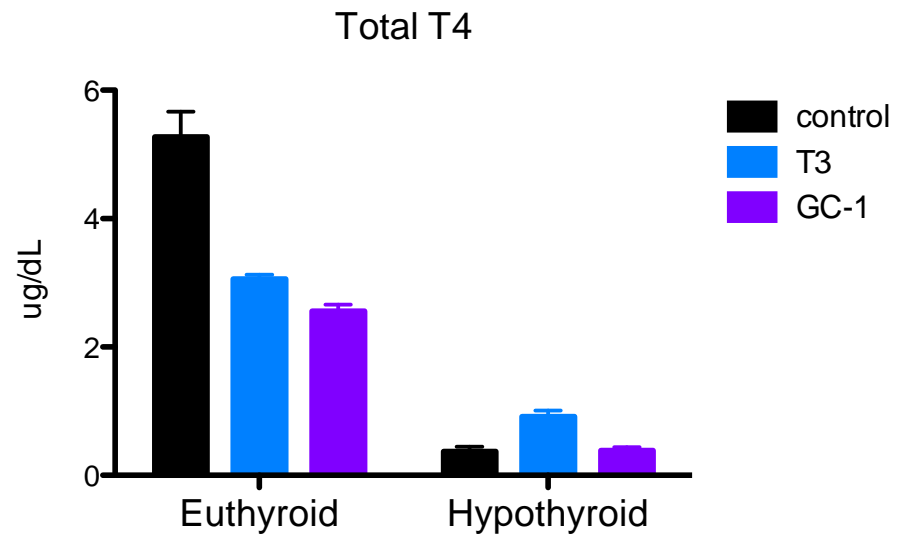


Fig. S1.

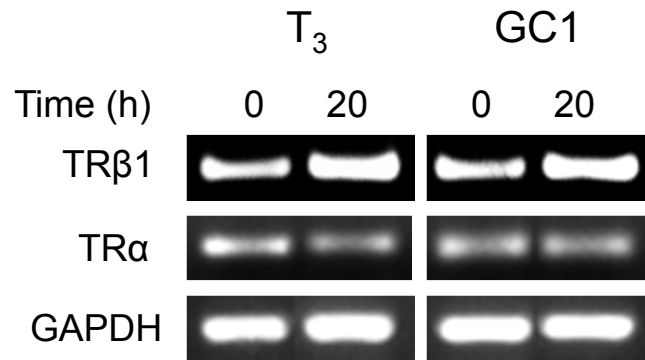


Fig. S2.

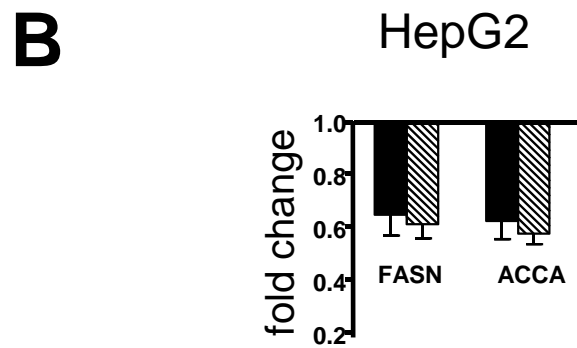
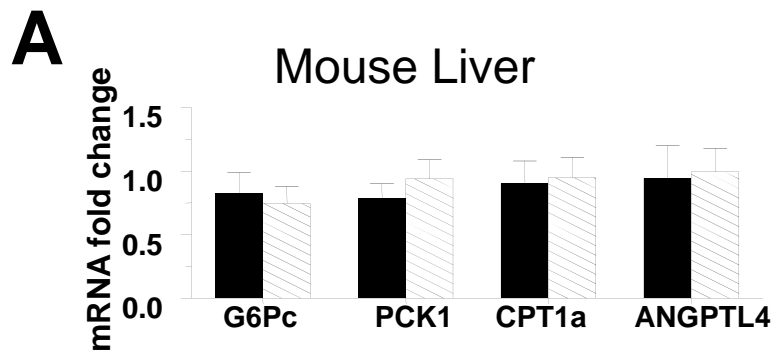


Fig. S3.

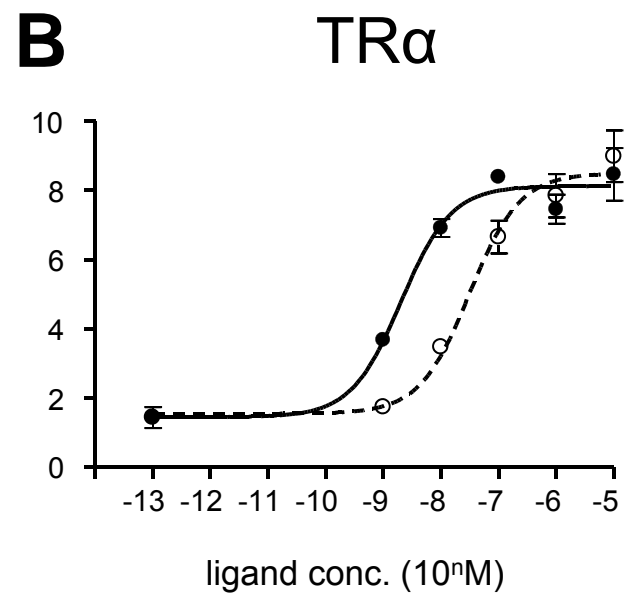
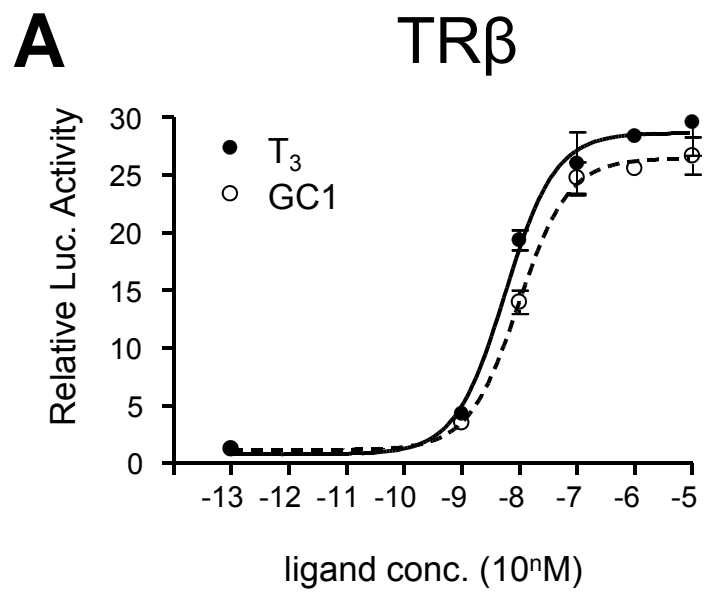


Fig. S4.