

Supporting Information for

Functional Toxicogenomic Assessment of Triclosan in Human HepG2 Cells Using Genome-wide CRISPR-Cas9 Screen

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Text S1. Supplemental information that describes process of ToxCast data retrieval and use

ToxCast data for TCS was downloaded from the ToxCast database (<https://www.epa.gov/chemical-research/toxicity-forecaster-toxcasttm-data>). ToxCast includes 941 “gene-based” assays whose biological activity is related with specific genes (i.e., *NR1I2*), and 251 other assays targeting apical cellular phenotype (i.e., cellular viability). To compare with CRISPR-Cas9 functional genomic profile consisting of resistant/sensitive genes, 177 “gene-based” assays testing TCS with AC50 (half-maximal activity) <10⁶ were selected. The scope of assays evaluation was further narrowed to 33 “gene-based HepG2” assays using HepG2 cells linked with 30 gene endpoints (i.e, Attagene platform measuring transcription factor activity of PPARG in HepG2 cells) using the same HepG2 cells to test TCS as the CRISPR-Cas9 screen conducted here. This step excluded “non-cell-based” assays (i.e., Novascreen platform testing receptor binding activity) and “non-HepG2-based” assays (i.e., Odyssey Thera platform using HEK293T cells). The gene targets from ToxCast “gene-based” assays were compared with gene-disease annotations from DisGeNET, which would reveal the number of genes from ToxCast “gene-based HepG2” assays annotated to disease terms. In some cases, genes may be tested in multiple assays, which result in multiple AC50 values for that gene. Here we assigned a calculated AC50 value for each gene. For instance, there were two “gene-based HepG2” assays (ATG_PPRE_CIS_up assay and ATG_PPARg_TRANS_up assay) in ToxCast whose endpoints are linked with *PPARG*, which have two AC50 values, 9.39 and 9.68 μM,

respectively. The two AC50 values were averaged and then log-transformed, resulting a calculated AC50 value, 0.98, for *PPARG*.

Finally, we compared enriched disease terms between genes from ToxCast “gene-based HepG2” assays and genes from the whole ToxCast 941 “gene-based” assays. A Fisher’s exact test was used and a p-value of 0.1 was used to determine a significant difference. Take obesity as instance, the R code for Fisher’s exact test is as following:

```
### Number of genes from “gene-based HepG2” assays annotated to obesity term  
a1<-19  
  
### Number of genes from “gene-based HepG2” assays not annotated to obesity  
term  
a2<-(30-a1)  
  
### Number of whole ToxCast genes annotated to obesity term  
b1<-165  
  
### Number of whole ToxCast genes not annotated to obesity term  
b2<-364-b1  
  
###Construction of 2 x2 contingency table  
Convictions <-matrix(c(a1-1, b1, a2, b2),  
nrow = 2,  
dimnames =list(c("My List", "Genome"),  
c("In Pathway", "Not In Pathway")))
```

Fisher's exact test

```
fisher.test(Convictions)
```

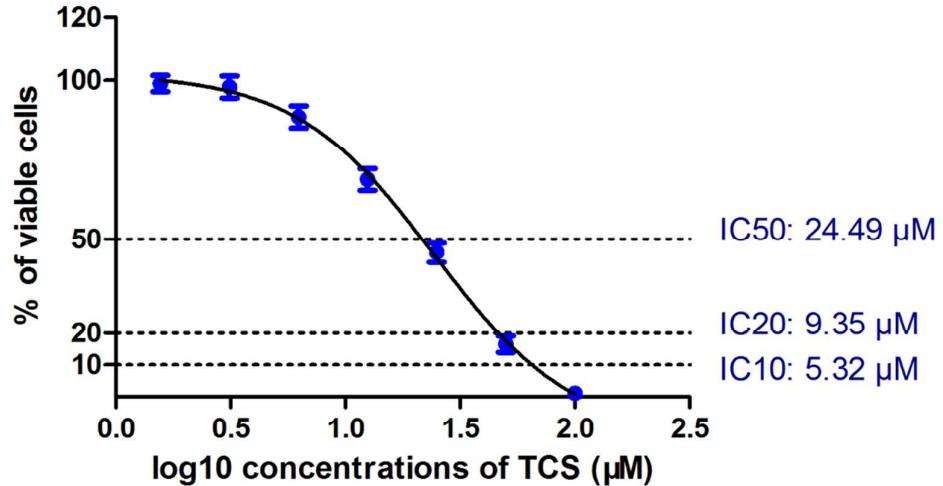


Figure S1. Cytotoxicity of TCS to HepG2 cell lines. Data represented are mean \pm SD of three identical experiments made in three replicate.

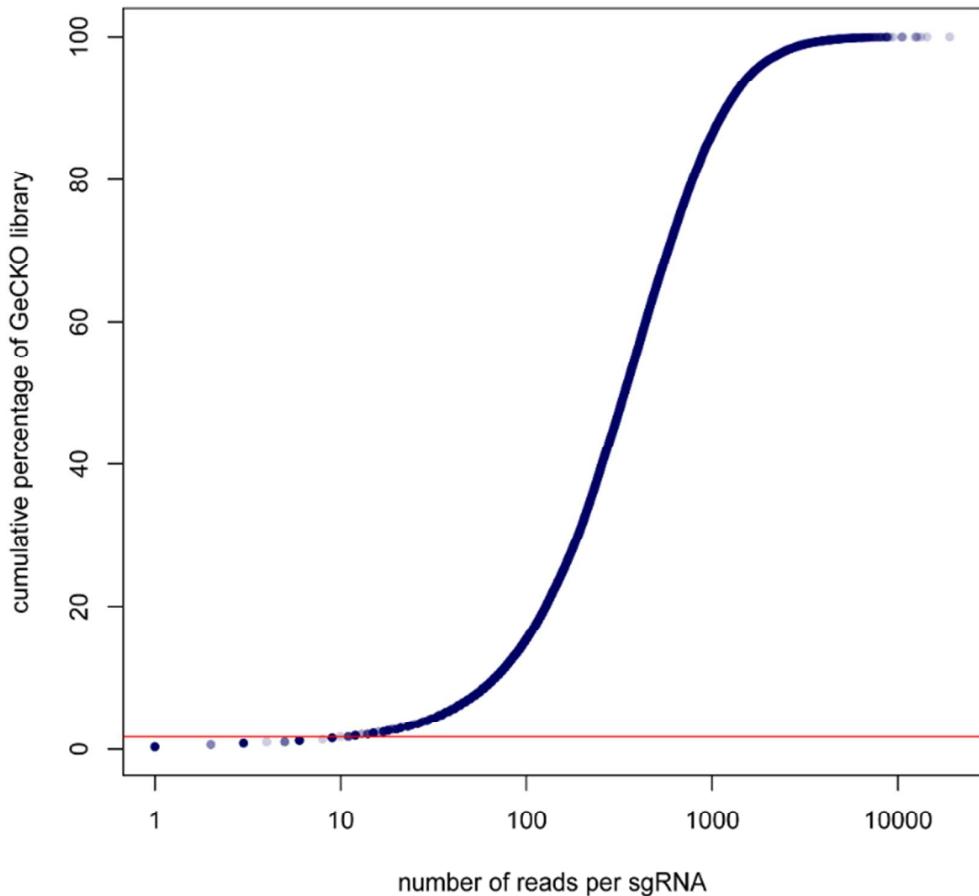


Figure S2. Cumulative distribution of the reads per sgRNA in GeCKO library. Each dot is a single sgRNA. Dots below the red line indicate that less than 3% sgRNAs are covered by less than 10 reads.

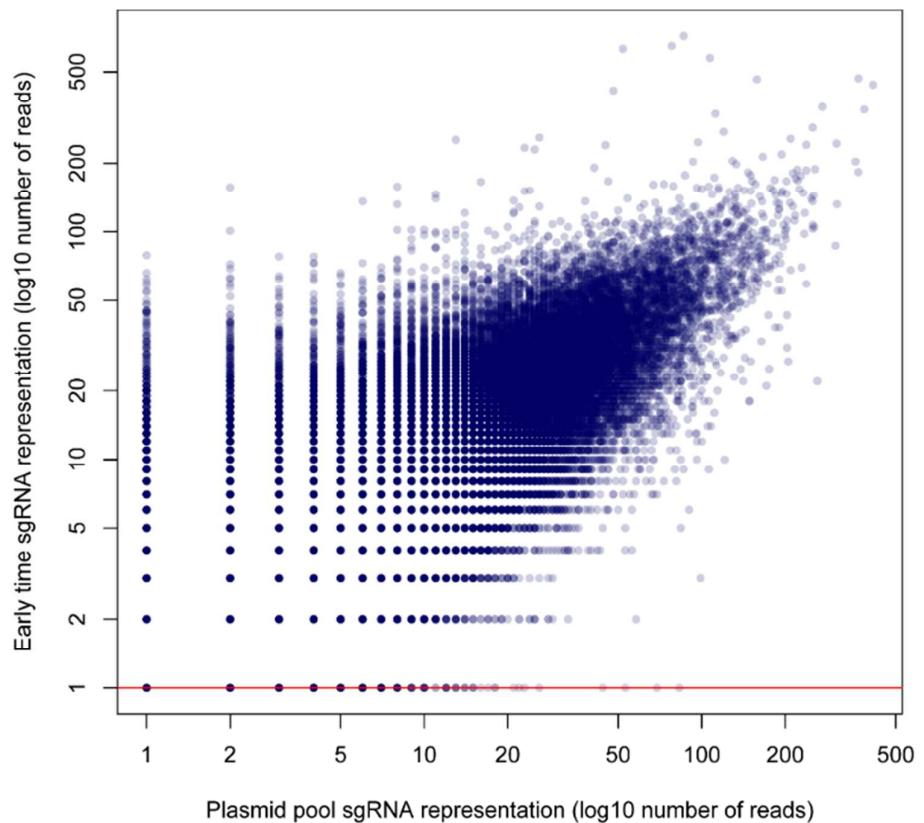


Figure S3. Comparison of sgRNA representation between the GeCKO plasmids pool and transduced cells. Dots below the red lines indicate that less than 0.17% of sgRNA were present at less than 10 reads.

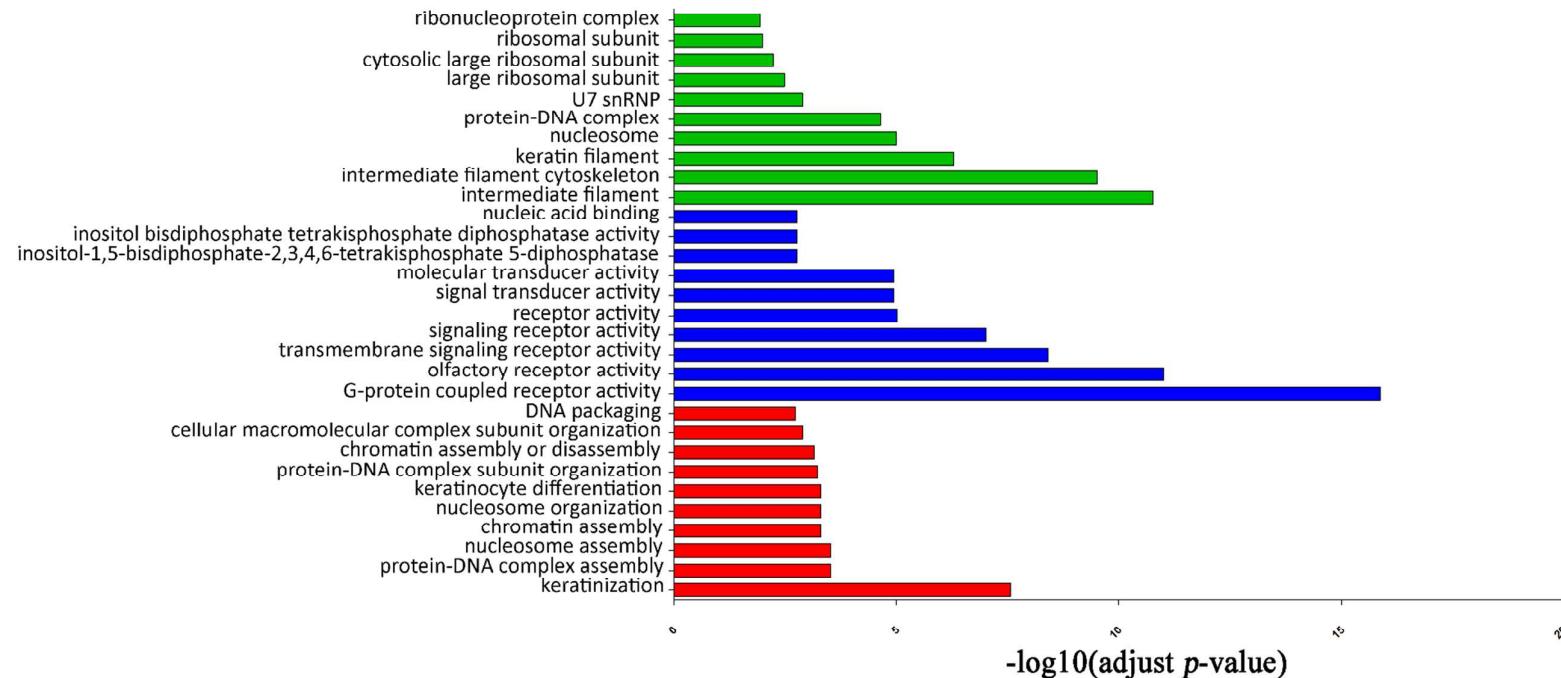


Figure S4. Gene Ontology (GO) terms enriched among the genes lost after transduction. Red, blue and green bars are GO terms of biological process (BP), molecular function (MF) and cellular component (CC), respectively.

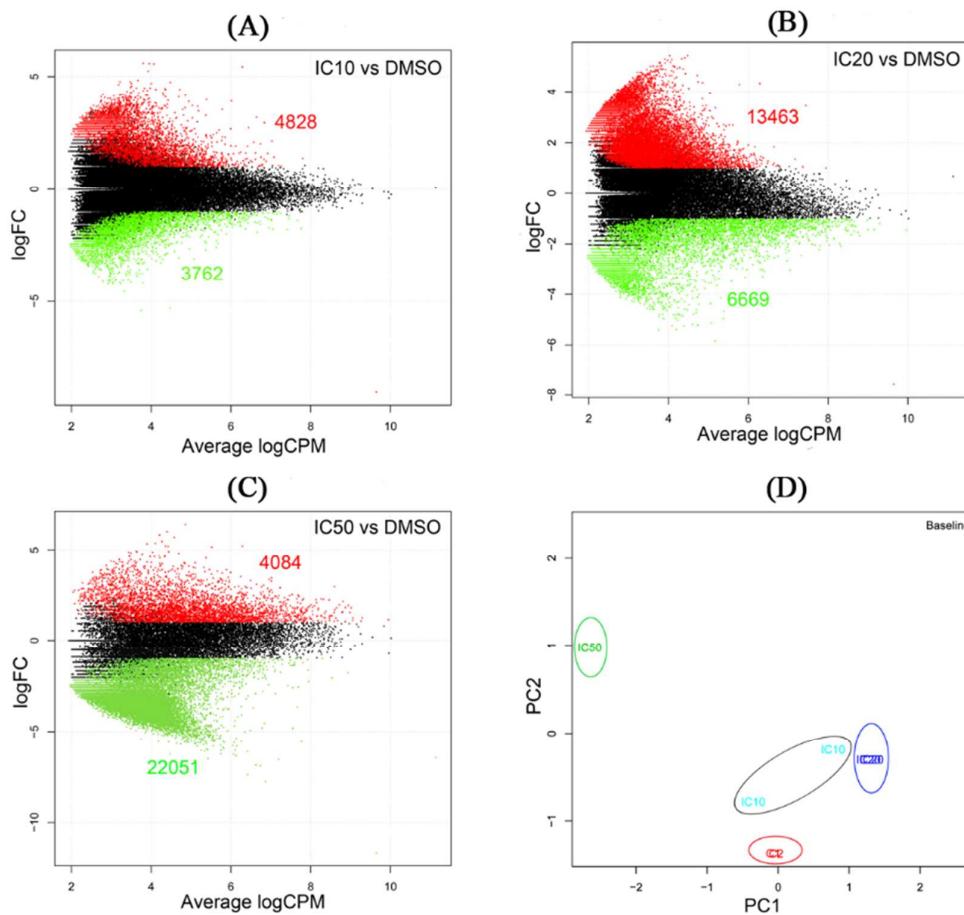


Figure S5. Analysis of sgRNA representation in each treatment group compared with vehicle control (DMSO). (A), (B) and (C) show significant overrepresentation (red dots) or underrepresentation (green dots) of sgRNAs ($FDR < 0.05$) in IC10, IC20 and IC50, respectively; (D) shows the principle component analysis of each treatment and vehicle control group with two replicate. “Baseline” means the abundance of sgRNAs at Day 0 for control group. Groups inside red, light blue, dark blue and green circles mean vehicle control, IC10, IC20 and IC50, respectively.

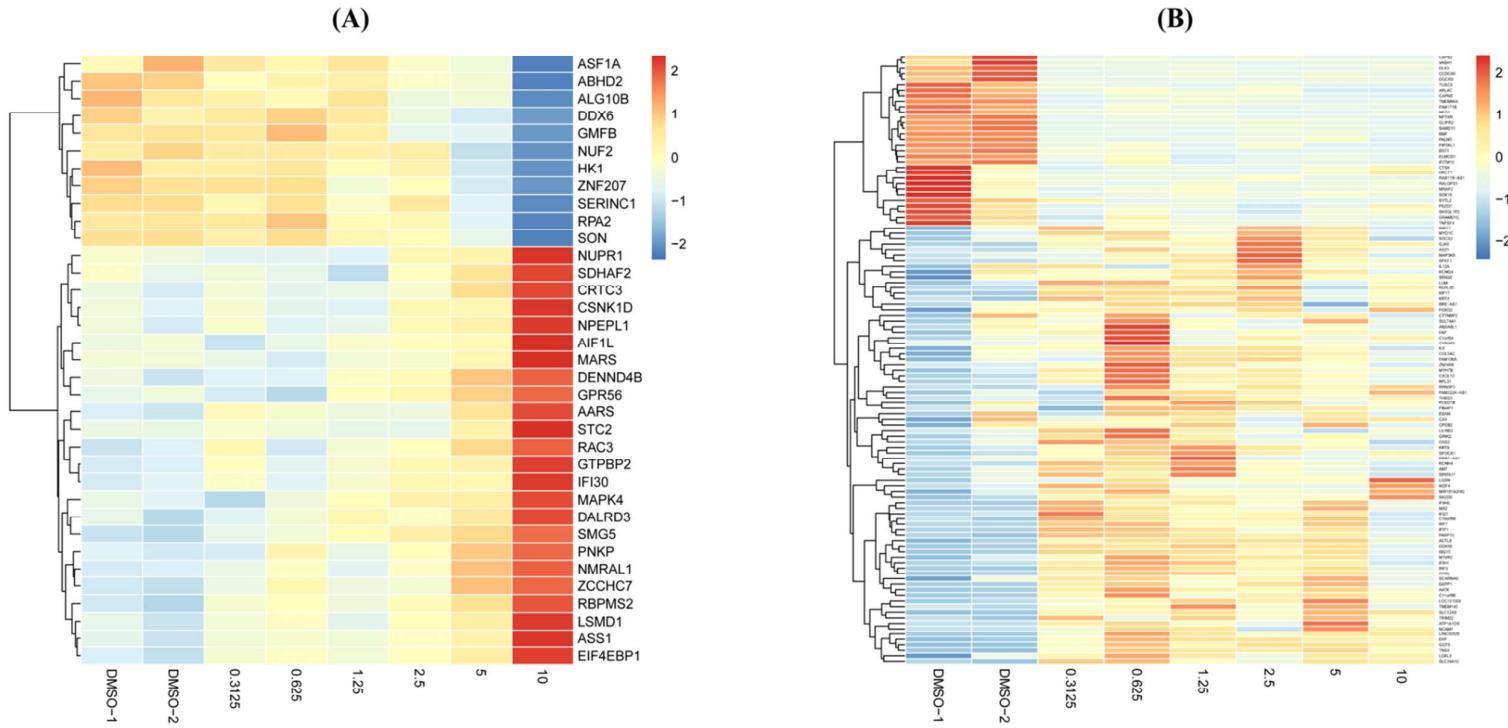


Figure S6. (A) Heatmap of expression of genes with significantly dose-dependent performance (adjusted p-value<0.2) of TCS transcriptomics in HepG2 cells. (B) Heatmap of expression of genes consistently altered (\log_2 fold changes >1.5 or <-1.5) in TCS transcriptomics in HepG2 cells.

The expressions were scaled by rows. The right columns are gene symbols, and the numbers in bottom rows are TCS concentrations of treatment.

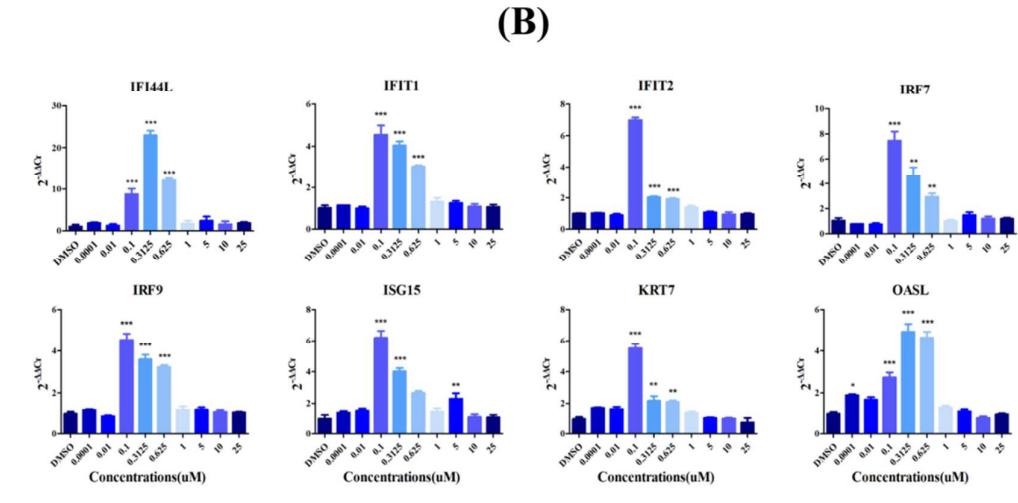
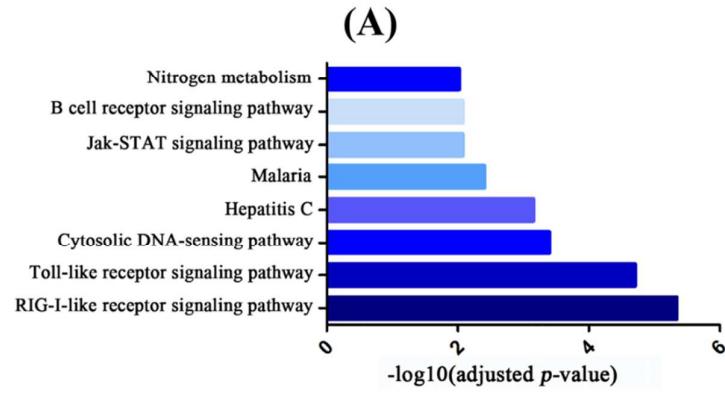
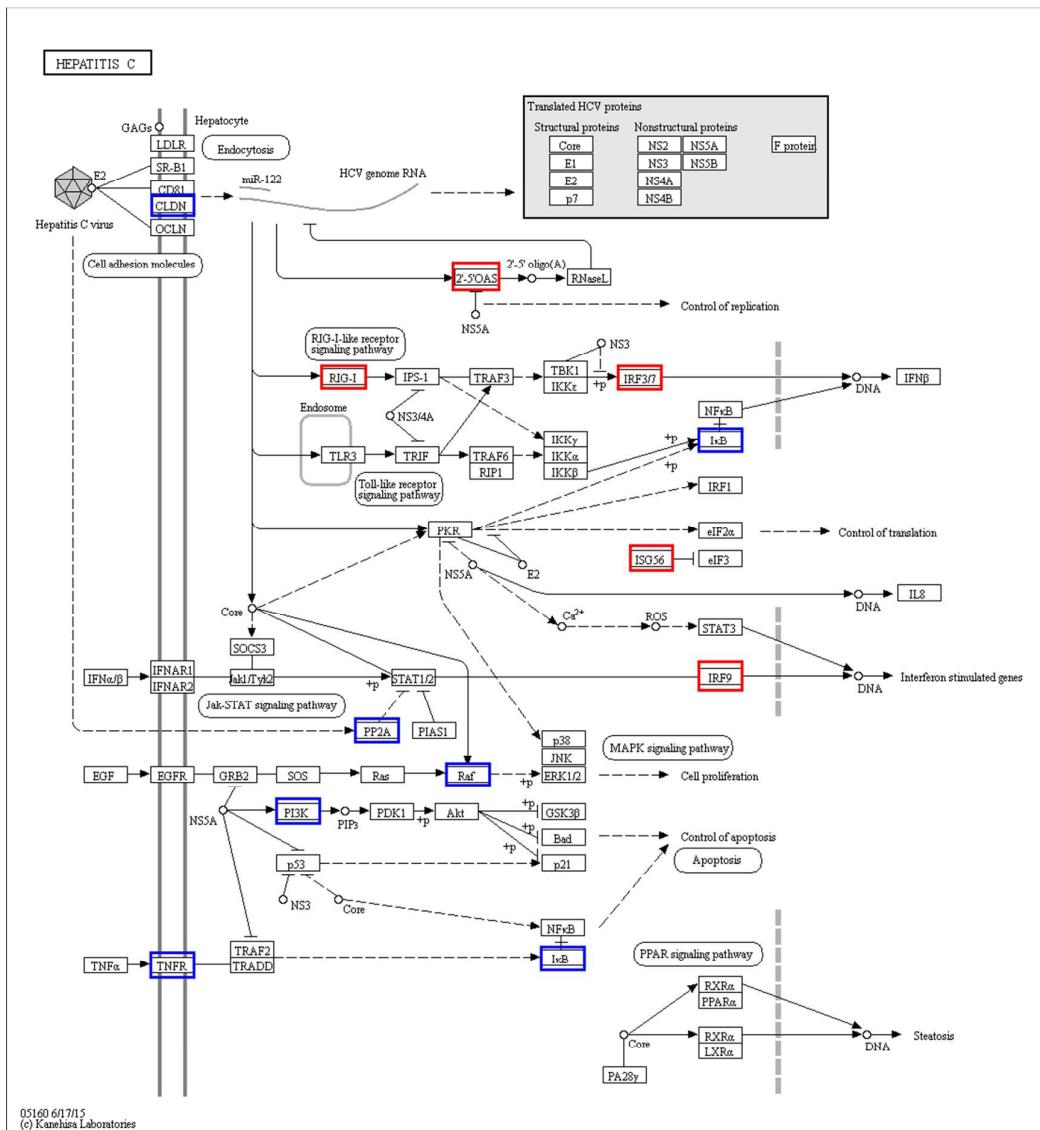
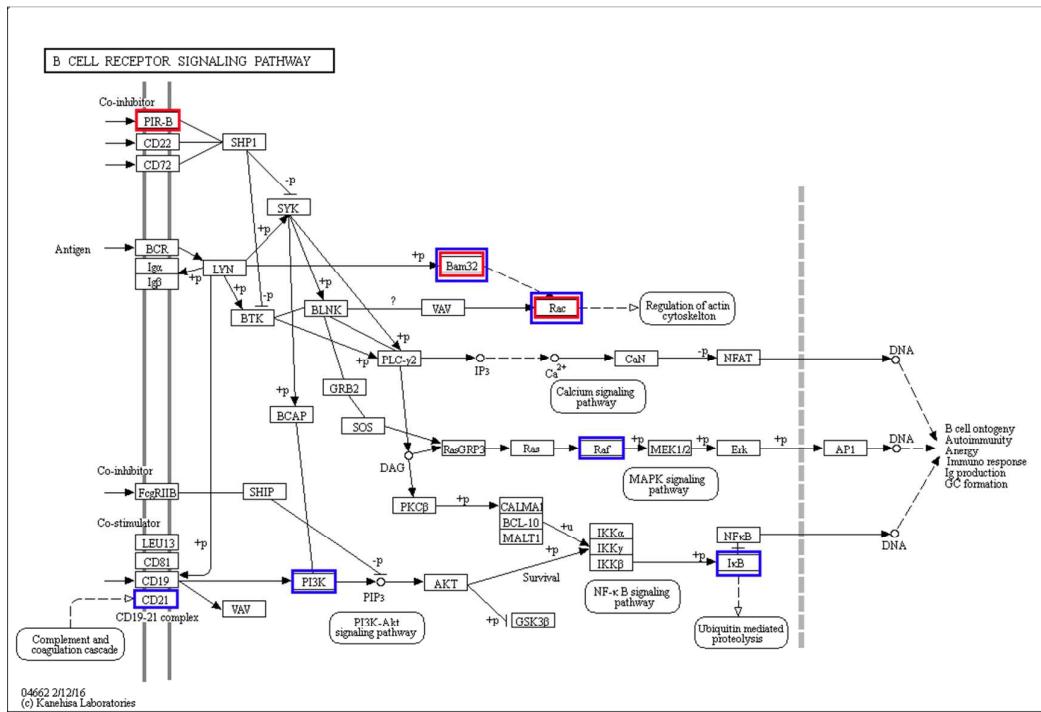


Figure S7. Transcriptome analysis of low doses of TCS. (A) The significantly enriched KEGG pathways associated with the DEGs and (B) qPCR validation of selected DEGs.

(A)



(B)



(C)

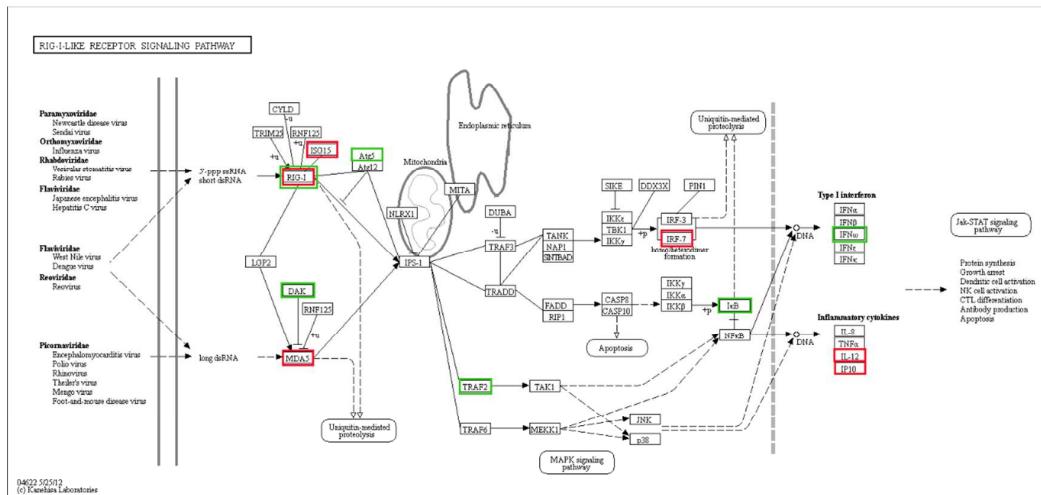


Figure S8. Common KEGG pathways significantly enriched by transcriptomic DEGs and CRISPR-Cas9 sensitive genes (IC10 and IC20). (A) Hepatitis C pathway; (B) B

cell receptor signaling pathway; (C) RIG-I-like receptor signaling pathway. The red, blue and green rectangles mean enriched transcriptomic DEGs, CRISPR-Cas9 IC10 sensitive genes and CRISPR-Cas9 IC20 sensitive genes, respectively.

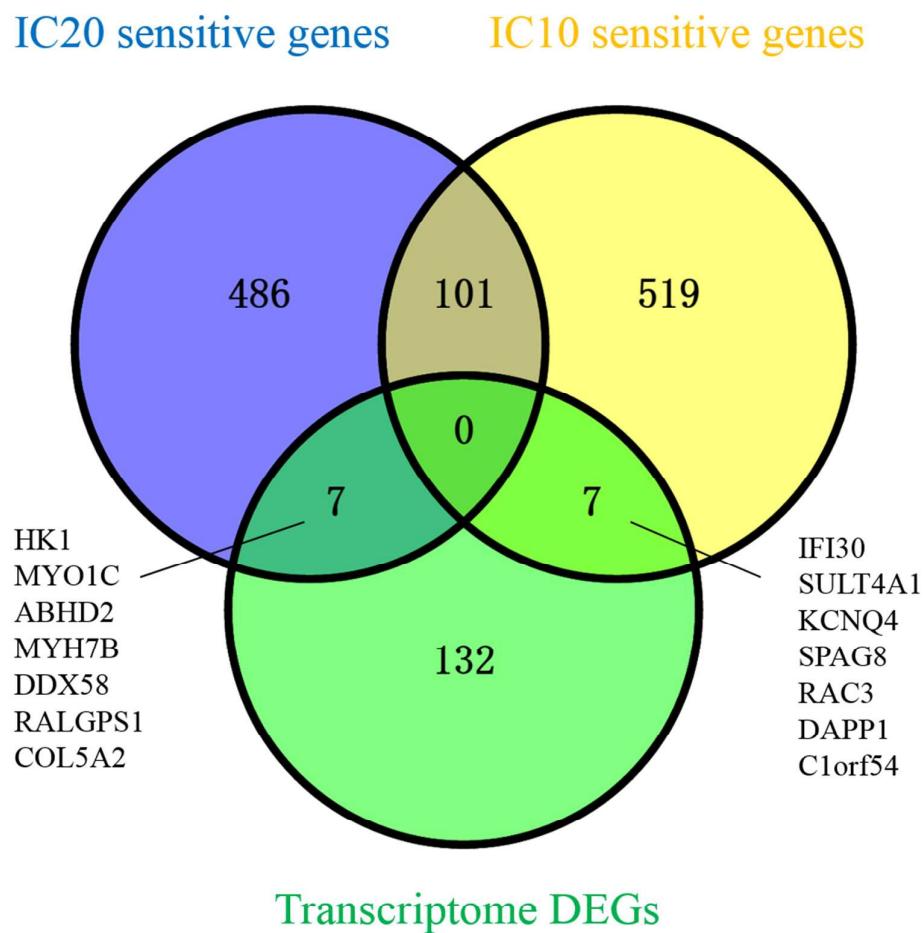


Figure S9. Comparison of genes between transcriptomic DEGs and CRISPR-Cas9 sensitive genes (IC10 and IC20).

Table S1. Primers sequences to amplify lentiCRISPR sgRNAs for the first PCR

Primers	Sequences
F1	AATGGACTATCATATGCTTACCGTAAC TGAAAGTATTTCG
R1	CTTAGTTGTATGTCTGTTGCTATTATGTCTACTATTCTTCC

*The PCR conditions included initial heat-denaturing step at 98°C for 2 min, 20 cycles of 98°C for 10 s, 60°C for 20s and 72°C for 30s, and a final extension step at 72°C for 3 min on SureCycler 8800 (Agilent technologies, Santa Clara, CA, US).

Table S2. Primers sequences to amplify lentiCRISPR sgRNAs for the second PCR

Primers	Sequences
F2-A	CCATCTCATCCCTGCGTGTCTCCGACTCAG ATCATIC GATTCTTGTGGAAAGGACGAAACACCG
F2-B	CCATCTCATCCCTGCGTGTCTCCGACTCAG ATCAGATC GATTCTTGTGGAAAGGACGAAACACCG
F2-C	CCATCTCATCCCTGCGTGTCTCCGACTCAG AAGAGGATT C GATTCTTGTGGAAAGGACGAAACACCG
F2-D	CCATCTCATCCCTGCGTGTCTCCGACTCAG AGGACGCACTGT GATTCTTGTGGAAAGGACGAAACACCG
F2-E	CCATCTCATCCCTGCGTGTCTCCGACTCAG CAGAGC GATTCTTGTGGAAAGGACGAAACACCG
F2-F	CCATCTCATCCCTGCGTGTCTCCGACTCAG ATCTGAGC GATTCTTGTGGAAAGGACGAAACACCG
F2-G	CCATCTCATCCCTGCGTGTCTCCGACTCAG ATAGGTTATA GATTCTTGTGGAAAGGACGAAACACCG
F2-H	CCATCTCATCCCTGCGTGTCTCCGACTCAG ACAGCTAGCTT G GATTCTTGTGGAAAGGACGAAACACCG
R2	CCACTACGCCCTCCGCTTCCTCTCTATGGGCAGTCGGTGATTCTACTATTCTTCCCCTGCACTGT

*Due to the sequencing length limitation of Ion Torrent Proton, we modified the reverse primers to make the length of second PCR products less than 200 base pairs. The sequences in red represent barcodes of each sequencing library.

Table S3. Oligo sequences for CRISPR-Cas9 plasmids construction for individual gene knockout

Gene symbols	Oligo sequences	Off-target score (OS)
<i>FTO</i>	AGCTTCGCGCTCTCGTCCT	56.7368
<i>MAP2K3</i>	CCGTGCGCATGTTGATGTCC	27.6316

Table S4. Primers of selected transcriptome differentially expressed genes for qPCR validation

Gene symbol	Sense primer	Antisense primer
<i>IFI44</i>	GTATAGCATATGTGGCCTTGCTTACT	ATGACCCGGCTTGAGAAGTC
<i>IFIT1</i>	GCAGCCAAGTTTACCGAAG	GCCCTATCTGGTGATGCAGT
<i>IFIT2</i>	CGAACAGCTGAGAATTGCAC	CAAGTTCCAGGTGAAATGGC
<i>IRF7</i>	TACCATCTACCTGGGCTTCG	AGGGTTCCAGCTTCACCA
<i>IRF9</i>	CCCGAAAACCTCCGGAAC TG	CAGCACACTCCGGGAAACT
<i>ISG15</i>	GGTGGACAAATGCGACGAA	ATGCTGGTGGAGGCCCTTA
<i>KRT7</i>	CTCTGTGATGAATTCCACTGGTG	CCCATGGTCCCCCGA
<i>OASL</i>	CCATCACGGTCACCATTGTG	ACCGCAGGCCTTGATCAG

Table S5. Top 20 IC50 resistant genes identified from CRISPR-Cas9 functional genomic screening on triclosan

Gene	Gene rank	p-value	p-value rank
C17orf98	1	0.0001	3
MAP2K3	2	0.0001	2
FTO	3	0.0001	1
FTSJD2	4	0.0003	4
CCDC48	5	0.001	10
SLC10A7	6	0.0013	16
C11orf63	7	0.0003	6
AARSD1	8	0.001	12
LDHAL6A	9	0.0003	5
POGZ	10	0.0014	19
KIAA1407	11	0.0005	7
PNLDC1	12	0.0005	8
FAM47E	13	0.0022	29
TBX15	14	0.0018	24
SHMT1	15	0.001	11
PDPR	16	0.0009	9
ORAI1	17	0.0012	14
GKN1	18	0.0027	35
EMR1	19	0.0014	17
BTBD9	20	0.0035	41

Table S6. Top 20 IC₂₀ resistant genes identified from CRISPR-Cas9 functional genomic screening on triclosan

Gene	Gene rank	p-value	p-value rank
MUC4	1	0.0002	5
PLEKHB2	2	0.0002	4
ARGLU1	3	0.0001	1
KRTAP10-10	4	0.0001	2
SRC	5	0.0003	8
ANKRD2	6	0.0008	11
PAN3	7	0.0003	7
EBAG9	8	0.0001	3
SDPR	9	0.0008	12
MCM7	10	0.0008	13
CD83	11	0.0013	20
TCERG1L	12	0.0003	6
DENND5B	13	0.0005	9
TRIM55	14	0.0017	26
AEN	15	0.0006	10
MPZ	16	0.0016	25
BIK	17	0.0023	34
CYBASC3	18	0.0026	40
UBE4B	19	0.0024	36
TUBGCP2	20	0.0024	35

Table S7. Top 20 IC10 resistant genes identified from CRISPR-Cas9 functional genomic screening on triclosan

Gene	Gene rank	p-value	p-value rank
GPC1	1	0.0002	4
DLC1	2	0.0001	3
CACHD1	3	0.0001	1
ENDOU	4	0.0004	5
CLCF1	5	0.0011	14
SLC9B1	6	0.0011	15
S1PR3	7	0.0001	2
PSMB2	8	0.0012	16
SAMSN1	9	0.0023	27
TCF4	10	0.0033	39
BCHE	11	0.0006	7
OR13A1	12	0.0006	6
HSD17B12	13	0.0007	8
RNF212	14	0.0009	12
OR10H3	15	0.0008	9
CACNG1	16	0.0008	10
CCDC51	17	0.0025	32
RAB11FIP5	18	0.0025	30
TMEM104	19	0.0009	11
IGSF8	20	0.0033	40

Table S8. Top 20 IC50 sensitive genes identified from CRISPR-Cas9 functional genomic screening on triclosan

Gene	Gene rank	p-value	p-value rank
NOTCH2	1	0.0003	4
EXOC1	2	0.0002	1
DTX2	3	0.0003	3
SLC5A10	4	0.0008	8
SQRDL	5	0.0008	9
RPA2	6	0.0008	10
ATP1A3	7	0.001	14
PNPLA8	8	0.0002	2
COL6A3	9	0.0012	17
CARD14	10	0.0003	5
ZNF317	11	0.0013	20
CCNY	12	0.0014	21
SIGLEC8	13	0.0005	7
CMKLR1	14	0.0004	6
PSKH1	15	0.0018	30
SCAF1	16	0.0023	35
RAD51AP1	17	0.0009	12
STEAP3	18	0.0025	37
C2orf65	19	0.001	13
CHODL	20	0.0024	36

Table S9. Top 20 IC₂₀ sensitive genes identified from CRISPR-Cas9 functional genomic screening on triclosan

Gene	Gene rank	p-value	p-value rank
ARHGAP12	1	0.0001	1
PTBP3	2	0.0012	9
TUBA8	3	0.0015	13
DAG1	4	0.0013	10
HS2ST1	5	0.0003	2
IFT27	6	0.0005	3
ETV3L	7	0.0025	30
CDKL4	8	0.001	5
NMU	9	0.0023	23
CELSR2	10	0.0024	25
TRAPPCL12	11	0.0009	4
ZNF317	12	0.003	35
KDM5C	13	0.0032	38
ELMOD2	14	0.0014	12
SFI1	15	0.0034	40
PHKG1	16	0.0036	41
KRT73	17	0.001	6
HIST1H4D	18	0.0011	8
CPNE3	19	0.0017	16
CPN2	20	0.0011	7

Table S10. Top 20 IC10 sensitive genes identified from CRISPR-Cas9 functional genomic screening on triclosan

Gene	Gene rank	p-value	p-value rank
IFI30	1	0.0001	1
SQRDL	2	0.0007	7
LTBP3	3	0.0008	8
FAM181A	4	0.0003	2
ABRA	5	0.001	9
C18orf54	6	0.0003	3
PRSS3	7	0.002	22
CRABP2	8	0.0015	15
GUCY2F	9	0.0004	4
INHBE	10	0.0005	5
RARS2	11	0.0006	6
BRD9	12	0.0018	19
ZNF365	13	0.0019	20
C1orf61	14	0.0021	24
TBC1D2	15	0.002	23
TTLL12	16	0.001	10
CELSR2	17	0.0023	25
KCNK2	18	0.0012	11
AJUBA	19	0.0027	34
DEDD	20	0.0013	13

Table S11. Gene-Disease association of CRISPR-Cas9 resistant/sensitive genes identified by using GeneAnalytics. (A) Disease terms scores of IC50 resistant genes; (B) Disease terms scores of IC50 sensitive genes; (C) Disease terms scores of IC20 resistant genes; (D) Disease terms scores of IC10 resistant genes

(A)

Score	Disease terms
15.29	Breast Cancer
14.94	Influenza

(B)

Score	Disease terms
12.52	Osteopontin-mediated Events
10.99	G-protein Signaling_K-RAS Regulation Pathway
10.03	EGFR1 Signaling Pathway
9.23	Spliceosome
8.82	PAK Pathway

(C)

Score	Disease terms
17.92	Breast Cancer
16.01	Obesity

(D)

Score	Disease terms
20.64	Colorectal Cancer
15.13	Breast Cancer
15.03	Malaria

*Disease terms scores of IC20 sensitive genes and IC10 sensitive genes were not exhibited, due to no medium scores were obtained by disease terms of the two groups of genes.

Table S12. Consistently differential expression genes of transcriptome analysis of low doses TCS. (A) Consistently up-regulated genes; (B) Consistently down-regulated genes

(A)

Genes	10	5	2.5	1.25	0.625	0.3125
AATK	1.868853	2.007438	1.745126	1.818239	1.884051	1.984244
ACTL8	1.927555	2.090689	2.180698	2.132054	1.655345	2.023035
AMT	1.690516	2.225618	2.988053	3.909662	2.877737	3.642763
ANXA8L1	2.275478	2.547546	1.988053	2.646627	3.578177	2.794766
ASZ1	2.012444	2.547546	3.40309	1.646627	2.462699	1.794766
ATP1A1OS	2.275478	3.032973	1.40309	1.909662	2.199665	2.472838
BIRC7	1.690516	2.225618	2.573015	1.909662	1.462699	2.642763
BRE-AS1	2.690516	2.650423	2.725018	2.646627	2.199665	2.057801
C11orf86	1.896377	1.804668	1.835722	1.406424	1.788752	1.757105
C19orf66	0.990076	2.319594	2.094968	1.872187	1.792007	2.714913
C1orf54	3.012444	1.810581	2.725018	1.909662	3.047662	2.057801
CA9	3.275478	2.810581	1.988053	2.909662	2.199665	2.472838
COL5A2	1.649874	1.610282	1.988053	1.8272	1.73018	1.432196
CPEB2	2.175943	2.810581	1.888517	2.810126	1.948126	2.543227
CTTNBP2	2.275478	3.225618	3.40309	2.324699	3.462699	3.057801
CXCL10	3.938443	4.51102	5.046946	4.909662	5.287128	4.93227
CYB5R3	1.690516	1.810581	2.40309	0.324699	3.784628	2.472838
DAPP1	2.860441	3.869474	3.795408	3.025139	3.401299	3.642763
DDX58	1.714822	2.310607	2.288342	2.519313	1.827861	2.603321

EHF	3.342593	3.032973	3.363919	3.324699	3.114776	2.969264
ESAM	2.275478	3.032973	2.40309	3.324699	3.047662	1.472838
FAM106A	1.828019	1.711045	2.251087	2.090234	1.948126	1.320835
FAM222A-AS1	2.629115	1.640656	1.90559	2.132054	1.685092	0.69523
FAP	2.175943	2.151618	2.168625	1.703211	2.685092	2.472838
FOXD2	2.912908	1.448011	2.518567	2.061665	1.877737	2.347307
GGT5	2.168563	1.910116	2.087588	1.726798	1.685092	1.709877
GJA5	2.690516	2.225618	3.210445	2.324699	1.462699	2.472838
GRIK2	1.583601	1.526788	1.087588	1.746163	1.940747	2.124915
IFI27	1.218447	2.225618	2.224753	2.06836	1.959267	3.123389
IFI44L	3.860441	4.769939	4.027581	4.597718	3.9652	5.116694
IFIH1	1.095772	1.623495	1.66937	2.040058	1.718132	1.914436
IFIT1	1.45855	2.052008	1.572652	2.152933	1.88833	2.532909
IKZF4	4.012444	1.810581	1.988053	1.909662	2.877737	3.642763
IL12A	2.105553	1.640656	2.725018	2.061665	0.614703	2.472838
IL6	2.690516	3.313081	3.862522	3.646627	3.632624	3.560301
IRF7	1.127783	2.084526	1.769141	1.644834	1.792373	2.291668
IRF9	1.646572	2.144005	2.067573	2.164659	2.021783	2.316822
ISG15	1.771204	2.3319	2.167874	2.418075	2.024304	2.629303
KCNH4	1.275478	1.547546	1.988053	2.784131	2.047662	2.794766
KCNQ4	1.690516	1.810581	2.210445	1.909662	1.199665	1.794766
KIF17	2.275478	1.225618	2.40309	2.324699	1.877737	2.472838
KLHL30	2.275478	0.225618	2.573015	2.025139	1.685092	2.173278
KRT4	2.275478	1.225618	2.988053	2.324699	2.199665	3.057801
KRT9	1.690516	2.225618	2.725018	3.132054	2.462699	2.472838

LGSN	3.690516	2.225618	2.40309	2.132054	2.337169	1.794766
LILRB3	2.012444	-0.77438	1.725018	2.324699	2.784628	2.93227
LINC00526	2.497871	2.032973	1.725018	2.132054	2.047662	1.794766
LOC151009	1.95355	2.427252	1.988053	2.212225	1.363164	1.735872
LOXL3	3.082833	2.68505	2.309981	2.784131	2.685092	2.794766
LUM	2.012444	1.00989	2.04052	1.581039	1.73018	2.369002
MAP3K8	1.275478	2.68505	3.795408	2.909662	2.199665	1.794766
MIR181A2HG	4.012444	2.547546	2.988053	2.909662	3.199665	3.472838
MTVR2	1.690516	2.225618	2.40309	2.324699	2.199665	2.057801
MX2	3.012444	4.032973	2.988053	3.324699	3.401299	4.280193
MYH7B	2.275478	1.810581	2.40309	1.909662	2.462699	2.472838
MYO1C	1.690516	2.225618	2.725018	1.646627	2.047662	2.642763
NCAM1	2.690516	2.926058	0.40309	2.494624	2.199665	1.794766
OAS2	0.690516	2.225618	1.988053	2.909662	2.685092	3.472838
OASL	2.244368	2.592989	2.368043	2.744777	2.389711	2.521074
PARP10	1.89215	2.60413	2.695872	2.810126	2.600203	3.238373
PCED1B	2.690516	1.810581	2.988053	3.132054	2.199665	1.472838
PIN4P1	1.690516	1.810581	1.988053	2.324699	1.877737	1.854075
PRR7-AS1	3.012444	2.225618	1.40309	4.494624	3.337169	3.472838
RPL31	1.583601	1.418263	1.917663	1.839272	2.114776	2.057801
RRN3P3	2.912908	1.962584	2.518567	1.739737	2.462699	0.887876
SCARNA6	1.990076	2.407822	2.194503	1.909662	1.932185	2.387108
SH2D5	2.73491	1.547546	1.651018	1.848261	1.578177	1.93227
SLC12A8	2.327946	2.055693	1.625482	1.962129	1.292774	1.887876
SLC39A10	2.275478	1.953539	1.38037	1.610102	1.831933	2.355481

SOCS2	1.690516	3.395543	4.10353	3.132054	3.199665	3.280193
SPAG8	2.690516	2.225618	2.988053	2.646627	1.877737	2.472838
SPATA17	1.275478	1.810581	1.988053	3.025139	1.877737	2.93227
SPEF1	2.275478	2.225618	3.40309	2.646627	1.877737	1.472838
SPOCK1	2.373326	1.263093	2.109359	2.584566	1.915212	2.00627
SULT4A1	1.597406	2.179815	1.210445	1.646627	1.9652	1.560301
THBS3	2.690516	1.547546	2.210445	2.646627	2.685092	0.472838
TMEM140	2.012444	3.473546	2.210445	3.717017	2.337169	2.472838
TNS4	2.197476	2.170336	2.158379	2.073548	1.866849	1.885161
TRIM22	2.275478	2.547546	1.818128	2.547092	0.877737	2.794766
ZNF668	0.690516	1.810581	1.988053	2.646627	2.877737	2.057801

(B)

Genes	10	5	2.5	1.25	0.625	0.3125
ARL4C	-2.7018	-3.1667	-1.18187	-1.74569	-1.70723	-1.59755
BMF	-2.69031	-1.93281	-1.86225	-3.05612	-3.00058	-2.40548
BST1	-1.89445	-2.35934	-2.18187	-2.26026	-1.70723	-1.11212
CAPN5	-3.89445	-3.35934	-1.85994	-1.93834	-2.3853	-4.11212
CAPS2	-3.11684	-3.58174	-2.40426	-3.48266	-2.92962	-3.33452
CCDC69	-1.7018	-1.58174	-1.98923	-1.48266	-2.51458	-2.33452
CTSK	-0.81198	-1.86184	-2.68437	-2.1778	-2.62476	-3.61462
DACT1	-0.30948	-1.77438	-2.59691	-2.6753	-3.12226	-2.52716
DGCR9	-1.72452	-1.77438	-2.59691	-2.09034	-3.12226	-1.9422
DLX3	-1.33696	-2.91734	-2.32483	-1.81826	-2.52826	-2.08516
ELMOD1	-1.89445	-1.77438	-2.18187	-3.26026	-1.3853	-1.52716

FAM171B	-1.49006	-1.77438	-1.98393	-1.76276	-1.56587	-1.80727
GLIPR2	-1.83305	-1.71298	-1.21358	-1.6139	-2.3239	-1.59129
GRAMD1C	-1.51112	-1.71298	-2.12047	-1.6139	-1.18639	-3.05072
IFITM10	-1.88064	-1.95126	-1.65349	-2.91631	-1.09478	-1.97967
MRAP2	-1.76892	-2.49685	-3.05634	-1.39777	-2.3593	-3.57156
NEO1	-2.33923	-5.38909	-4.21162	-2.12009	-2.27754	-2.14187
NPTXR	-2.47941	-2.41379	-2.47733	-1.84523	-2.46211	-2.69709
PALM3	-3.83305	-1.29794	-2.12047	-2.19886	-3.06086	-2.05072
PDZD7	-0.47941	-1.94431	-2.76683	-1.5233	-1.97026	-2.11212
PIP5KL1	-2.30948	-2.77438	-1.01195	-2.6753	-1.5373	-1.52716
RAB11B-AS1	-2.06437	-2.52927	-1.3518	-2.10826	-2.55522	-1.96012
RALGPS1	-1.89445	-2.77438	-3.18187	-2.26026	-4.70723	-2.52716
SAMD11	-1.70977	-1.98622	-1.56548	-2.07558	-2.45696	-1.96139
SH3GL1P2	-0.89445	-1.77438	-3.18187	-2.26026	-1.70723	-2.11212
SOX18	-1.57252	-1.55199	-1.85994	-1.6753	-2.3853	-2.52716
SYTL2	-2.89445	-3.35934	-3.18187	-2.26026	-3.70723	-0.7902
TMEM86A	-2.27296	-4.05978	-2.29735	-1.63877	-3.40767	-4.81256
TNFSF4	-3.21637	-2.68127	-2.5038	-2.58219	-2.02915	-3.43405
TUSC3	-2.7018	-3.1667	-1.98923	-3.06762	-2.92962	-1.91948
VASH1	-1.89445	-2.35934	-3.18187	-2.26026	-2.70723	-2.11212

Numbers in first row were concentrations of TCS used in transcriptome experiment.

Numbers in other rows are log2 fold change value of genes.

Table S13. 22 disease terms (Score>20) associated with TCS retrieved from CTD databases

Disease Name	Disease ID	Inference Score	Reference Count
Reperfusion Injury	MESH:D015427	41.43	28
Breast Neoplasms	MESH:D001943	38.35	42
Carcinoma, Hepatocellular	MESH:D006528	33.58	27
Inflammation	MESH:D007249	31.05	37
Prostatic Neoplasms	MESH:D011471	29.9	49
Arthritis, Experimental	MESH:D001169	29.23	14
Infertility, Female	MESH:D007247	28.07	5
Arthritis, Rheumatoid	MESH:D001172	27.46	13
Obesity	MESH:D009765	27.31	13
Kidney Failure, Chronic	MESH:D007676	27.04	4
Heat Stroke	MESH:D018883	26.24	1
Colonic Neoplasms	MESH:D003110	25.91	16

Diabetes Mellitus, Experimental	MESH:D003921	25.74	15
Brain Ischemia	MESH:D002545	24.28	13
Stomach Neoplasms	MESH:D013274	22.28	18
Diabetes Mellitus, Type 2	MESH:D003924	22.12	15
HIV Wasting Syndrome	MESH:D019247	21.25	1
Burns	MESH:D002056	21.23	3
Thyroid Neoplasms	MESH:D013964	20.95	4
Alzheimer Disease	MESH:D000544	20.41	8
Drug-Induced Liver Injury	MESH:D056486	20.28	20

Table S14. ToxCast Assays testing TCS

Assay names	Log10(AC50)	Endpoints	AssayType	Platforms	CellType
NVS_TR_hNET	-0.33	SLC6A2	binding reporter	Novascreen	NA
TOX21_MMP_ratio_down	0.15	NA	membrane potential reporter	Tox21/NCGC	HepG2
NVS_ADME_hCYP2C19	0.26	CYP2C19	enzyme reporter	Novascreen	NA
NHEERL_ZF_144hpf_TERATOSCORE_up	0.42	NA	NA	National Health and Environmental Effects Research Lab - Padilla Lab	zebrafish embryo
ATG_PXRE_CIS_up	0.51	NR1I2	inducible reporter	Attagene	HepG2
NVS_GPCR_rV1	0.53	Avpr1a	binding reporter	Novascreen	NA
ATG_NRF2_ARE_CIS_up	0.54	NFE2L2	inducible reporter	Attagene	HepG2
ATG_PXR_TRANS_up	0.61	NR1I2	inducible reporter	Attagene	HepG2
ATG_VDRE_CIS_up	0.66	VDR	inducible reporter	Attagene	HepG2
ATG_BRE_CIS_up	0.67	SMAD1	inducible reporter	Attagene	HepG2

ATG_PBREM_CIS_up	0.67	NR1I3	inducible reporter	Attagene	HepG2
BSK_hDFCGF_EGFR_down	0.67	EGFR	binding reporter	Bioseek	foreskin fibroblast
BSK_hDFCGF_Proliferation_down	0.69	NA	viability reporter	Bioseek	foreskin fibroblast
BSK_hDFCGF_CollagenIII_down	0.69	COL3A1	binding reporter	Bioseek	foreskin fibroblast
NVS_ENZ_hLck_Activator	0.72	LCK	enzyme reporter	Novascreen	NA
BSK_hDFCGF_VCAM1_down	0.72	VCAM1	binding reporter	Bioseek	foreskin fibroblast
NVS_ADME_hCYP2C8	0.72	CYP2C8	enzyme reporter	Novascreen	NA
BSK_LPS_PGE2_down	0.74	PTGER2	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
NVS_ADME_hCYP2C9	0.77	CYP2C9	enzyme reporter	Novascreen	NA
ATG_RXRb_TRANS_up	0.77	RXR β	inducible reporter	Attagene	HepG2

NVS_MP_rPBR	0.78	Tspo	binding reporter	Novascreen	NA
BSK_4H_VEGFRII_down	0.81	KDR	binding reporter	Bioseek	umbilical vein endothelium
BSK_hDFCGF_PA11_down	0.82	SERPINE1	binding reporter	Bioseek	foreskin fibroblast
NVS_ADME_hCYP1A2	0.82	CYP1A2	enzyme reporter	Novascreen	NA
BSK_3C_Proliferation_down	0.83	NA	viability reporter	Bioseek	umbilical vein endothelium
ATG_ISRE_CIS_dn	0.83	IRF1	inducible reporter	Attagene	HepG2
BSK_hDFCGF_MCSF_down	0.83	CSF1	binding reporter	Bioseek	foreskin fibroblast
NVS_GPCR_hAdra2C	0.83	ADRA2C	binding reporter	Novascreen	NA
BSK_SAg_Proliferation_down	0.83	NA	viability reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
NVS_NR_hPPARg	0.85	PPARG	binding reporter	Novascreen	NA

BSK_3C_TissueFactor_down	0.85	F3	binding reporter	Bioseek	umbilical vein endothelium
ATG_CMV_CIS_up	0.86	NA	inducible reporter	Attagene	HepG2
BSK_3C_uPAR_down	0.86	PLAUR	binding reporter	Bioseek	umbilical vein endothelium
BSK_CASM3C_IL6_down	0.86	IL6	binding reporter	Bioseek	coronary artery smooth muscle cells
BSK_hDFCGF_IP10_down	0.87	CXCL10	binding reporter	Bioseek	foreskin fibroblast
ATG_TCF_b_cat_CIS_dn	0.87	LEF1 TCF7 TCF7L1 TCF7L2	inducible reporter	Attagene	HepG2
BSK_3C_SRБ_down	0.87	NA	viability reporter	Bioseek	umbilical vein endothelium
APR_HepG2_CellCycleArrest_24h_dn	0.88	NA	morphology reporter	Apredica	HepG2
BSK_4H_MCP1_down	0.89	CCL2	binding reporter	Bioseek	umbilical vein endothelium
ATG_Sox_CIS_up	0.89	SOX1	inducible reporter	Attagene	HepG2
BSK_hDFCGF_SRБ_down	0.89	NA	viability reporter	Bioseek	foreskin

fibroblast					
BSK_LPS_CD40_down	CD40	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells	0.90
APR_Hepat_DNATexture_1hr_dn	NA	conformation reporter	Apredica	hepatocyte	0.90
BSK_SAg_IL8_down	CXCL8	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells	0.90
ATG_AP_1_CIS_up	0.91	JUN FOS	inducible reporter	Attagene	HepG2
ATG_EGR_CIS_up	0.91	EGR1	inducible reporter	Attagene	HepG2
APR_HepG2_CellCycleArrest_72h_dn	NA	morphology reporter	Apredica	HepG2	0.92
NVS_ENZ_hBACE	0.92	BACE1	enzyme reporter	Novascreen	NA
BSK_SAg_MCP1_down	CCL2	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear	0.92

cells					
ATG_Pax6_CIS_up	0.92	PAX6	inducible reporter	Attagene	HepG2
BSK_SAg_CD40_down		CD40	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
	0.93				
BSK_4H_Pselectin_down	0.93	SELP	binding reporter	Bioseek	umbilical vein endothelium
ATG_Xbp1_CIS_up	0.93	XBP1	inducible reporter	Attagene	HepG2
BSK_SAg_CD38_down		CD38	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
	0.94				
BSK_KF3CT_TGFb1_down		TGFB1	binding reporter	Bioseek	keratinocytes and foreskin fibroblasts
	0.94				
BSK_hDFCGF_MMP1_down	0.94	MMP1	binding reporter	Bioseek	foreskin fibroblast

ATG_Oct_MLP_CIS_up	0.94	POU2F1	inducible reporter	Attagene	HepG2
BSK_SAg_PBMCCytotoxicity_down	0.94	NA	viability reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
ATG_MRE_CIS_up	0.94	MTF1	inducible reporter	Attagene	HepG2
BSK_hDFCGF_MIG_down	0.95	CXCL9	binding reporter	Bioseek	foreskin fibroblast
NVS_NR_hAR	0.95	AR	binding reporter	Novascreen	NA
BSK_3C_Vis_down	0.95	NA	morphology reporter	Bioseek	umbilical vein endothelium
BSK_SAg_Eselectin_down	0.95	SELE	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
TOX21_TR_LUC_GH3_Antagonist	0.96	THRB THRA	inducible reporter	Tox21/NCGC	GH3
ATG_Sp1_CIS_up	0.96	SP1	inducible reporter	Attagene	HepG2

APR_HepG2_MitoMembPot_24h_dn	0.96	NA	membrane potential reporter	Apredica	HepG2
NVS_ENZ_rMAOAP	0.96	Maoa	enzyme reporter	Novascreen	NA
NCCT_HEK293T_CellTiterGLO	0.97	NA	viability reporter	NCCT's Simmons Lab	HEK293T
BSK_hDFCGF_TIMP1_down	0.97	TIMP1	binding reporter	Bioseek	foreskin fibroblast
ATG_PPRE_CIS_up	0.97	PPARA PPARD PPARG	inducible reporter	Attagene	HepG2
OT_AR_ARSRC1_0480	0.99	AR SRC	binding reporter	Odyssey Thera	HEK293T
APR_HepG2_MitoMembPot_72h_dn	0.99	NA	membrane potential reporter	Apredica	HepG2
BSK_KF3CT_MMP9_down	0.99	MMP9	binding reporter	Bioseek	keratinocytes and foreskin fibroblasts
BSK_SAg_CD69_down	0.99	CD69	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
ATG_PPARg_TRANS_up	0.99	PPARG	inducible reporter	Attagene	HepG2

BSK_LPS_IL1a_down		IL1A	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
	1.00				
TOX21_FXR_BLA_agonist_ch2	1.00	NR1H4	background reporter	Tox21/NCGC	HEK293T
ATG_RXRa_TRANS_up	1.00	RXRA	inducible reporter	Attagene	HepG2
BSK_3C_HLADR_down	1.00	HLA-DRA	binding reporter	Bioseek	umbilical vein endothelium
BSK_KF3CT_MCP1_down		CCL2	binding reporter	Bioseek	keratinocytes and foreskin fibroblasts
	1.00				
NVS_ADME_rCYP2D2	1.01	Cyp2d2	enzyme reporter	Novascreen	NA
BSK_CASM3C_Proliferation_down		NA	viability reporter	Bioseek	coronary artery smooth muscle cells
	1.01				
BSK_4H_SRБ_down	1.02	NA	viability reporter	Bioseek	umbilical vein endothelium
BSK_SAg_MIG_down	1.02	CXCL9	binding reporter	Bioseek	umbilical vein endothelium and

					peripheral blood mononuclear cells
BSK_4H_uPAR_down	1.03	PLAUR	binding reporter	Bioseek	umbilical vein endothelium
BSK_LPS_Eselectin_down		SELE	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
ATG_DR4_LXR_CIS_dn	1.03	NR1H3 NR1H2	inducible reporter	Attagene	HepG2
BSK_3C_Eselectin_down	1.03	SELE	binding reporter	Bioseek	umbilical vein endothelium
BSK_KF3CT_SRB_down	1.03	NA	viability reporter	Bioseek	keratinocytes and foreskin fibroblasts
BSK_4H_Eotaxin3_down	1.04	CCL26	binding reporter	Bioseek	umbilical vein endothelium
TOX21_ARE_BLA_agonist_ratio	1.04	NFE2L2	inducible reporter	Tox21/NCGC	HepG2
BSK_LPS_TissueFactor_down	1.05	F3	binding reporter	Bioseek	umbilical vein

					endothelium and peripheral blood mononuclear cells
NVS_GPCR_hOpiate_D1	1.05	OPRD1	binding reporter	Novascreen	NA
BSK_SAg_SRБ_down		NA	viability reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
	1.05				
BSK_LPS_MCSF_down		CSF1	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
	1.05				
APR_HepG2_CellLoss_24h_dn	1.06	NA	viability reporter	Apredica	HepG2
BSK_3C_VCAM1_down	1.06	VCAM1	binding reporter	Bioseek	umbilical vein endothelium
BSK_LPS_MCP1_down		CCL2	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear
	1.06				

cells					
APR_HepG2_p53Act_72h_up	1.07	TP53	viability reporter	Apredica	HepG2
BSK_CASM3C_TissueFactor_down	1.08	F3	binding reporter	Bioseek	coronary artery smooth muscle cells
BSK_LPS_SRБ_down	1.08	NA	viability reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
BSK_BE3C_PAII_down	1.08	SERPINE1	binding reporter	Bioseek	bronchial epithelial cells
BSK_BE3C_tPA_down	1.08	PLAT	binding reporter	Bioseek	bronchial epithelial cells
BSK_BE3C_TGFb1_down	1.08	TGFB1	binding reporter	Bioseek	bronchial epithelial cells
BSK_LPS_IL8_down	1.08	CXCL8	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear

cells					
BSK_CASM3C_uPAR_down	1.09	PLAUR	binding reporter	Bioseek	coronary artery smooth muscle cells
BSK_KF3CT_IL1a_down	1.09	IL1A	binding reporter	Bioseek	keratinocytes and foreskin fibroblasts
BSK_BE3C_IP10_down	1.10	CXCL10	binding reporter	Bioseek	bronchial epithelial cells
BSK_3C_IL8_down	1.10	CXCL8	binding reporter	Bioseek	umbilical vein endothelium
NVS_TR_rNET	1.10	Slc6a2	binding reporter	Novascreen	NA
BSK_hDFCGF_IL8_down	1.10	CXCL8	binding reporter	Bioseek	foreskin fibroblast
BSK_BE3C_uPAR_down	1.10	PLAUR	binding reporter	Bioseek	bronchial epithelial cells
BSK_KF3CT_IP10_down	1.11	CXCL10	binding reporter	Bioseek	keratinocytes and foreskin fibroblasts

ACEA_T47D_80hr_Negative	1.11	NA	growth reporter	ACEA Biosciences	T47D
BSK_4H_VCAM1_down	1.12	VCAM1	binding reporter	Bioseek	umbilical vein endothelium
BSK_LPS_VCAM1_down	1.12	VCAM1	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
NVS_ADME_rCYP2C13	1.12	Cyp2c13	enzyme reporter	Novascreen	NA
BSK_KF3CT_uPA_down	1.12	PLAU	binding reporter	Bioseek	keratinocytes and foreskin fibroblasts
BSK_3C_MCP1_down	1.13	CCL2	binding reporter	Bioseek	umbilical vein endothelium
BSK_CASM3C_LDLR_down	1.14	LDLR	binding reporter	Bioseek	coronary artery smooth muscle cells
APR_Hepat_DNA Damage_1hr_dn	1.14	TP53	viability reporter	Apredica	hepatocyte
BSK_BE3C_MMP1_down	1.14	MMP1	binding reporter	Bioseek	bronchial

					epithelial cells
BSK_CASM3C_HLADR_down	1.14	HLA-DRA	binding reporter	Bioseek	coronary artery smooth muscle cells
NVS_NR_hPXR	1.14	NR1I2	binding reporter	Novascreen	NA
BSK_BE3C_HLADR_down	1.15	HLA-DRA	binding reporter	Bioseek	bronchial epithelial cells
BSK_3C_ICAM1_down	1.15	ICAM1	binding reporter	Bioseek	umbilical vein endothelium
OT_FXR_FXRSRC1_0480	1.15	NR1H4 SRC	binding reporter	Odyssey Thera	HEK293T
BSK_CASM3C_SRБ_down	1.16	NA	viability reporter	Bioseek	coronary artery smooth muscle cells
BSK_LPS_TNF α _down	1.16	TNF	binding reporter	Bioseek	umbilical vein endothelium and peripheral blood mononuclear cells
BSK_CASM3C_MCSF_down	1.16	CSF1	binding reporter	Bioseek	coronary artery smooth muscle

					cells
BSK_CASM3C_MCP1_down	1.17	CCL2	binding reporter	Bioseek	coronary artery smooth muscle cells
BSK_CASM3C_SAA_down	1.17	SAA1	binding reporter	Bioseek	coronary artery smooth muscle cells
TOX21_ARE_BLA_Agonist_ch2	1.17	NFE2L2	background reporter	Tox21/NCGC	HepG2
BSK_3C_MIG_down	1.17	CXCL9	binding reporter	Bioseek	umbilical vein endothelium
TOX21_AR_LUC_MDAKB2_Antagonist2	1.18	NA	inducible reporter	Tox21/NCGC	NA
BSK_BE3C_SRB_down	1.19	NA	viability reporter	Bioseek	bronchial epithelial cells
NVS_TR_hDAT	1.19	SLC6A3	binding reporter	Novascreen	NA
BSK_BE3C_uPA_down	1.21	PLAU	binding reporter	Bioseek	bronchial epithelial cells
BSK_KF3CT_TIMP2_down	1.21	TIMP2	binding reporter	Bioseek	keratinocytes and foreskin fibroblasts

BSK_BE3C_MIG_down	1.21	CXCL9	binding reporter	Bioseek	bronchial epithelial cells
BSK_KF3CT_ICAM1_down	1.21	ICAM1	binding reporter	Bioseek	keratinocytes and foreskin fibroblasts
NVS_NR_cAR	1.22	AR	binding reporter	Novascreen	NA
NVS_ENZ_hMMP7	1.24	MMP7	enzyme reporter	Novascreen	NA
NVS_GPCR_hOpiate_mu	1.28	OPRM1	binding reporter	Novascreen	NA
APR_Hepat_Apoptosis_1hr_dn	1.31	CYCS	morphology reporter	Apredica	hepatocyte
TOX21_AR_BLA_Antagonist_viability	1.34	NA	viability reporter	Tox21/NCGC	HEK293T
NVS_GPCR_rSST	1.35	Sstr1	binding reporter	Novascreen	NA
NVS_ENZ_oCOX2	1.37	PTGS2	enzyme reporter	Novascreen	NA
BSK_BE3C_IL1a_down	1.38	IL1A	binding reporter	Bioseek	bronchial epithelial cells
TOX21_Aromatase_Inhibition	1.39	CYP19A1	inducible reporter	Tox21/NCGC	MCF-7
APR_Hepat_CellLoss_1hr_dn	1.40	NA	viability reporter	Apredica	hepatocyte
NCCT_QuantiLum_inhib_dn	1.40	NA	enzyme reporter	NCCT's	NA

Simmons Lab					
TOX21_AR_BLA_Antagonist_ch2	1.40	AR	background reporter	Tox21/NCGC	HEK293T
NVS_NR_rAR	1.40	Ar	binding reporter	Novascreen	NA
Tanguay_ZF_120hpf_MORT_up	1.41	NA	NA	Tanguay Lab	dechorionated zebrafish embryo
NVS_NR_bPR	1.41	PGR	binding reporter	Novascreen	NA
NVS_TR_gDAT	1.42	Slc6a3	binding reporter	Novascreen	NA
TOX21_GR_BLA_Agonist_ch1	1.46	NR3C1	background reporter	Tox21/NCGC	HeLa
NVS_ENZ_rMAOAC	1.46	Maoa	enzyme reporter	Novascreen	NA
TOX21_HSE_BLA_agonist_ch1	1.47	HSF1	background reporter	Tox21/NCGC	HeLa
NVS_GPCR_mCCKAPeripheral	1.48	Cckar	binding reporter	Novascreen	NA
APR_HepG2_MitoticArrest_72h_up	1.48	H3F3A	morphology reporter	Apredica	HepG2
TOX21_AR_BLA_Antagonist_ratio	1.48	AR	inducible reporter	Tox21/NCGC	HEK293T
APR_HepG2_MitoMass_24h_dn	1.49	NA	morphology reporter	Apredica	HepG2
APR_HepG2_OxidativeStress_72h_up	1.50	H2AFX	viability reporter	Apredica	HepG2

TOX21_AR_LUC_MDAKB2_Antagonist	1.51	AR	inducible reporter	Tox21/NCGC	MDA-kb2
ATG_XTT_Cytotoxicity_up	1.51	NA	viability reporter	Attagene	HepG2
TOX21_p53_BLA_p1_viability	1.51	NA	viability reporter	Tox21/NCGC	HCT116
BSK_CASM3C_Thrombomodulin_down		THBD	binding reporter	Bioseek	coronary artery smooth muscle cells
BSK_CASM3C_VCAM1_down	1.52	VCAM1	binding reporter	Bioseek	coronary artery smooth muscle cells
BSK_CASM3C_IL8_down	1.52	CXCL8	binding reporter	Bioseek	coronary artery smooth muscle cells
BSK_CASM3C_MIG_down	1.52	CXCL9	binding reporter	Bioseek	coronary artery smooth muscle cells
NVS_GPCR_hNK2	1.53	TACR2	binding reporter	Novascreen	NA
APR_HepG2_OxidativeStress_24h_up	1.53	H2AFX	viability reporter	Apredica	HepG2
NVS_GPCR_hAdrb1	1.54	ADRB1	binding reporter	Novascreen	NA

TOX21_ERa_BLA_Antagonist_ratio	1.54	ESR1	inducible reporter	Tox21/NCGC	HEK293T
APR_HepG2_p53Act_24h_up	1.54	TP53	viability reporter	Apredica	HepG2
APR_HepG2_CellLoss_72h_dn	1.54	NA	viability reporter	Apredica	HepG2
NVS_GPCR_h5HT7	1.55	HTR7	binding reporter	Novascreen	NA
TOX21_HSE_BLA_agonist_ratio	1.56	HSF1	inducible reporter	Tox21/NCGC	HeLa
TOX21_NFkB_BLA_agonist_viability	1.56	NA	viability reporter	Tox21/NCGC	ME-180
TOX21_PPARd_BLA_Agonist_viability	1.56	NA	viability reporter	Tox21/NCGC	HEK293T
TOX21_NFkB_BLA_agonist_ch1	1.57	NFKB1	background reporter	Tox21/NCGC	ME-180
TOX21_p53_BLA_p1_ch1	1.57	TP53	background reporter	Tox21/NCGC	HCT116
TOX21_GR_BLA_Antagonist_ch2	1.59	NR3C1	background reporter	Tox21/NCGC	HeLa
TOX21_ERa_BLA_Antagonist_viability	1.59	NA	viability reporter	Tox21/NCGC	HEK293T
NVS_ENZ_rMAOBP	1.61	Maob	enzyme reporter	Novascreen	NA
NVS_ENZ_hAKT2	1.61	AKT2	enzyme reporter	Novascreen	NA
TOX21_GR_BLA_Agonist_ratio	1.61	NR3C1	inducible reporter	Tox21/NCGC	HeLa
TOX21_VDR_BLA_antagonist_viability	1.62	NA	viability reporter	Tox21/NCGC	HEK293T

TOX21_ESRE_BLA_ch1	1.62	ATF6	background reporter	Tox21/NCGC	HeLa
Tanguay_ZF_120hpf_ActivityScore	1.63	NA	NA	Tanguay Lab	dechorionated zebrafish embryo
TOX21_p53_BLA_p4_viability	1.63	NA	viability reporter	Tox21/NCGC	HCT116
TOX21_p53_BLA_p2_viability	1.63	NA	viability reporter	Tox21/NCGC	HCT116
TOX21_p53_BLA_p5_viability	1.65	NA	viability reporter	Tox21/NCGC	HCT116
TOX21_ESRE_BLA_ratio	1.66	ATF6	inducible reporter	Tox21/NCGC	HeLa
TOX21_p53_BLA_p4_ch1	1.66	TP53	background reporter	Tox21/NCGC	HCT116
APR_Hepat_MitoFxnl_1hr_dn	1.67	NA	membrane potential reporter	Apredica	hepatocyte
TOX21_p53_BLA_p2_ch1	1.67	TP53	background reporter	Tox21/NCGC	HCT116
NCCT_TPO_AUR_dn	1.68	Tpo	enzyme reporter	NCCT's Simmons Lab	NA
APR_HepG2_StressKinase_72h_up	1.68	JUN	enzyme reporter	Apredica	HepG2
TOX21_FXR_BLA_antagonist_ratio	1.69	NR1H4	inducible reporter	Tox21/NCGC	HEK293T
TOX21_GR_BLA_Antagonist_viability	1.69	NA	viability reporter	Tox21/NCGC	HeLa

TOX21_HSE_BLA_agonist_viability	1.69	NA	viability reporter	Tox21/NCGC	HeLa
TOX21_p53_BLA_p5_ch1	1.77	TP53	background reporter	Tox21/NCGC	HCT116
TOX21_p53_BLA_p3_viability	1.78	NA	viability reporter	Tox21/NCGC	HCT116
TOX21_p53_BLA_p3_ch1	1.79	TP53	background reporter	Tox21/NCGC	HCT116
APR_HepG2_NuclearSize_24h_dn	1.80	NA	morphology reporter	Apredica	HepG2
TOX21_FXR_BLA_antagonist_viability	1.81	NA	viability reporter	Tox21/NCGC	HEK293T
APR_HepG2_MitoticArrest_24h_up	1.81	H3F3A	morphology reporter	Apredica	HepG2
APR_Hepat_CellLoss_24hr_dn	1.82	NA	viability reporter	Apredica	hepatocyte
TOX21_VDR_BLA_Agonist_viability	1.84	NA	viability reporter	Tox21/NCGC	HEK293T
APR_HepG2_MicrotubuleCSK_72h_dn	1.85	TUBA1A	conformation reporter	Apredica	HepG2
TOX21_ERa_LUC_BG1_Antagonist	1.85	ESR1	inducible reporter	Tox21/NCGC	BG1
APR_Hepat_DNATexture_48hr_up	1.85	NA	conformation reporter	Apredica	hepatocyte
APR_Hepat_CellLoss_48hr_dn	1.86	NA	viability reporter	Apredica	hepatocyte
TOX21_p53_BLA_p1_ratio	1.86	TP53	inducible reporter	Tox21/NCGC	HCT116
APR_Hepat_DNADamage_48hr_up	1.87	TP53	viability reporter	Apredica	hepatocyte

APR_Hepat_Apoptosis_48hr_up	1.87	CYCS	morphology reporter	Apredica	hepatocyte
APR_Hepat_Steatosis_48hr_up	1.88	NA	morphology reporter	Apredica	hepatocyte
APR_Hepat_DNATexture_24hr_up	1.88	NA	conformation reporter	Apredica	hepatocyte
TOX21_p53_BLA_p5_ratio	1.89	TP53	inducible reporter	Tox21/NCGC	HCT116
APR_Hepat_NuclearSize_48hr_dn	1.89	NA	morphology reporter	Apredica	hepatocyte
APR_Hepat_Apoptosis_24hr_up	1.90	CYCS	morphology reporter	Apredica	hepatocyte
APR_Hepat_DNADamage_24hr_up	1.91	TP53	viability reporter	Apredica	hepatocyte
TOX21_p53_BLA_p4_ratio	1.91	TP53	inducible reporter	Tox21/NCGC	HCT116
TOX21_p53_BLA_p3_ratio	1.91	TP53	inducible reporter	Tox21/NCGC	HCT116
TOX21_AR_BLA_Agonist_ratio	1.93	AR	inducible reporter	Tox21/NCGC	HEK293T
APR_Hepat_NuclearSize_24hr_dn	1.94	NA	morphology reporter	Apredica	hepatocyte
APR_Hepat_MitoFxnl_48hr_dn	1.97	NA	membrane potential reporter	Apredica	hepatocyte
TOX21_ARE_BLA_Agonist_ch1	2.00	NFE2L2	background reporter	Tox21/NCGC	HepG2
APR_Hepat_Steatosis_1hr_dn	2.01	NA	morphology reporter	Apredica	hepatocyte
APR_HepG2_OxidativeStress_1h_up	2.04	H2AFX	viability reporter	Apredica	HepG2

APR_HepG2_NuclearSize_1h_dn	2.04	NA	morphology reporter	Apredica	HepG2
TOX21_p53_BLA_p2_ratio	2.05	TP53	inducible reporter	Tox21/NCGC	HCT116
APR_HepG2_MitoMass_1h_dn	2.06	NA	morphology reporter	Apredica	HepG2
APR_HepG2_CellCycleArrest_1h_dn	2.07	NA	morphology reporter	Apredica	HepG2
APR_Hepat_MitoFxnl_24hr_dn	2.08	NA	membrane potential reporter	Apredica	hepatocyte
APR_HepG2_CellLoss_1h_dn	2.09	NA	viability reporter	Apredica	HepG2
TOX21_ESRE_BLA_viability	2.26	NA	viability reporter	Tox21/NCGC	HeLa
TOX21_NFkB_BLA_agonist_ratio	2.40	NFKB1	inducible reporter	Tox21/NCGC	ME-180

*The rows in grey color are 33 selected “gene-based HepG2” assays

Table S15. Six overlapped genes between ToxCast responsive genes and CRISPR-Cas9 resistant/sensitive genes of triclosan

Gene Symbols	CRISPR-Cas9 resistant/sensitive genes	Obesity	Breast cancer
NR1I2	IC50 Sensitive Genes	Y	Y
PAX6	IC50 Resistant Genes	Y	N
XBP1	IC20 Resistant Genes	Y	Y
SP1	IC50 Sensitive Genes	N	Y
PPARG	IC50 Resistant Genes	Y	Y
NR1H3	IC50 Sensitive Genes	Y	N

Y: The gene may be potentially associated with the disease term according to DisGeNET database

N: The gene may not be potentially associated with the disease term according to DisGeNET database