

Supplementary Table 3. Detailed information on the characterization of gene and drug members of unified conserved drug-induced (CODI) modules, CODI-associated modules of rat liver and selected cell line-specific modules linked to certain MOA.

CODI module 1

108 genes, 41 chemicals

Functional enrichment of genes:

Annotation Cluster 1		Enrichment Score: 32.82	
Category	Term		PValue
GOTERM_BP_FAT	GO:0022403~cell cycle phase		2.17E-49
GOTERM_BP_FAT	GO:0022402~cell cycle process		3.14E-47
GOTERM_BP_FAT	GO:0000279~M phase		1.13E-46
GOTERM_BP_FAT	GO:0000278~mitotic cell cycle		2.02E-45
GOTERM_BP_FAT	GO:0007049~cell cycle		3.92E-43
GOTERM_BP_FAT	GO:0000280~nuclear division		6.23E-43
GOTERM_BP_FAT	GO:0007067~mitosis		6.23E-43
GOTERM_BP_FAT	GO:0000087~M phase of mitotic cell cycle		1.41E-42
SP_PIR_KEYWORDS	cell cycle		1.45E-42
GOTERM_BP_FAT	GO:0048285~organelle fission		5.27E-42
SP_PIR_KEYWORDS	cell division		2.94E-39
SP_PIR_KEYWORDS	mitosis		3.45E-39
GOTERM_BP_FAT	GO:0051301~cell division		2.17E-32
GOTERM_CC_FAT	GO:0005819~spindle		3.78E-30
GOTERM_CC_FAT	GO:0015630~microtubule cytoskeleton		7.66E-28
GOTERM_CC_FAT	GO:0044430~cytoskeletal part		5.66E-22
GOTERM_CC_FAT	GO:0005856~cytoskeleton		6.46E-18
GOTERM_CC_FAT	GO:0043228~non-membrane-bounded organelle		4.09E-17
GOTERM_CC_FAT	GO:0043232~intracellular non-membrane-bounded organelle		4.09E-17
SP_PIR_KEYWORDS	cytoskeleton		2.01E-12
SP_PIR_KEYWORDS	coiled coil		2.77E-04
Annotation Cluster 2		Enrichment Score: 15.65	
Category	Term		PValue
GOTERM_BP_FAT	GO:0007017~microtubule-based process		1.03E-24
GOTERM_BP_FAT	GO:0000226~microtubule cytoskeleton organization		1.22E-17
GOTERM_BP_FAT	GO:0007051~spindle organization		4.79E-12
GOTERM_BP_FAT	GO:0007010~cytoskeleton organization		3.98E-11
Annotation Cluster 3		Enrichment Score: 10.90	
Category	Term		PValue
GOTERM_BP_FAT	GO:0007059~chromosome segregation		1.36E-16
GOTERM_BP_FAT	GO:0000819~sister chromatid segregation		2.94E-13
GOTERM_BP_FAT	GO:0000070~mitotic sister chromatid segregation		2.94E-13
GOTERM_BP_FAT	GO:0051276~chromosome organization		1.33E-09
GOTERM_BP_FAT	GO:0051640~organelle localization		3.15E-09
GOTERM_BP_FAT	GO:0051656~establishment of organelle localization		7.56E-08

Genes:

probe set	Gene Symbol	Ensembl ID	Protein name	# of cell lines
201088_at	KPNA2	ENSP00000332455	karyopherin alpha 2 (RAG cohort 1, importin alpha 1)	3
201291_s_at	TOP2A	ENSP00000411532	topoisomerase (DNA) II alpha 170kDa	3
201896_s_at	PSRC1	ENSP00000358925	proline/serine-rich coiled-coil 1	3
202240_at	PLK1	ENSP00000300093	polo-like kinase 1	3
202705_at	CCNB2	ENSP00000288207	cyclin B2	3
202870_s_at	CDC20	ENSP00000308450	cell division cycle 20 homolog (S. cerevisiae)	3
202954_at	UBE2C	ENSP00000348838	ubiquitin-conjugating enzyme E2C	3

203554_x_at	PTTG1	ENSP00000344936	pituitary tumor-transforming 1	3
203755_at	BUB1B	ENSP00000287598	budding uninhibited by benzimidazoles 1 homolog beta (yeast)	3
203764_at	DLGAP5	ENSP00000247191	discs, large (Drosophila) homolog-associated protein 5	3
204092_s_at	AURKA	ENSP00000216911	aurora kinase A	3
204170_s_at	CKS2	ENSP00000364976	CDC28 protein kinase regulatory subunit 2	3
204641_at	NEK2	ENSP00000355966	NIMA (never in mitosis gene a)-related kinase 2	3
204649_at	TROAP	ENSP00000257909	trophinin associated protein (tastin)	3
204709_s_at	KIF23	ENSP00000260363	kinesin family member 23	3
204826_at	CCNF	ENSP00000380256	cyclin F	3
204962_s_at	CENPA	ENSP00000336868	centromere protein A	3
205046_at	CENPE	ENSP00000265148	centromere protein E, 312kDa	3
205240_at	GPSM2	ENSP00000264126	G-protein signaling modulator 2	3
206364_at	KIF14	ENSP00000356319	kinesin family member 14	3
207165_at	HMMR	ENSP00000377492	hyaluronan-mediated motility receptor (RHAMM)	3
207828_s_at	CENPF	ENSP00000355922	centromere protein F, 350/400kDa (mitosin)	3
209408_at	KIF2C	ENSP00000361298	kinesin family member 2C	3
209464_at	AURKB	ENSP00000313950	aurora kinase B	3
209642_at	BUB1	ENSP00000302530	budding uninhibited by benzimidazoles 1 homolog (yeast)	3
210052_s_at	TPX2	ENSP00000300403	TPX2, microtubule-associated, homolog (Xenopus laevis)	3
212020_s_at	MKI67	ENSP00000357643	antigen identified by monoclonal antibody Ki-67	3
214710_s_at	CCNB1	ENSP00000256442	cyclin B1	3
218009_s_at	PRC1	ENSP00000377793	protein regulator of cytokinesis 1	3
218039_at	NUSAP1	ENSP00000260359	nucleolar and spindle associated protein 1	3
218355_at	KIF4A	ENSP00000363524	kinesin family member 4A	3
218726_at	HJURP	ENSP00000414109	Holliday junction recognition protein	3
218755_at	KIF20A	ENSP00000378356	kinesin family member 20A	3
219918_s_at	ASPM	ENSP00000356379	asp (abnormal spindle) homolog, microcephaly associated (Drosophila)	3
220295_x_at	DEPDC1	ENSP00000412292	DEP domain containing 1	3
221436_s_at	CDCA3	ENSP00000229265	cell division cycle associated 3	3
221520_s_at	CDCA8	ENSP00000316121	cell division cycle associated 8	3
222039_at	KIF18B	ENSP00000341466	kinesin family member 18B	3
201774_s_at	NCAPD2	ENSP00000325017	non-SMC condensin I complex, subunit D2	2
201853_s_at	CDC25B	ENSP00000245960	cell division cycle 25 homolog B (S. pombe)	2
202094_at	BIRC5	ENSP00000301633	baculoviral IAP repeat containing 5	2
202779_s_at	UBE2S	ENSP00000264552	ubiquitin-conjugating enzyme E2S	2
203145_at	SPAG5	ENSP00000323300	sperm associated antigen 5	2
203213_at	CDK1	ENSP00000306043	cyclin-dependent kinase 1	2
203418_at	CCNA2	ENSP00000274026	cyclin A2	2
204162_at	NDC80	ENSP00000261597	NDC80 homolog, kinetochore complex component (S. cerevisiae)	2
204244_s_at	DBF4	ENSP00000265728	DBF4 homolog (S. cerevisiae)	2
204315_s_at	GTSE1	ENSP00000160874	G-2 and S-phase expressed 1	2
204444_at	KIF11	ENSP00000260731	kinesin family member 11	2
204822_at	TTK	ENSP00000230510	TTK protein kinase	2
205167_s_at	CDC25C	ENSP00000321656	cell division cycle 25 homolog C (S. pombe)	2
209714_s_at	CDKN3	ENSP00000335357	cyclin-dependent kinase inhibitor 3	2
212738_at	ARHGAP19	ENSP00000351333	Rho GTPase activating protein 19	2
212832_s_at	CKAP5	ENSP00000346566	cytoskeleton associated protein 5	2
218252_at	CKAP2	ENSP00000367276	cytoskeleton associated protein 2	2

218308_at	TACC3	ENSP00000326550	transforming, acidic coiled-coil containing protein 3	2
218542_at	CEP55	ENSP00000360540	centrosomal protein 55kDa	2
219544_at	C13ORF34	ENSP00000375082	Protein aurora borealis	2
219787_s_at	ECT2	ENSP00000232458	epithelial cell transforming sequence 2 oncogene	2
221258_s_at	KIF18A	ENSP00000263181	kinesin family member 18A	2
221591_s_at	FAM64A	ENSP00000308470	family with sequence similarity 64, member A	2
221685_s_at	CCDC99	ENSP00000265295	coiled-coil domain containing 99	2
222077_s_at	RACGAP1	ENSP00000309871	Rac GTPase activating protein 1	2
200974_at	ACTA2	ENSP00000224784	actin, alpha 2, smooth muscle, aorta	1
201236_s_at	BTG2	ENSP00000290551	BTG family, member 2	1
201464_x_at	JUN	ENSP00000360266	jun proto-oncogene	1
201663_s_at	SMC4	ENSP00000341382	structural maintenance of chromosomes 4	1
201795_at	LBR	ENSP00000272163	lamin B receptor	1
202149_at	NEDD9	ENSP00000368759	neural precursor cell expressed, developmentally down-regulated 9	1
202227_s_at	BRD8	ENSP00000254900	bromodomain containing 8	1
202284_s_at	CDKN1A	ENSP00000244741	cyclin-dependent kinase inhibitor 1A (p21, Cip1)	1
202672_s_at	ATF3	ENSP00000344352	activating transcription factor 3	1
202859_x_at	IL8	ENSP00000306512	interleukin 8	1
203409_at	DDB2	ENSP00000256996	damage-specific DNA binding protein 2, 48kDa	1
203574_at	NFIL3	ENSP00000297689	nuclear factor, interleukin 3 regulated	1
203725_at	GADD45A	ENSP00000360025	growth arrest and DNA-damage-inducible, alpha	1
204285_s_at	PMAIP1	ENSP00000326119	phorbol-12-myristate-13-acetate-induced protein 1	1
204492_at	ARHGAP11A	ENSP00000355090	Rho GTPase activating protein 11A	1
204748_at	PTGS2	ENSP00000356438	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	1
204780_s_at	FAS	ENSP00000347979	Fas (TNF receptor superfamily, member 6)	1
204817_at	ESPL1	ENSP00000257934	extra spindle pole bodies homolog 1 (S. cerevisiae)	1
204855_at	SERPINB5	ENSP00000372221	serpin peptidase inhibitor, clade B (ovalbumin), member 5	1
204977_at	DDX10	ENSP00000314348	DEAD (Asp-Glu-Ala-Asp) box polypeptide 10	1
205114_s_at	CCL3	ENSP00000225245	chemokine (C-C motif) ligand 3	1
205220_at	GPR109B	ENSP00000375066	G protein-coupled receptor 109B	1
205235_s_at	KIF20B	ENSP00000260753	kinesin family member 20B	1
205266_at	LIF	ENSP00000249075	leukemia inhibitory factor (cholinergic differentiation factor)	1
205281_s_at	PIGA	ENSP00000369820	phosphatidylinositol glycan anchor biosynthesis, class A	1
205436_s_at	H2AFX	ENSP00000364310	H2A histone family, member X	1
205967_at	HIST1H4C	ENSP00000367034	histone cluster 1, H4c	1
207813_s_at	FDXR	ENSP00000293195	ferredoxin reductase	1
208808_s_at	HMGB2	ENSP00000296503	high-mobility group box 2	1
208886_at	H1F0	ENSP00000344504	H1 histone family, member 0	1
209122_at	PLIN2	ENSP00000276914	perilipin 2	1
209457_at	DUSP5	ENSP00000358596	dual specificity phosphatase 5	1
209610_s_at	SLC1A4	ENSP00000234256	solute carrier family 1 (glutamate/neutral amino acid transporter), member 4	1
209795_at	CD69	ENSP00000228434	CD69 molecule	1
210609_s_at	TP53I3	ENSP00000238721	tumor protein p53 inducible protein 3	1
211935_at	ARL6IP1	ENSP00000306788	ADP-ribosylation factor-like 6 interacting protein 1	1
212949_at	NCAPH	ENSP00000240423	non-SMC condensin I complex, subunit H	1
217373_x_at	MDM2	ENSP00000417281	Mdm2 p53 binding protein homolog (mouse)	1
217996_at	PHLDA1	ENSP00000266671	pleckstrin homology-like domain, family A, member 1	1
218346_s_at	SESN1	ENSP00000306734	sestrin 1	1

218662_s_at	NCAPG	ENSP00000251496	non-SMC condensin I complex, subunit G	1
219306_at	KIF15	ENSP00000324020	kinesin family member 15	1
219392_x_at	PRR11	ENSP00000262293	proline rich 11	1
219936_s_at	GPR87	ENSP00000260843	G protein-coupled receptor 87	1
221586_s_at	E2F5	ENSP00000398124	E2F transcription factor 5, p130-binding	1

Drug annotation:

No enriched terms found.

Drugs	# of cell lines	Drug annotation	Literature evidence
ciclopirox	3	cell cycle blocker; antifungal (ATC: D01AE14)	(Zhou <i>et al.</i> , 2010)
etoposide	3	cell cycle blocker; anticancer (ATC:L01CB01)	(Gordaliza <i>et al.</i> , 2004)
methotrexate	3	cell cycle blocker; antimetabolite (ATC: L01BA01)	(Hertz <i>et al.</i> , 1956)
monobenzone	3	depigmentation agent (ATC:D11AX13)	
pyrimethamine	3	cell cycle blocker; antimalarial (ATC:P01BD01)	(Giammarioli <i>et al.</i> , 2008)
trifluridine	3	cell cycle blocker; thymidine analog/antiviral (ATC:S01AD02)	(Temmink <i>et al.</i> , 2004)
vidarabine	3	cell cycle blocker; antiviral (ATC: J05AB03)	(Brink & Lepage, 1965)
thioguanosine	2	cell cycle blocker; guanine analog	(Lepage, 1963)
triamterene	2	diuretic (ATC:C03DB02)	
vinburnine	2	vasodilator (ATC: C04AX17)	
(+)-chelidone	1	cell cycle blocker	(Panzer <i>et al.</i> , 2001)
15-delta prostaglandin J2	1	NSAID; inhibition of cell proliferation	(Kim <i>et al.</i> , 2007)
8-azaguanine	1	cell cycle blocker; purine analog	(Colsky <i>et al.</i> , 1955)
atovaquone	1	an analog of ubiquinone (ATC: P01AX06); cytotoxic derivatives	(Zhou <i>et al.</i> , 2009)
betulinic acid	1	anti-retroviral, anti-malarial, and anti-inflammatory; cell cycle blocker	(Fulda, 2008)
cefotiam	1	inhibit proliferation; antibiotic (ATC:J01DC07)	(Akira <i>et al.</i> , 2000)
cinchonine	1	alkaloid	
clioquinol	1	cell cycle blocker; antifungal (ATC:G01AC02)	(Zhai <i>et al.</i> , 2010)
dequalinium chloride	1	anticarcinogenic activity; antiseptic (ATC: D08AH01)	(Weiss <i>et al.</i> , 1987)
diethylstilbestrol	1	inhibit proliferation of human prostate cancer cell lines; nonsteroidal estrogen (ATC: G03CB02)	(Koike <i>et al.</i> , 2005)
ethaverine	1	Vasodilator and antispasmodic; structurally similar to papaverine	
ethoxyquin	1	antioxidant; genotoxic/induce apoptosis	(Błaszczuk & Skolimowski, 2005)
gossypol	1	antiproliferative activity	(Le Blanc <i>et al.</i> , 2002)
hycanthone	1	cytotoxic; cell cycle blocker; inhibit rna synthesis	(Sieber <i>et al.</i> , 1973; Wong <i>et al.</i> , 1990)
mephentermine	1	cardiac stimulant (ATC: C01CA11)	
methylbenzethonium chloride	1	induce apoptosis	(Yip <i>et al.</i> , 2006)
nifuroxazide	1	inhibit myeloma survival; antibiotic (ATC: A07AX03)	(Nelson <i>et al.</i> , 2008)
paclitaxel	1	cell cycle blocker; stabilizing microtubules	(Jordan <i>et al.</i> , 1993)
primaquine	1	antimalaria (ATC:P01BA03)	
progesterone	1	inhibit epithelial cell proliferation; hormon (ATC:G03DA04)	(Hsu <i>et al.</i> , 2008)
pyrvinium	1	inhibit proliferation in colon cancer ; antiparasitic (ATC:P02CX01)	(Thorne <i>et al.</i> , 2010)
rimexolone	1	cell cycle blocker; H02 Corticosteroids for systemic use (ATC: H02AB12)	(Spies <i>et al.</i> , 2010)
seneciophylline	1	cytotoxic/mutagenic (not antiproliferative)	(Griffin & Segall, 1986)
sirolimus	1	inhibit proliferation; immunosuppressant (ATC:L04AA10)	(Wang <i>et al.</i> , 2007)
sulconazole	1	antifungal (ATC: D01AC09)	
thioridazine	1	cytogenetic damage; inhibit cell proliferation; antipsychotic drug (ATC: N05AC02)	(Strobl <i>et al.</i> , 1990)

ticarcillin	1	antiproliferative effect on human cell lines; b-lactam inhibitor(antibiotic) (ATC: J01CA13)	(Weston <i>et al</i> , 1986)
trifluoperazine	1	reduce cell proliferation; anticalmodulin and blocker of phospholipase A2; antipsychotic (ATC:N05AB06)	(Izaguirre Roncal <i>et al</i> , 2001)
trimethylcolchicinic acid	1	cell cycle blocker; inhibit microtubule polymerization	(Lessner <i>et al</i> , 1963)
zalcitabine	1	mitochondrial toxicity; nucleoside analog reverse transcriptase inhibitor (ATC: J05AF03)	(Walker <i>et al</i> , 2003)
zidovudine	1	cell cycle blocker;nucleoside analog reverse-transcriptase inhibitor (ATC:J05AF01)	(Wagner <i>et al</i> , 1997)

CODI module 2

62 genes, 63 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 19.04	
Category	Term	PValue
SP_PIR_KEYWORDS	lipid synthesis	3.64E-30
SP_PIR_KEYWORDS	Steroid biosynthesis	1.08E-29
GOTERM_BP_FAT	GO:0016126~sterol biosynthetic process	2.97E-25
GOTERM_BP_FAT	GO:0006694~sterol biosynthetic process	2.38E-24
SP_PIR_KEYWORDS	sterol biosynthesis	1.19E-23
GOTERM_BP_FAT	GO:0016125~sterol metabolic process	3.59E-23
GOTERM_BP_FAT	GO:0008202~sterol metabolic process	4.89E-23
GOTERM_BP_FAT	GO:0008610~lipid biosynthetic process	7.93E-21
GOTERM_BP_FAT	GO:0008203~cholesterol metabolic process	1.27E-18
GOTERM_BP_FAT	GO:0006695~cholesterol biosynthetic process	2.22E-18
SP_PIR_KEYWORDS	Cholesterol biosynthesis	5.52E-18
KEGG_PATHWAY	hsa00100:Steroid biosynthesis	2.16E-17
SP_PIR_KEYWORDS	oxidoreductase	6.00E-09
GOTERM_BP_FAT	GO:0055114~oxidation reduction	9.65E-08
SP_PIR_KEYWORDS	nadp	2.53E-07
Annotation Cluster 2	Enrichment Score: 9.49	
Category	Term	PValue
KEGG_PATHWAY	hsa00100:Steroid biosynthesis	2.16E-17
GOTERM_CC_FAT	GO:0005783~endoplasmic reticulum	1.10E-15
GOTERM_CC_FAT	GO:0042175~nuclear envelope-endoplasmic reticulum network	1.11E-09
GOTERM_CC_FAT	GO:0005789~endoplasmic reticulum membrane	6.74E-09
GOTERM_CC_FAT	GO:0044432~endoplasmic reticulum part	1.21E-08
GOTERM_CC_FAT	GO:0012505~endomembrane system	1.53E-06
GOTERM_CC_FAT	GO:0031090~organelle membrane	1.07E-04
Annotation Cluster 3	Enrichment Score: 9.38	
Category	Term	PValue
SP_PIR_KEYWORDS	sterol biosynthesis	1.19E-23
GOTERM_BP_FAT	GO:0008203~cholesterol metabolic process	1.27E-18
GOTERM_BP_FAT	GO:0006695~cholesterol biosynthetic process	2.22E-18
SP_PIR_KEYWORDS	Cholesterol biosynthesis	5.52E-18
GOTERM_BP_FAT	GO:0008299~isoprenoid biosynthetic process	4.13E-08
KEGG_PATHWAY	hsa00900:Terpenoid backbone biosynthesis	4.10E-07
GOTERM_BP_FAT	GO:0006720~isoprenoid metabolic process	1.27E-06
SP_PIR_KEYWORDS	Isoprene biosynthesis	9.93E-04
GOTERM_CC_FAT	GO:0042579~microbody	0.014490138
GOTERM_CC_FAT	GO:0005777~peroxisome	0.014490138
SP_PIR_KEYWORDS	peroxisome	0.066043141

Genes:

probe	gene symbol	Protein name	cluster label	# of cell lines	Selected genes for siRNA screening
201790_s_at	DHCR7	7-dehydrocholesterol reductase	blue	3	Not tested
202245_at	LSS	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)	blue	3	Not tested

201275_at	FDPS	farnesyl diphosphate synthase	blue	3	Not tested
208647_at	FDFT1	farnesyl-diphosphate farnesyltransferase 1	blue	3	Not tested
200831_s at	SCD	stearoyl-CoA desaturase (delta-9-desaturase)	blue	3	Not tested
202539_s at	HMGCR	3-hydroxy-3-methylglutaryl-Coenzyme A reductase	blue	3	3 siRNAs
211423_s at	SC5DL	sterol-C5-desaturase (ERG3 delta-5-desaturase homolog, <i>S. cerevisiae</i>)-like	blue	3	Not tested
209218_at	SQLE	squalene epoxidase	blue	3	2 siRNAs
201625_s at	INSIG1	insulin induced gene 1	blue	3	2 siRNAs
204615_x at	IDI1	isopentenyl-diphosphate delta isomerase 1	blue	3	Not tested
209146_at	SC4MOL	sterol-C4-methyl oxidase-like	blue	3	Not tested
220081_x at	HSD17B7	hydroxysteroid (17-beta) dehydrogenase 7	green	3	Not tested
202218_s at	FADS2	fatty acid desaturase 2	blue	2	Not tested
212272_at	LPIN1	lipin 1	blue	2	2 siRNAs
212218_s at	FASN	fatty acid synthase	blue	2	Not tested
202679_at	NPC1	Niemann-Pick disease, type C1	blue	2	3 siRNAs
208926_at	NEU1	sialidase 1 (lysosomal sialidase)	blue	2	Not tested
209608_s at	ACAT2	acetyl-CoA acetyltransferase 2	blue	2	Not tested
202314_at	CYP51A1	cytochrome P450, family 51, subfamily A, polypeptide 1	blue	2	Not tested
209279_s at	NSDHL	NAD(P) dependent steroid dehydrogenase-like	blue	2	Not tested
202067_s at	LDLR	low density lipoprotein receptor	blue	2	3 siRNAs
221249_s at	FAM117A	family with sequence similarity 117, member A	green	2	2 siRNAs
212622_at	TMEM41B	transmembrane protein 41B	green	2	4 siRNAs
209118_s at	TUBA1A	tubulin, alpha 1a	blue	1	4 siRNAs
203027_s at	MVD	mevalonate (diphospho) decarboxylase	blue	1	Not tested
202735_at	EBP	emopamil binding protein (sterol isomerase)	blue	1	Not tested
201127_s at	ACLY	ATP citrate lyase	blue	1	Not tested
200862_at	DHCR24	24-dehydrocholesterol reductase	blue	1	Not tested
202562_s at	C14orf1	chromosome 14 open reading frame 1	blue	1	Not tested
208962_s at	FADS1	fatty acid desaturase 1	blue	1	Not tested
205822_s at	HMGCS1	3-hydroxy-3-methylglutaryl-CoA synthase 1 (soluble)	blue	1	Not tested
201193_at	IDH1	isocitrate dehydrogenase 1 (NADP+), soluble	blue	1	4 siRNAs
217869_at	HSD17B12	hydroxysteroid (17-beta) dehydrogenase 12	blue	1	Not tested
200632_s at	NDRG1	N-myc downstream regulated 1	brown	1	Not tested
209122_at	PLIN2	perilipin 2	brown	1	Not tested
202497_x at	SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 3	brown	1	Not tested
216236_s at	SLC2A14	solute carrier family 2 (facilitated glucose transporter), member 14	brown	1	3 siRNAs
202988_s at	RGS1	regulator of G-protein signaling 1	brown	1	4 siRNAs
209875_s at	SPP1	secreted phosphoprotein 1	brown	1	4 siRNAs
204014_at	DUSP4	dual specificity phosphatase 4	dark green	1	4 siRNAs
204698_at	ISG20	interferon stimulated exonuclease gene 20kDa	dark green	1	4 siRNAs
219117_s at	FKBP11	FK506 binding protein 11, 19 kDa	green	1	2 siRNAs
209173_at	AGR2	anterior gradient homolog 2 (<i>Xenopus laevis</i>)	green	1	4 siRNAs
202375_at	SEC24D	SEC24 family, member D (<i>S. cerevisiae</i>)	green	1	Not tested
218696_at	EIF2AK3	eukaryotic translation initiation factor 2-alpha kinase 3	green	1	4 siRNAs
219390_at	FKBP14	FK506 binding protein 14, 22 kDa	green	1	Not tested
210041_s at	PGM3	phosphoglucomutase 3	green	1	4 siRNAs
217858_s at	ARMCX3	armadillo repeat containing, X-linked 3	green	1	4 siRNAs
212345_s at	CREB3L2	cAMP responsive element binding protein 3-like 2	green	1	Not tested
211936_at	HSPA5	heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa)	green	1	4 siRNAs

202842_s_at	DNAJB9	DnaJ (Hsp40) homolog, subfamily B, member 9	green	1	4 siRNAs
217168_s_at	HERPUD1	homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	green	1	Not tested
203675_at	NUCB2	nucleobindin 2	green	1	2 siRNAs
202721_s_at	GFPT1	glutamine--fructose-6-phosphate transaminase 1	green	1	Not tested
203827_at	WIPI1	WD repeat domain, phosphoinositide interacting 1	green	1	4 siRNAs
202769_at	CCNG2	cyclin G2	green	1	Not tested
202887_s_at	DDIT4	DNA-damage-inducible transcript 4	green	1	Not tested
202341_s_at	TRIM2	tripartite motif containing 2	green	1	4 siRNAs
218437_s_at	LZTFL1	leucine zipper transcription factor-like 1	green	1	4 siRNAs
218976_at	DNAJC12	DnaJ (Hsp40) homolog, subfamily C, member 12	green	1	4 siRNAs
206683_at	ZNF165	zinc finger protein 165	green	1	4 siRNAs
205014_at	FGFBP1	fibroblast growth factor binding protein 1	light blue	1	4 siRNAs

Drug annotation:

Annotation type	Enriched term	q-value
Drug target	HTR2A; 5-hydroxytryptamine (serotonin) receptor 2A	3.60E-05
Drug target	HRH1; histamine receptor H1	8.94E-03
Drug target	DRD1; dopamine receptor D1	1.10E-02
Drug target	DRD2; dopamine receptor D2	1.45E-02
Drug target	HTR1A; 5-hydroxytryptamine (serotonin) receptor 1A	1.48E-02
Drug target	DRD4; dopamine receptor D4	2.22E-02
Drug target	CHRM5; cholinergic receptor, muscarinic 5	2.40E-02
Drug target	SLC6A4; solute carrier family 6 (neurotransmitter transporter, serotonin), member 4	2.65E-02
Drug target	DRD3; dopamine receptor D3	2.72E-02
Drug target	CYP2D6; cytochrome P450, family 2, subfamily D, polypeptide 6	3.04E-02
Drug target	CHRM3; cholinergic receptor, muscarinic 3	3.10E-02
Drug target	SLC6A2; solute carrier family 6 (neurotransmitter transporter, noradrenalin), member 2	3.10E-02
Drug target	ADRA1A; adrenergic, alpha-1A-, receptor	3.58E-02
Drug target	HTR2C; 5-hydroxytryptamine (serotonin) receptor 2C	6.47E-02
Drug target	CHRM1; cholinergic receptor, muscarinic 1	6.53E-02
Drug target	CHRM4; cholinergic receptor, muscarinic 4	8.95E-02
ATC code (2nd level)	N05; Psycholeptics	4.25E-03
Side effect	paralytic ileus	2.00E-04
Side effect	galactorrhea	3.33E-04
Side effect	adenitis	3.33E-04
Side effect	gynecomastia	6.19E-03
Side effect	SIADH	1.07E-02
Side effect	breast enlargement	1.21E-02
Side effect	testicular swelling	1.57E-02
Chemical Fragment	<chem>O=C(c1ccc(F)cc1)CCC</chem>	7.73E-04
Chemical Fragment	<chem>c1c3OCOc3(cc2c1CN(C)CC2)</chem>	7.73E-04
Chemical Fragment	<chem>C(c1cccc1)c2ccccc2</chem>	7.73E-04
Chemical Fragment	<chem>C(=C(NCc1cnc(nc1(N))C)C)S</chem>	7.73E-04
Chemical Fragment	<chem>c1ccc(cc1)C[N+](C)C</chem>	7.73E-04
Chemical Fragment	<chem>C1N(C)CCCC1</chem>	7.73E-04
Chemical Fragment	<chem>Cc1c(ccc1Cl)Cl</chem>	2.02E-03
Chemical Fragment	<chem>c1ccc(cc1)CN2CCN(C)CC2</chem>	7.68E-03

Drugs	# of cell lines	Drug annotation	Literature evidence
metixene	3	N04 Anti-parkinson drugs	
tetrandrine	3	calcium channel blocker	(Chen <i>et al</i> , 2011)
astemizole	2	histamine H1-receptor antagonist	
fluspirilene	2	N05 Psycholeptics	
maprotiline	2	N06 Psychoanaleptics	
metergoline	2	A dopamine agonist and serotonin antagonist (ATC: G02CB05)	(Hamon <i>et al</i> , 1981)
nortriptyline	2	N05 Psycholeptics	
perhexiline	2	antianginal agent (ATC: C08EX02)	
perphenazine	2	N05 Psycholeptics	
prochlorperazine	2	N05 Psycholeptics	
pregnenolone	1	GABAA antagonist and increases neurogenesis in the hippocampus	(Mayo <i>et al</i> , 2005)
mometasone	1	D07 Corticosteroids, dermatological preparations; glucocorticosteroid (ATC: D07AC13)	
nifuroxazide	1	inhibit myeloma survival; antibiotic (ATC: A07AX03)	(Nelson <i>et al</i> , 2008)
thiostrepton	1	oligo peptide antibiotic	
pimozide	1	N05 Psycholeptics	
karakoline	1	Ganglioblocker; nicotinic receptor antagonis	
trimethylcolchicinic acid	1	cell cycle blocker; inhibit microtubule polymerization	(Lessner <i>et al</i> , 1963)
piperacetazine	1	antipsychotic prodrug	(Rada & Donlon, 1974)
amodiaquine	1	anti-inflammatory (ATC: P01BA06)	
amoxapine	1	N06 Psychoanaleptics	
etiocholanolone	1	metabolite of testosterone	
suloctidil	1	vasodilator (ATC: C04AX19)	
chlorpromazine	1	N05 Psycholeptics	
chlorprothixene	1	N05 Psycholeptics	
ciclopirox	1	cell cycle blocker; antifungal (ATC: D01AE14)	(Zhou <i>et al</i> , 2010)
ciclosporin	1	immunosuppressant drug (ATC: L04AD01)	
dequalinium chloride	1	anticarcinogenic activity; antiseptic (ATC: D08AH01)	(Weiss <i>et al</i> , 1987)
desipramine	1	N06 Psychoanaleptics	
dydrogesterone	1	progesterone hormone (ATC: G03DB01)	
econazole	1	antifungal (ATC: D01AC03)	
ethaverine	1	Vasodilator and antispasmodic	
famprofazone	1	non-steroidal anti-inflammatory agent	
fluoxetine	1	N06 Psychoanaleptics	
geldanamycin	1	HSP90 inhibitors	(Miyata, 2005a)
glafenine	1	N02 Analgesics	
hecogenin	1	antioxidant and anti-inflammatory properties	(Santos Cerqueira <i>et al</i> , 2012)
homochlorcyclizine	1	antihistamine	(Haraguchi <i>et al</i> , 1997)
hydrocotarnine	1	alkaloid	
ketoconazole	1	antifungal drug (ATC: D01AC08)	
loperamide	1	opioid drug used against diarrhea (ATC: A07DA03)	
mestranol	1	estrogen	
metitepine	1	antipsychotic	(Monachon <i>et al</i> , 1972)
methylbenzethonium chloride	1	induce apoptosis	(Yip <i>et al</i> , 2006)
nabumetone	1	non-steroidal anti-inflammatory drug	(Gonzalo-Garijo <i>et al</i> , 2007)
nitrendipine	1	calcium channel blocker (ATC: C08CA08)	
oxetacaine	1	local anesthetic (ATC: C05AD06)	
papaverine	1	antispasmodic (ATC: A03AD01); inhibition of the enzyme	

		phosphodiesterase causing elevation of cyclic AMP	
procyclidine	1	N04 Anti-parkinson drugs	
promazine	1	N05 Psycholeptics	
propafenone	1	anti-arrhythmic medication (ATC: C01BC03)	
protriptyline	1	N06 Psychoanaleptics	
puromycin	1	antibiotic; protein synthesis inhibitor	
raloxifene	1	selective estrogen receptor modulator (ATC: G03XC01)	
terconazole	1	antifungal (ATC: G01AG02)	
thiethylperazine	1	antiemetic (ATC: R06AD03); potential antipsychotic activity	(Rotrosen <i>et al</i> , 1978)
thioridazine	1	N05 Psycholeptics (ATC: N05AC02); cytogenetic damage; inhibit cell proliferation;	(Strobl <i>et al</i> , 1990)
tracazolate	1	anxiolytic	(Patel & Malick, 1982)
trimipramine	1	N06 Psychoanaleptics	
saquinavir	1	antiretroviral (ATC: J05AE01)	
atovaquone	1	an analog of ubiquinone (ATC: P01AX06)	(Ittarat <i>et al</i> , 1995)
emetine	1	anti-protozoal; protein synthesis inhibitor	
thiopropazine	1	N05 Psycholeptics	
norcyclobenzaprine	1	structurally similar to tricyclic antidepressants	(Van Hoey)

CODI module 3

58 genes, 51 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 5.10	
Category	Term	PValue
SP_PIR_KEYWORDS	citrullination	8.85E-12
SP_PIR_KEYWORDS	nucleosome core	2.58E-11
INTERPRO	IPR007125:Histone core	4.91E-11
GOTERM_CC_FAT	GO:0000786~nucleosome	3.85E-10
SP_PIR_KEYWORDS	methylation	8.40E-10
GOTERM_CC_FAT	GO:0032993~protein-DNA complex	1.93E-08
GOTERM_BP_FAT	GO:0006334~nucleosome assembly	4.46E-08
GOTERM_BP_FAT	GO:0031497~chromatin assembly	6.02E-08
KEGG_PATHWAY	hsa05322:Systemic lupus erythematosus	7.18E-08
GOTERM_BP_FAT	GO:0065004~protein-DNA complex assembly	1.06E-07
SP_PIR_KEYWORDS	DNA binding	1.12E-07
GOTERM_BP_FAT	GO:0034728~nucleosome organization	1.21E-07
GOTERM_CC_FAT	GO:0000785~chromatin	1.42E-07
INTERPRO	IPR002119:Histone H2A	3.17E-07
SMART	SM00414:H2A	6.64E-07
GOTERM_BP_FAT	GO:0006323~DNA packaging	7.45E-07
SP_PIR_KEYWORDS	dna-binding	9.17E-07
SP_PIR_KEYWORDS	chromosomal protein	1.02E-06
PIR_SUPERFAMILY	PIRSF002048:histone H2A	1.13E-06
GOTERM_BP_FAT	GO:0006333~chromatin assembly or disassembly	1.44E-06
SP_PIR_KEYWORDS	ubl conjugation	7.21E-06
SP_PIR_KEYWORDS	isopeptide bond	9.47E-06
GOTERM_MF_FAT	GO:0003677~DNA binding	1.32E-05
UP_SEQ_FEATURE	cross-link:Glycyl lysine isopeptide (Lys-Gly) (interchain with G-Cter in ubiquitin)	2.62E-05
GOTERM_CC_FAT	GO:0044427~chromosomal part	4.99E-05
INTERPRO	IPR009072:Histone-fold	5.53E-05
SP_PIR_KEYWORDS	acetyllysine	1.13E-04
GOTERM_CC_FAT	GO:0005694~chromosome	1.76E-04
GOTERM_BP_FAT	GO:0034622~cellular macromolecular complex assembly	0.001213214
SP_PIR_KEYWORDS	nucleus	0.001282232
GOTERM_BP_FAT	GO:0034621~cellular macromolecular complex subunit organization	0.002299677
GOTERM_BP_FAT	GO:0006325~chromatin organization	0.002814147

SP_PIR_KEYWORDS	methylated amino acid	0.00376949
SP_PIR_KEYWORDS	transcription regulation	0.010608754
GOTERM_BP_FAT	GO:0051276~chromosome organization	0.012543863
GOTERM_BP_FAT	GO:0065003~macromolecular complex assembly	0.022578447
GOTERM_BP_FAT	GO:0043933~macromolecular complex subunit organization	0.029709331
UP_SEQ_FEATURE	mutagenesis site	0.036883111
GOTERM_CC_FAT	GO:0043232~intracellular non-membrane-bounded organelle	0.230087898
GOTERM_CC_FAT	GO:0043228~non-membrane-bounded organelle	0.230087898
SP_PIR_KEYWORDS	acetylation	0.625796507
Annotation Cluster 2	Enrichment Score: 2.79	
Category	Term	PValue
GOTERM_BP_FAT	GO:0006915~apoptosis	8.31E-04
GOTERM_BP_FAT	GO:0016265~death	8.76E-04
GOTERM_BP_FAT	GO:0012501~programmed cell death	9.47E-04
GOTERM_BP_FAT	GO:0008219~cell death	0.003019056
SP_PIR_KEYWORDS	Apoptosis	0.005314882

Drug annotation:

Annotation type	Enriched term	q-value
Drug target	CYP2D6; cytochrome P450, family 2, subfamily D, polypeptide 6	2.19E-02
Drug target	KCNH2; potassium voltage-gated channel, subfamily H (eag-related), member 2	2.40E-02
Drug target	CYP3A4; cytochrome P450, family 3, subfamily A, polypeptide 4	2.40E-02
Drug target	CALM1; calmodulin 1 (phosphorylase kinase, delta)	3.04E-02

Drugs	# of cell lines	Drug annotation	Literature evidence
anisomycin	3	protein synthesis inhibitor	(Chan, 2004)
cephaeline	3	protein synthesis inhibitor	(Chan, 2004)
emetine	3	protein synthesis inhibitor; anti-protozoal (ATC: P01AX02)	(Jiménez <i>et al</i> , 1977)
cicloheximide	2	protein synthesis inhibitor	(Baliga <i>et al</i> , 1969)
digoxigenin	2	Na ⁺ /K ⁺ -ATPase inhibition	(Yoda, 1974)
azacyclonol	2	ataractive	(Braun <i>et al</i> , 1956)
helveticoside	2	Na ⁺ /K ⁺ -ATPase inhibition	(Yoda, 1974)
astemizole	2	histamine H1-receptor antagonist	
suloctidil	2	vasodilator (ATC: C04AX19)	
digoxin	2	Na ⁺ /K ⁺ -ATPase inhibition; cardiac glycoside (ATC: C01AA05)	
econazole	2	antifungal (ATC: D01AC03)	
lanatoside C	2	Na ⁺ /K ⁺ -ATPase inhibition; cardiac glycoside (ATC: C01AA06)	
lycorine	2	toxic alkaloid	
mefloquine	2	quinine analogue; anti-malarial (ATC: P01BC02)	
ouabain	2	Na ⁺ /K ⁺ -ATPase inhibition; cardiac glycoside (ATC: C01AC01)	
strophanthidin	2	Na ⁺ /K ⁺ -ATPase inhibition	(Deitmer & Ellis, 1978)
digitoxigenin	2	Na ⁺ /K ⁺ -ATPase inhibition	(Erenkamp <i>et al</i> , 1998)
thioridazine	2	cytogenetic damage; inhibit cell proliferation; antipsychotic drug (ATC: N05AC02)	(Strobl <i>et al</i> , 1990)
prenylamine	2	calcium channel blocker (ATC: C01DX02)	
mometasone	1	D07 Corticosteroids, dermatological preparations; glucocorticosteroid (ATC: D07AC13)	
pimozide	1	N05 Psycholeptics	
bepridil	1	calcium channel blocker (ATC:C08EA02)	
bisacodyl	1	Na ⁺ /K ⁺ -ATPase inhibition; stimulant laxative drug (ATC: A06AB02)	(Schreiner <i>et al</i> , 1980)
chlorprothixene	1	N05 Psycholeptics	
clioquinol	1	cell cycle blocker; antifungal (ATC:G01AC02)	(Zhai <i>et al</i> , 2010)

dicycloverine	1	muscarinic receptor antagonist (ATC: A03AA07)	
felodipine	1	calcium channel blocker (ATC:C08CA02)	
fluoxetine	1	N06 Psychoanaleptics	
fluspirilene	1	N05 Psycholeptics	
hexestrol	1	steroid used by veterinarians	
hexetidine	1	anti-bacterial and anti-fungal (ATC: A01AB12)	
isoconazole	1	antifungal drug (ATC: D01AC05)	
vanoxerine	1	nicotinic acetylcholine receptor antagonist	PUBCHEM ID: 104920
Prestwick-664	1	nicotinic acetylcholine receptor antagonist	PUBCHEM ID: 104920
loperamide	1	opioid drug used against diarrhea (ATC: A07DA03)	
LY-294002	1	PI3Ks inhibitor	(Maira <i>et al</i> , 2009)
8-azaguanine	1	cell cycle blocker; purine analog	(Colsky <i>et al</i> , 1955)
methylbenzethonium chloride	1	induce apoptosis	(Yip <i>et al</i> , 2006)
mianserin	1	psychoactive drug (ATC: N06AX03)	
miconazole	1	antifungal (ATC: D01AC02)	
beta-escin	1		
oxybutynin	1	anticholinergic medication(ATC:G04BD04)	
perhexiline	1	antianginal agent (ATC: C08EX02)	
proadifen	1	inhibitor of cytochrome P450 enzymes	(Marshall & Williamson, 1964)
propofol	1	hypnotic agent (ATC: N01AX10)	
sulconazole	1	antifungal (ATC: D01AC09)	
tamoxifen	1	estrogen receptor antagonist (ATC: L02BA01)	
tonzonium bromide	1	mono-catioine detergent	
ticlopidine	1	antiplatelet drug (ATC:B01AC05)	
trimipramine	1	N06 Psychoanaleptics	
quinisocaine	1	antipruritic (ATC: D04AB05)	

CODI module 4

173 genes, 43 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 6.59	
Category	Term	PValue
GOTERM_BP_FAT	GO:0009611~response to wounding	3.46E-08
GOTERM_BP_FAT	GO:0006952~defense response	8.47E-08
GOTERM_BP_FAT	GO:0006954~inflammatory response	5.52E-06
Annotation Cluster 2	Enrichment Score: 5.25	
Category	Term	PValue
SP_PIR_KEYWORDS	signal	2.38E-08
UP_SEQ_FEATURE	signal peptide	2.47E-08
GOTERM_CC_FAT	GO:0005576~extracellular region	4.26E-06
SP_PIR_KEYWORDS	disulfide bond	5.11E-06
UP_SEQ_FEATURE	disulfide bond	1.09E-05
GOTERM_CC_FAT	GO:0044421~extracellular region part	1.91E-05
SP_PIR_KEYWORDS	glycoprotein	2.10E-05
UP_SEQ_FEATURE	glycosylation site:N-linked (GlcNAc...)	3.97E-05
GOTERM_CC_FAT	GO:0005615~extracellular space	4.67E-05
SP_PIR_KEYWORDS	Secreted	2.79E-04
Annotation Cluster 3	Enrichment Score: 4.26	
Category	Term	PValue
SP_PIR_KEYWORDS	chelation	2.00E-06
SP_PIR_KEYWORDS	metal-thiolate cluster	9.05E-06
UP_SEQ_FEATURE	metal ion-binding site:Divalent metal cation; cluster B	9.09E-06

UP_SEQ_FEATURE	region of interest:Beta	9.09E-06
UP_SEQ_FEATURE	region of interest:Alpha	9.09E-06
UP_SEQ_FEATURE	metal ion-binding site:Divalent metal cation; cluster A	9.09E-06
INTERPRO	IPR000006:metallothionein, vertebrate	1.07E-05
INTERPRO	IPR018064:metallothionein, vertebrate, metal binding site	1.07E-05
INTERPRO	IPR003019:metallothionein superfamily, eukaryotic	1.07E-05
PIR_SUPERFAMILY	PIRSF002564:metallothionein	1.97E-05
SP_PIR_KEYWORDS	metal binding	4.08E-05
SP_PIR_KEYWORDS	cadmium	1.38E-04
GOTERM_MF_FAT	GO:0046870~cadmium ion binding	2.79E-04
SP_PIR_KEYWORDS	acetylated amino end	0.001450927
SP_PIR_KEYWORDS	copper	0.019899055
GOTERM_MF_FAT	GO:0005507~copper ion binding	0.036920952

Drug annotation:

Annotation type	Enriched term	q-value
Drug target	NR3C1; nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor)	1.45E-02
ATC code (2nd level)	D07; Corticosteroids, dermatological preparations	4.40E-18
ATC code (2nd level)	R01; Nasal preparations	1.10E-06
ATC code (2nd level)	H02; Corticosteroids for systemic use	2.36E-06
ATC code (2nd level)	R03; Drugs for obstructive airway diseases	8.18E-04
Side effect	striae	1.94E-13
Side effect	skin atrophy	1.69E-09
Side effect	hypopigmentation	9.66E-07
Side effect	miliaria	9.74E-07
Side effect	cataract	4.65E-05
Side effect	hypertrichosis	1.93E-04
Side effect	folliculitis	1.93E-04
Side effect	Aseptic necrosis	3.33E-04
Side effect	paraparesis	7.45E-04
Side effect	nasal septum perforation	7.45E-04
Side effect	alkalosis	9.74E-04
Side effect	ocular infection	1.18E-03
Side effect	exophthalmos	2.37E-03
Side effect	paraplegia	3.12E-03
Side effect	glaucoma	6.89E-03
Side effect	osteoporosis	1.07E-02
Side effect	pseudotumor cerebri	2.11E-02
Side effect	arachnoiditis	3.90E-02
Side effect	latent diabetes	3.97E-02
Side effect	infection	5.10E-02
Side effect	pathological fracture	5.65E-02
Side effect	abscess	5.65E-02
Side effect	papilledema	5.65E-02
Chemical Fragment	C=C(NC)NCC	2.45E-12
Chemical Fragment	C(=NCCCCC)N	9.28E-10
Chemical Fragment	C(=NCCCC)N	9.38E-10
Chemical Fragment	C(=NCCCCC)N	3.62E-09
Chemical Fragment	c1ccc(cc1)CC	1.87E-08
Chemical Fragment	C(=NCCCC)N	3.20E-08
Chemical Fragment	C(=NCCCC)N	4.62E-08
Chemical Fragment	C(=C(NC)C1CNC(N)C)C)S	5.01E-08
Chemical Fragment	C(=NOC(C)C)C1NC(N)sc1	4.20E-07
Chemical Fragment	C=C1CCCC2(C)C(C)C(C)C12	1.07E-06
Chemical Fragment	Cc1c(cccc1Cl)Cl	1.07E-06
Chemical Fragment	C(C)CCCC(C)C	1.48E-06
Chemical Fragment	C(c1ccccc1)c2ccccc2	5.73E-06
Chemical Fragment	C(C)CCCC(C)C	6.09E-06
Chemical Fragment	C(=NCCCCC)N	6.70E-06
Chemical Fragment	C(=NOC)C1NC(N)sc1	1.88E-05
Chemical Fragment	C(=NCCCCC)N	4.12E-05

Chemical Fragment	<chem>C(c1ccccc1)CC</chem>	4.69E-05
Chemical Fragment	<chem>C(C)(C)CC(C)(C)C</chem>	4.69E-05
Chemical Fragment	<chem>C(=NCCCCCN=CN)N</chem>	2.08E-04
Chemical Fragment	<chem>c1ccc(cc1)C[N+](C)C</chem>	2.42E-03
Chemical Fragment	<chem>CCc1ccc(cc1)Cl</chem>	2.42E-03
Chemical Fragment	<chem>C(NC)NCCS</chem>	2.42E-03

Drugs	# of cell lines	Drug annotation	Literature evidence
alclometasone	2	D07 Corticosteroids, dermatological preparations	
beclometasone	2	D07 Corticosteroids, dermatological preparations	
betamethasone	2	D07 Corticosteroids, dermatological preparations	
budesonide	2	D07 Corticosteroids, dermatological preparations	
dexamethasone	2	D07 Corticosteroids, dermatological preparations	
diflorasone	2	D07 Corticosteroids, dermatological preparations	
fludrocortide	2	D07 Corticosteroids, dermatological preparations	
flumetasone	2	D07 Corticosteroids, dermatological preparations	
fluorometholone	2	D07 Corticosteroids, dermatological preparations	
halcinonide	2	D07 Corticosteroids, dermatological preparations	
methylprednisolone	2	D07 Corticosteroids, dermatological preparations	
mometasone	2	D07 Corticosteroids, dermatological preparations; glucocorticosteroid (ATC: D07AC13)	
prednisolone	2	D07 Corticosteroids, dermatological preparations	
triamcinolone	2	D07 Corticosteroids, dermatological preparations	
fludrocortisone	2	H02 Corticosteroids for systemic use	
rimexolone	2	H02 Corticosteroids for systemic use (ATC: H02AB12); cell cycle blocker	(Spies <i>et al</i> , 2010)
corticosterone	2	corticosteroid (steroid hormone)	
flunisolide	2	corticosteroid (ATC: R03BA03)	
fluticasone	2	glucocorticoid (synthetic, ATC: D07AC17)	
isoflupredone	2	antiinflammatory steroid	
simvastatin	2	hypolipidemic drug (ATC: C10AA01)	
tracazolate	2	anxiolytic	(Patel & Malick, 1982)
(+)-chelidonine	1	cell cycle blocker	(Panzer <i>et al</i> , 2001)
amylocaine	1	local anesthetic	
carbachol	1	acetylcholine receptor (ATC: N07AB01)	
cyclic adenosine monophosphate	1	second messenger for intracellular signal transduction	
etynodiol	1	hormonal contraceptive (ATC:G03DC06)	
gabexate	1	serine protease inhibitor	(Yuksel <i>et al</i> , 2003)
haloperidol	1	antipsychotic (ATC:N05AD01)	
hemicholinium	1	indirect acetylcholine antagonist	(Sandberg & Coyle, 1985)
isosorbide	1	Diuretics	(McLean <i>et al</i> , 1994)
letrozole	1	non-steroidal aromatase inhibitor (ATC:L02BG04)	
lithocholic acid	1	bile acid	
metergoline	1	A dopamine agonist and serotonin antagonist (ATC: G02CB05)	(Hamon <i>et al</i> , 1981)
moracizine	1	antiarrhythmic (ATC: C01BG01)	
naloxone	1	opioid antagonist (ATC: V03AB15)	
phenylpropanolamine	1	psychoactive drug	
piretanide	1	Diuretics (ATC: C03CA03)	
practolol	1	selective beta blocker (ATC:C07AB01)	
repaglinide	1	treatment of type II diabetes (ATC: A10BX02)	
ribavirin	1	anti-viral drug (ATC: J05AB04)	

rolipram	1	PDE4-inhibitor; anti-inflammatory drug	
terbutaline	1	ADRB2 agonist (ATC: R03AC03)	

CODI module 5

111 genes, 23 chemicals

Functional enrichment of genes:

Annotation Cluster 1		Enrichment Score: 14.76	
Category	Term		PValue
GOTERM_BP_FAT	GO:0006986~response to unfolded protein		6.64E-19
SP_PIR_KEYWORDS	stress response		2.10E-18
GOTERM_BP_FAT	GO:0051789~response to protein stimulus		1.52E-16
SP_PIR_KEYWORDS	Chaperone		2.07E-16
GOTERM_BP_FAT	GO:0006457~protein folding		1.71E-15
GOTERM_BP_FAT	GO:0010033~response to organic substance		5.82E-13
GOTERM_MF_FAT	GO:0051082~unfolded protein binding		9.75E-10
Annotation Cluster 2		Enrichment Score: 3.62	
Category	Term		PValue
SP_PIR_KEYWORDS	molecular chaperone		6.86E-11
INTERPRO	IPR013126:Heat shock protein 70		7.22E-06
INTERPRO	IPR001023:Heat shock protein Hsp70		7.22E-06
INTERPRO	IPR018181:Heat shock protein 70, conserved site		1.07E-05
KEGG_PATHWAY	hsa04612:Antigen processing and presentation		4.83E-04
PIR_SUPERFAMILY	PIRSF002581:chaperone HSP70		0.007261831
SP_PIR_KEYWORDS	ATP		0.073358956
KEGG_PATHWAY	hsa03040:Spliceosome		0.421685642
KEGG_PATHWAY	hsa04144:Endocytosis		0.581097351

Drug annotation:

No enriched terms found.

Drugs	# of cell lines	Drug annotation	Literature evidence
alvespimycin	3	hsp90 inhibitor	(Taldone <i>et al.</i> , 2008)
geldanamycin	3	HSP90 inhibitors	(Miyata, 2005a)
monorden	3	HSP90 inhibitor	(Sharma <i>et al.</i> , 1998)
tanespimycin	3	HSP90 inhibitors	
securinine	3	GABAA receptor antagonist	(Beutler <i>et al.</i> , 1985)
15-delta prostaglandin J2	3	NSAID; inhibition of cell proliferation	(Kim <i>et al.</i> , 2007)
disulfiram	3	treatment of chronic alcoholism; proteasome inhibitor	(Cvek & Dvorak, 2008)
parthenolide	3	apoptosis/antiparasitic/anticancer/microtubule interfering/anti-inflammatory; HDAC1 depletion	(López-Franco <i>et al.</i> , 2006; Gopal <i>et al.</i> , 2007)
thiostrepton	3	oligo peptide antibiotic	
ebselen	2	antiinflammatory antioxidant	(Schewe, 1995)
LY-294002	2	PI3Ks inhibitor	(Maira <i>et al.</i> , 2009)
oxyphenbutazone	2	anti-inflammatory (ATC: M01AA03)	
puromycin	2	antibiotic; protein synthesis inhibitor	
(+)-chelidone	1	cell cycle blocker	(Panzer <i>et al.</i> , 2001)
etacrynic acid	1	diuretic (ATC: C03CC01)	
mefloquine	1	quinine analogue; anti-malarial (ATC: P01BC02)	
mometasone	1	D07 Corticosteroids, dermatological preparations; glucocorticosteroid (ATC: D07AC13)	
myricetin	1	flavonoid/anti-oxidant; hsp70 inhibitor	(Jinwal <i>et al.</i> , 2009)
nifuroxazide	1	inhibit myeloma survival; antibiotic (ATC: A07AX03)	(Nelson <i>et al.</i> , 2008)
oxolamine	1	anti-inflammatory/cough suppressant (ATC: R05DB07)	
scoulerine	1	GABAA receptor agonist	(Eisenreich <i>et al.</i> ,

			2003)
Prestwick-642	1	cystic acne (ATC:D10AD04)	
Prestwick-674	1	oral anaesthetic (ATC: N01BX02)	

CODI module 6

75 genes, 21 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 1.42	
Category	Term	PValue
UP_SEQ_FEATURE	domain:LIM zinc-binding 2	0.02025079
UP_SEQ_FEATURE	domain:LIM zinc-binding 1	0.02025079
SP_PIR_KEYWORDS	LIM domain	0.04782628
INTERPRO	IPR001781:Zinc finger, LIM-type	0.048255967
SMART	SM00132:LIM	0.078441179

Drug annotation:

Annotation type	Enriched term	q-value
Chemical Fragment	C(=NOC(C)C)c1nc(N)sc1	9.47E-03

Drugs	# of cell lines	Drug annotation	Literature evidence
vorinostat	2	Histone deacetylase inhibitor	
trichostatin A	2	Histone deacetylase (HDAC, class I/II) inhibitor	(Vanhaecke <i>et al</i> , 2004)
fulvestrant	1	estrogen receptor antagonist (ATC: L02BA03)	
bufexamac	1	anti-inflammatory (ATC: M01AB17); HDAC inhibitor	(Bantscheff <i>et al</i> , 2011)
parthenolide	1	apoptosis/antiparasitic/anticancer/microtubule interfering/anti-inflammatory; HDAC1 depletion	(López-Franco <i>et al</i> , 2006; Gopal <i>et al</i> , 2007)
alprostadil	1	prostaglandin; treatment of erectile dysfunction (ATC: G04BE01); Alprostadil results in increased phosphorylation of ADRB2 protein	(Davis <i>et al</i> , 2011)
tanespimycin	1	HSP90 inhibitors	
dilazep	1	adenosine reuptake inhibitor (ATC: C01DX10)	
ellipticine	1	antineoplastic agent, uncoupling agent	
geldanamycin	1	HSP90 inhibitors	(Miyata, 2005b)
hycanthone	1	cytotoxic; cell cycle blocker; inhibit rna synthesis	(Sieber <i>et al</i> , 1973; Wong <i>et al</i> , 1990)
LY-294002	1	PI3Ks inhibitor	(Maira <i>et al</i> , 2009)
thiostrepton	1	oligo peptide antibiotic	
15-delta prostaglandin J2	1	NSAID; inhibition of cell proliferation	(Kim <i>et al</i> , 2007)
protriptyline	1	N06 Psychoanaleptics	
monorden	1	HSP90 inhibitor	(Sharma <i>et al</i> , 1998)
raloxifene	1	selective estrogen receptor modulator (ATC: G03XC01)	
solasodine	1	glycoalkaloid	
syrosingopine	1		
corticosterone	1	corticosteroid (steroid hormone)	
alvespimycin	1	hsp90 inhibitor	(Taldone <i>et al</i> , 2008)

CODI module 7

74 genes, 20 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 1.88	

Category	Term	PValue
SP_PIR_KEYWORDS	rna-binding	0.001024947
GOTERM_MF_FAT	GO:0003723~RNA binding	0.002184082
SMART	SM00360:RRM	0.005501749
INTERPRO	IPR000504:RNA recognition motif, RNP-1	0.005810571
INTERPRO	IPR012677:Nucleotide-binding, alpha-beta plait	0.006337525
UP_SEQ_FEATURE	domain:RRM 1	0.11692093
UP_SEQ_FEATURE	domain:RRM 2	0.11692093
UP_SEQ_FEATURE	domain:RRM	0.130687405
Annotation Cluster 2		Enrichment Score: 1.40
Category	Term	PValue
KEGG_PATHWAY	hsa00240:Pyrimidine metabolism	0.016908657
KEGG_PATHWAY	hsa00230:Purine metabolism	0.04279547
GOTERM_BP_FAT	GO:0006259~DNA metabolic process	0.084506223
Annotation Cluster 3		Enrichment Score: 1.39
Category	Term	PValue
GOTERM_BP_FAT	GO:0006396~RNA processing	6.02E-04
GOTERM_BP_FAT	GO:0006397~mRNA processing	0.016105021
SP_PIR_KEYWORDS	mrna processing	0.02283707
GOTERM_BP_FAT	GO:0016071~mRNA metabolic process	0.028036716
GOTERM_BP_FAT	GO:0008380~RNA splicing	0.03948499
SP_PIR_KEYWORDS	mrna splicing	0.045741516
GOTERM_BP_FAT	GO:0000375~RNA splicing, via transesterification reactions	0.300744596
GOTERM_BP_FAT	GO:0000377~RNA splicing, via transesterification reactions with bulged adenosine as nucleophile	0.300744596
GOTERM_BP_FAT	GO:0000398~nuclear mRNA splicing, via spliceosome	0.300744596

Drug annotation:

Annotation type	Enriched term	q-value
Drug target	CYP1B1;cytochrome P450, family 1, subfamily B, polypeptide 1	1.14E-02
Chemical Fragment	C(=NCCCCC)N	1.84E-04

Drugs	# of cell lines	Drug annotation	Literature evidence
luteolin	3	flavonoid; controls nucleic acid syntheses	(Harris <i>et al</i> , 2012)
apigenin	3	flavonoid	
acacetin	3	flavonoid	
harmol	2	Metabolite of harmine that binds to yeast RNA	(Nafisi <i>et al</i> , 2010)
nifedipine	2	calcium channel blocker (ATC: C08CA05); decrease RNA synthesis	(Lijnen <i>et al</i> , 1998)
nocodazole	2	anti-neoplastic agent; depolymerize microtubules	
harmine	2	fluorescent harmala alkaloid; inhibits monoamine oxidase A; binds to yeast RNA	(Nafisi <i>et al</i> , 2010)
atovaquone	1	an analog of ubiquinone (ATC: P01AX06)	
simvastatin	1	hypolipidemic drug (ATC: C10AA01)	
harman	1	monoamine oxidase inhibitor; binds to yeast RNA	(Nafisi <i>et al</i> , 2010)
kaempferol	1	flavonoid; decrease RNA synthesis	(Kanakis <i>et al</i> , 2006; Nose, 1984)
quercetin	1	flavonoid; decrease RNA synthesis	(Kanakis <i>et al</i> , 2006; Nose, 1984)
minoxidil	1	vasodilator (ATC: D11AX01)	
meptazinol	1	opoid and acetylcholinesterase inhibitor (ATC: N02AX05)	
hycanthone	1	cytotoxic; cell cycle blocker; inhibit rna synthesis	(Sieber <i>et al</i> , 1973; Wong <i>et al</i> , 1990)
nystatin	1	antifungal (ATC: D01AA01)	
ellipticine	1	antineoplastic agent, uncoupling agent	
cyclopenthiiazide	1	diuretics (ATC: C03AA07)	
canavanine	1	non-proteinogenic α -amino acid found in certain leguminous plants	(McMahon & Langstroth, 1972)

molindone	1	antipsychotic (ATC: N05AE02)	
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CODI module 8

115 genes, 32 chemicals

Functional enrichment of genes:

Annotation Cluster 1		Enrichment Score: 4.16	
Category	Term	PValue	
GOTERM_CC_FAT	GO:0005576~extracellular region	6.40E-06	
SP_PIR_KEYWORDS	signal	2.53E-05	
UP_SEQ_FEATURE	signal peptide	2.59E-05	
SP_PIR_KEYWORDS	Secreted	2.79E-05	
SP_PIR_KEYWORDS	glycoprotein	8.35E-05	
UP_SEQ_FEATURE	disulfide bond	2.69E-04	
UP_SEQ_FEATURE	glycosylation site:N-linked (GlcNAc...)	3.43E-04	
SP_PIR_KEYWORDS	disulfide bond	5.42E-04	
Annotation Cluster 2		Enrichment Score: 1.95	
Category	Term	PValue	
GOTERM_BP_FAT	GO:0048839~inner ear development	0.004380241	
GOTERM_BP_FAT	GO:0043583~ear development	0.00938752	
GOTERM_BP_FAT	GO:0007423~sensory organ development	0.033885801	
Annotation Cluster 3		Enrichment Score: 1.35	
Category	Term	PValue	
GOTERM_CC_FAT	GO:0044421~extracellular region part	7.30E-04	
GOTERM_CC_FAT	GO:0031012~extracellular matrix	0.016885878	
GOTERM_CC_FAT	GO:0005578~proteinaceous extracellular matrix	0.039250179	
GOTERM_BP_FAT	GO:0007155~cell adhesion	0.06362705	
GOTERM_BP_FAT	GO:0022610~biological adhesion	0.06362705	
SP_PIR_KEYWORDS	extracellular matrix	0.255837168	
SP_PIR_KEYWORDS	cell adhesion	0.605670239	

Drug annotation:

No enriched terms found.

CODI module 9

176 genes, 56 chemicals

Functional enrichment of genes:

Annotation Cluster 1		Enrichment Score: 4.60	
Category	Term	PValue	
GOTERM_CC_FAT	GO:0031981~nuclear lumen	9.54E-07	
GOTERM_CC_FAT	GO:0005654~nucleoplasm	7.86E-06	
GOTERM_CC_FAT	GO:0070013~intracellular organelle lumen	1.36E-05	
GOTERM_CC_FAT	GO:0031974~membrane-enclosed lumen	1.63E-05	
GOTERM_CC_FAT	GO:0043233~organelle lumen	2.19E-05	
GOTERM_CC_FAT	GO:0005730~nucleolus	0.006116859	
Annotation Cluster 2		Enrichment Score: 2.16	
Category	Term	PValue	
SP_PIR_KEYWORDS	Rotamase	9.73E-04	
GOTERM_MF_FAT	GO:0003755~peptidyl-prolyl cis-trans isomerase activity	0.001343264	
GOTERM_MF_FAT	GO:0016859~cis-trans isomerase activity	0.001585145	
SP_PIR_KEYWORDS	Isomerase	0.003811761	
INTERPRO	IPR002130:Peptidyl-prolyl cis-trans isomerase, cyclophilin-type	0.02067277	
UP_SEQ_FEATURE	domain:PP1ase cyclophilin-type	0.022566346	
GOTERM_MF_FAT	GO:0008144~drug binding	0.036267974	
GOTERM_BP_FAT	GO:0006457~protein folding	0.039090865	
Annotation Cluster 3		Enrichment Score: 2.12	
Category	Term	PValue	

SP_PIR_KEYWORDS	rna-binding	1.65E-05
UP_SEQ_FEATURE	domain:RRM 2	0.013041137
UP_SEQ_FEATURE	domain:RRM 1	0.013041137
INTERPRO	IPR000504:RNA recognition motif, RNP-1	0.018483294
INTERPRO	IPR012677:Nucleotide-binding, alpha-beta plait	0.020470083
UP_SEQ_FEATURE	domain:RRM 3	0.029104132
SMART	SM00360:RRM	0.041657864
Annotation Cluster 4	Enrichment Score: 2.06	
Category	Term	PValue
SP_PIR_KEYWORDS	dna-binding	7.39E-04
SP_PIR_KEYWORDS	transcription regulation	0.002432614
GOTERM_MF_FAT	GO:0003677~DNA binding	0.004340302
SP_PIR_KEYWORDS	Transcription	0.00444635
GOTERM_BP_FAT	GO:0006350~transcription	0.004866742
GOTERM_BP_FAT	GO:0045449~regulation of transcription	0.00989707
GOTERM_MF_FAT	GO:0030528~transcription regulator activity	0.024243333
GOTERM_BP_FAT	GO:0051252~regulation of RNA metabolic process	0.059107977
GOTERM_BP_FAT	GO:0006355~regulation of transcription, DNA-dependent	0.105091817

Drug annotation:

No enriched terms found.

CODI module 10

51 genes, 55 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 2.91	
Category	Term	PValue
INTERPRO	IPR019782:WD40 repeat 2	4.68E-04
UP_SEQ_FEATURE	repeat:WD 3	5.72E-04
INTERPRO	IPR017986:WD40 repeat, region	5.92E-04
INTERPRO	IPR019781:WD40 repeat, subgroup	6.39E-04
UP_SEQ_FEATURE	repeat:WD 1	6.65E-04
UP_SEQ_FEATURE	repeat:WD 2	6.65E-04
SP_PIR_KEYWORDS	wd repeat	6.68E-04
INTERPRO	IPR001680:WD40 repeat	9.77E-04
INTERPRO	IPR019775:WD40 repeat, conserved site	0.001170208
SMART	SM00320:WD40	0.001624547
INTERPRO	IPR015943:WD40/YVTN repeat-like	0.001664433
UP_SEQ_FEATURE	repeat:WD 5	0.002967375
UP_SEQ_FEATURE	repeat:WD 4	0.003871282
UP_SEQ_FEATURE	repeat:WD 6	0.013103737
Annotation Cluster 2	Enrichment Score: 2.29	
Category	Term	PValue
GOTERM_CC_FAT	GO:0044430~cytoskeletal part	0.00125971
GOTERM_CC_FAT	GO:0005856~cytoskeleton	0.004753477
GOTERM_CC_FAT	GO:0043232~intracellular non-membrane-bounded organelle	0.010529529
GOTERM_CC_FAT	GO:0043228~non-membrane-bounded organelle	0.010529529

Drug annotation:

No enriched terms found.

CODI module 11

154 genes, 66 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 3.09	
Category	Term	PValue
GOTERM_BP_FAT	GO:0046907~intracellular transport	1.39E-06
GOTERM_BP_FAT	GO:0034613~cellular protein localization	1.80E-05
GOTERM_BP_FAT	GO:0070727~cellular macromolecule localization	1.95E-05
GOTERM_BP_FAT	GO:0006886~intracellular protein transport	2.96E-05

GOTERM_BP_FAT	GO:0008104~protein localization	3.00E-04
GOTERM_BP_FAT	GO:0015031~protein transport	4.32E-04
GOTERM_BP_FAT	GO:0045184~establishment of protein localization	4.79E-04
GOTERM_BP_FAT	GO:0006605~protein targeting	6.91E-04
GOTERM_BP_FAT	GO:0006913~nucleocytoplasmic transport	0.002762323
GOTERM_BP_FAT	GO:0051169~nuclear transport	0.002942796
GOTERM_BP_FAT	GO:0017038~protein import	0.006407508
GOTERM_BP_FAT	GO:0006606~protein import into nucleus	0.007359192
GOTERM_BP_FAT	GO:0051170~nuclear import	0.007972003
GOTERM_BP_FAT	GO:0033365~protein localization in organelle	0.009997456
GOTERM_BP_FAT	GO:0034504~protein localization in nucleus	0.010008898
SP_PIR_KEYWORDS	protein transport	0.178793179
Annotation Cluster 2		
Enrichment Score: 2.06		
Category	Term	PValue
GOTERM_BP_FAT	GO:0051674~localization of cell	0.001738566
GOTERM_BP_FAT	GO:0048870~cell motility	0.001738566
GOTERM_BP_FAT	GO:0006928~cell motion	0.0035237
GOTERM_BP_FAT	GO:0016477~cell migration	0.011982647
GOTERM_BP_FAT	GO:0030036~actin cytoskeleton organization	0.052259267
GOTERM_BP_FAT	GO:0030029~actin filament-based process	0.06519111

Drug annotation:

No enriched terms found.

CODI module 12

106 genes, 118 chemicals

Functional enrichment of genes:

Annotation Cluster 1		Enrichment Score: 1.33
Category	Term	PValue
SP_PIR_KEYWORDS	isopeptide bond	0.017434813
SP_PIR_KEYWORDS	ubl conjugation	0.024665376
UP_SEQ_FEATURE	cross-link:Glycyl lysine isopeptide (Lys-Gly) (interchain with G-Cter in ubiquitin)	0.235862924

Drug annotation:

Annotation type	Enriched term	q-value
Side Effect	exfoliative dermatitis	9.96E-02

CODI module 13

53 genes, 41 chemicals

Functional enrichment of genes:

Annotation Cluster 1		Enrichment Score: 10.32
Category	Term	PValue
UP_SEQ_FEATURE	region of interest:Alpha	5.55E-14
UP_SEQ_FEATURE	region of interest:Beta	5.55E-14
UP_SEQ_FEATURE	metal ion-binding site:Divalent metal cation; cluster B	1.22E-13
UP_SEQ_FEATURE	metal ion-binding site:Divalent metal cation; cluster A	1.22E-13
INTERPRO	IPR018064:metallothionein, vertebrate, metal binding site	1.66E-13
SP_PIR_KEYWORDS	metal-thiolate cluster	2.34E-13
PIR_SUPERFAMILY	PIRSF002564:metallothionein	2.71E-13
INTERPRO	IPR003019:metallothionein superfamily, eukaryotic	3.30E-13
INTERPRO	IPR000006:metallothionein, vertebrate	3.30E-13
SP_PIR_KEYWORDS	cadmium	5.96E-12
SP_PIR_KEYWORDS	chelation	5.96E-12
GOTERM_MF_FAT	GO:0046870~cadmium ion binding	5.34E-11
SP_PIR_KEYWORDS	metal binding	1.21E-09
SP_PIR_KEYWORDS	copper	4.04E-07
GOTERM_MF_FAT	GO:0005507~copper ion binding	2.08E-06
SP_PIR_KEYWORDS	acetylated amino end	6.67E-06

SP_PIR_KEYWORDS	acetylation	0.039761968
Annotation Cluster 2	Enrichment Score: 4.56	
Category	Term	PValue
SP_PIR_KEYWORDS	zinc	5.26E-08
GOTERM_MF_FAT	GO:0008270~zinc ion binding	6.71E-07
GOTERM_MF_FAT	GO:0046914~transition metal ion binding	1.53E-05
SP_PIR_KEYWORDS	metal-binding	3.38E-05
GOTERM_MF_FAT	GO:0046872~metal ion binding	7.15E-04
GOTERM_MF_FAT	GO:0043169~cation binding	8.29E-04
GOTERM_MF_FAT	GO:0043167~ion binding	0.00104236

Drug annotation:

Annotation type	Enriched term	q-value
Drug target	SERPINE1;serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	3.47E-02

CODI module 14

91 genes, 52 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 13.35	
Category	Term	PValue
SP_PIR_KEYWORDS	endoplasmic reticulum	1.43E-24
GOTERM_CC_FAT	GO:0005783~endoplasmic reticulum	6.25E-20
GOTERM_CC_FAT	GO:0044432~endoplasmic reticulum part	1.72E-16
GOTERM_CC_FAT	GO:0005789~endoplasmic reticulum membrane	3.84E-11
GOTERM_CC_FAT	GO:0042175~nuclear envelope-endoplasmic reticulum network	1.02E-10
GOTERM_CC_FAT	GO:0012505~endomembrane system	6.60E-10
GOTERM_CC_FAT	GO:0031090~organelle membrane	8.81E-06
Annotation Cluster 2	Enrichment Score: 5.73	
Category	Term	PValue
GOTERM_CC_FAT	GO:0012505~endomembrane system	6.60E-10
GOTERM_BP_FAT	GO:0015031~protein transport	1.87E-07
GOTERM_BP_FAT	GO:0045184~establishment of protein localization	2.18E-07
SP_PIR_KEYWORDS	er-golgi transport	4.26E-07
GOTERM_BP_FAT	GO:0006886~intracellular protein transport	6.53E-07
GOTERM_BP_FAT	GO:0046907~intracellular transport	1.28E-06
GOTERM_BP_FAT	GO:0008104~protein localization	1.34E-06
GOTERM_BP_FAT	GO:0034613~cellular protein localization	1.95E-06
GOTERM_BP_FAT	GO:0070727~cellular macromolecule localization	2.18E-06
GOTERM_CC_FAT	GO:0031090~organelle membrane	8.81E-06
SP_PIR_KEYWORDS	protein transport	5.74E-05
GOTERM_BP_FAT	GO:0016192~vesicle-mediated transport	9.64E-05
SP_PIR_KEYWORDS	transport	0.001130058
Annotation Cluster 3	Enrichment Score: 5.42	
Category	Term	PValue
UP_SEQ_FEATURE	topological domain:Luminal	1.16E-12
SP_PIR_KEYWORDS	membrane	7.28E-06
UP_SEQ_FEATURE	transmembrane region	7.55E-06
SP_PIR_KEYWORDS	transmembrane	8.49E-06
UP_SEQ_FEATURE	topological domain:Cytoplasmic	2.37E-05
GOTERM_CC_FAT	GO:0031224~intrinsic to membrane	8.63E-04
GOTERM_CC_FAT	GO:0016021~integral to membrane	9.16E-04
Annotation Cluster 4	Enrichment Score: 5.41	
Category	Term	PValue
INTERPRO	IPR000348:emp24/gp25L/p24	3.97E-07
UP_SEQ_FEATURE	domain:GOLD	3.36E-06
INTERPRO	IPR009038:GOLD	3.62E-06

GOTERM_CC_FAT	GO:0005793~ER-Golgi intermediate compartment	4.61E-05
Annotation Cluster 5	Enrichment Score: 3.61	
Category	Term	PValue
UP_SEQ_FEATURE	short sequence motif:Prevents secretion from ER	2.02E-11
GOTERM_CC_FAT	GO:0005788~endoplasmic reticulum lumen	3.21E-07
INTERPRO	IPR000886:Endoplasmic reticulum, targeting sequence	2.96E-05
SP_PIR_KEYWORDS	Isomerase	1.27E-04
GOTERM_CC_FAT	GO:0048770~pigment granule	3.86E-04
GOTERM_CC_FAT	GO:0042470~melanosome	3.86E-04
GOTERM_CC_FAT	GO:0043233~organelle lumen	0.905523772
GOTERM_CC_FAT	GO:0031974~membrane-enclosed lumen	0.919959277
GOTERM_CC_FAT	GO:0070013~intracellular organelle lumen	0.937638533

Drug annotation:

Annotation type	Enriched term	q-value
Chemical Fragment	<chem>c1c(cc(cc1))I</chem>	7.11E-05
Chemical Fragment	<chem>Cc1c(cccc1Cl)Cl</chem>	4.31E-04

CODI module 15

55 genes, 48 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 2.54	
Category	Term	PValue
GOTERM_BP_FAT	GO:0006563~L-serine metabolic process	9.28E-04
KEGG_PATHWAY	hsa00260:Glycine, serine and threonine metabolism	0.004319529
GOTERM_BP_FAT	GO:0009069~serine family amino acid metabolic process	0.005756289
Annotation Cluster 2	Enrichment Score: 2.00	
Category	Term	PValue
SP_PIR_KEYWORDS	Aminoacyl-tRNA synthetase	2.25E-05
KEGG_PATHWAY	hsa00970:Aminoacyl-tRNA biosynthesis	3.21E-05
GOTERM_MF_FAT	GO:0016875~ligase activity, forming carbon-oxygen bonds	4.25E-05
GOTERM_MF_FAT	GO:0016876~ligase activity, forming aminoacyl-tRNA and related compounds	4.25E-05
GOTERM_MF_FAT	GO:0004812~aminoacyl-tRNA ligase activity	4.25E-05
GOTERM_BP_FAT	GO:0043038~amino acid activation	5.85E-05
GOTERM_BP_FAT	GO:0043039~tRNA aminoacylation	5.85E-05
GOTERM_BP_FAT	GO:0006418~tRNA aminoacylation for protein translation	5.85E-05
GOTERM_BP_FAT	GO:0006399~tRNA metabolic process	0.002320177
GOTERM_MF_FAT	GO:0000049~tRNA binding	0.002875221
SP_PIR_KEYWORDS	ligase	0.006586294
INTERPRO	IPR014729:Rossmann-like alpha/beta/alpha sandwich fold	0.013913194
SP_PIR_KEYWORDS	protein biosynthesis	0.014425618
GOTERM_BP_FAT	GO:0034660~ncRNA metabolic process	0.027120096
GOTERM_BP_FAT	GO:0006412~translation	0.076127375
GOTERM_MF_FAT	GO:0003723~RNA binding	0.201133504
GOTERM_MF_FAT	GO:0032555~purine ribonucleotide binding	0.28648941
GOTERM_MF_FAT	GO:0032553~ribonucleotide binding	0.28648941
SP_PIR_KEYWORDS	nucleotide-binding	0.319792205
GOTERM_MF_FAT	GO:0017076~purine nucleotide binding	0.332015222
GOTERM_MF_FAT	GO:0005524~ATP binding	0.381221624
GOTERM_MF_FAT	GO:0032559~adenyl ribonucleotide binding	0.389970012
GOTERM_MF_FAT	GO:0000166~nucleotide binding	0.399117334
SP_PIR_KEYWORDS	atp-binding	0.43133076
GOTERM_MF_FAT	GO:0030554~adenyl nucleotide binding	0.441515712
GOTERM_MF_FAT	GO:0001883~purine nucleoside binding	0.454652627
GOTERM_MF_FAT	GO:0001882~nucleoside binding	0.462299836

Drug annotation:

Annotation type	Enriched term	q-value
Drug target	SLC6A2; solute carrier family 6 (neurotransmitter transporter, noradrenalin), member 2	3.87E-03
Drug target	HRH1; histamine receptor H1	3.87E-03
Drug target	HTR2A; 5-hydroxytryptamine (serotonin) receptor 2A	4.58E-03
Drug target	ADCY1; adenylate cyclase 1 (brain)	6.13E-03
Drug target	SLC6A4; solute carrier family 6 (neurotransmitter transporter, serotonin), member 4	8.45E-03
Drug target	DRD1; dopamine receptor D1	1.10E-02
Drug target	ADRA1A; adrenergic, alpha-1A-, receptor	1.45E-02
Drug target	DRD2; dopamine receptor D2	1.45E-02
Drug target	CHRM2; cholinergic receptor, muscarinic 2	2.22E-02
Drug target	CHRM5; cholinergic receptor, muscarinic 5	2.40E-02
Drug target	DRD3; dopamine receptor D3	2.72E-02
Drug target	CHRM4; cholinergic receptor, muscarinic 4	2.87E-02
Drug target	HTR2C; 5-hydroxytryptamine (serotonin) receptor 2C	6.47E-02
Drug target	CHRM1; cholinergic receptor, muscarinic 1	6.53E-02
Drug target	CYP1B1; cytochrome P450, family 1, subfamily B, polypeptide 1	8.95E-02
Side effect	paralytic ileus	3.18E-04
Side effect	breast enlargement	3.33E-04
Side effect	galactorrhea	4.41E-04
Side effect	weight gain	2.13E-03
Side effect	testicular swelling	6.19E-03
Side effect	gynecomastia	1.83E-02
Side effect	adenitis	7.94E-02
Side effect	agitation	9.23E-02
Chemical Fragment	c1ccc(cc1)CN2CCN(C)CC2	1.85E-03

Drugs	# of cell lines	Drug annotation	Literature evidence
methylbenzethonium chloride	2	induce apoptosis	(Yip <i>et al</i> , 2006)
astemizole	2	histamine H1-receptor antagonist	
ciclosporin	2	immunosuppressant drug (ATC: L04AD01)	
loperamide	2	opioid drug used against diarrhea (ATC: A07DA03)	
alexidine	2	disinfectant	
gossypol	2	antiproliferative activity	(Le Blanc <i>et al</i> , 2002)
mefloquine	2	quinine analogue; anti-malarial (ATC: P01BC02)	
niclosamide	2	teniacide (ATC: P02DA01)	
pyrvinium	2	inhibit proliferation in colon cancer ; antiparasitic (ATC:P02CX01)	
15-delta prostaglandin J2	1	NSAID; inhibition of cell proliferation	(Kim <i>et al</i> , 2007)
nifuroxazide	1	inhibit myeloma survival; antibiotic (ATC: A07AX03)	(Nelson <i>et al</i> , 2008)
econazole	1	antifungal (ATC: D01AC03)	
desipramine	1	N06 Psychoanaleptics	
mometasone	1	D07 Corticosteroids, dermatological preparations; glucocorticosteroid (ATC: D07AC13)	
metixene	1	N04 Anti-parkinson drugs	
chlorpromazine	1	N05 Psycholeptics	
perphenazine	1	N05 Psycholeptics	
pimozide	1	N05 Psycholeptics	
prochlorperazine	1	N05 Psycholeptics	
thioridazine	1	cytogenetic damage; inhibit cell proliferation; antipsychotic drug (ATC: N05AC02)	(Strobl <i>et al</i> , 1990)
maprotiline	1	N06 Psychoanaleptics	
trimipramine	1	N06 Psychoanaleptics	
norcyclobenzaprine	1	structurally similar to tricyclic antidepressants	(Van Hoey)
suloctidil	1	vasodilator (ATC: C04AX19)	

abamectin	1	insecticide (ATCvet:QP54AA02)	
amiodarone	1	antiarrhythmic agent (ATC: C01BD01)	
azacyclonol	1	ataractive	(Braun <i>et al</i> , 1956)
bepriidil	1	calcium channel blocker (ATC:C08EA02)	
butoconazole	1	antifungal (ATC: G01AF15)	
clioquinol	1	cell cycle blocker; antifungal (ATC:G01AC02)	(Zhai <i>et al</i> , 2010)
cyclobenzaprine	1	muscle relaxant medication (ATC: M03BX08)	
depropine	1	antihistamine with anticholinergic properties (ATC: R06AX16)	
dequalinium chloride	1	anticarcinogenic activity; antiseptic (ATC: D08AH01)	(Weiss <i>et al</i> , 1987)
hexetidine	1	antibacterial and antifungal (ATC: A01AB12)	
ivermectin	1	antiparasitic avermectin (ATC: P02CF01)	
lasalocid	1	antibacterial (ATCvet: QP51AH02)	
meclizine	1	antihistamine (ATC:R06AE05)	
miconazole	1	antifungal (ATC: D01AC02)	
naftifine	1	antifungal (ATC:D01AE22)	
pizotifen	1	prevention of vascular headache (ATC: N02CX01)	
prenylamine	1	calcium channel blocker (ATC: C01DX02)	
quinisocaine	1	antipruritic (ATC: D04AB05)	
tamoxifen	1	estrogen receptor antagonist (ATC: L02BA01)	
thiethylperazine	1	antiemetic (ATC: R06AD03);potential antipsychotic activity	
thioguanosine	1	cell cycle blocker; guanine analog	(Lepage, 1963)
ticlopidine	1	antiplatelet drug (ATC:B01AC05)	
tonzonium bromide	1	mono-catioinc detergent	
tribenoside	1	vasoprotective (ATC: C05AX05)	

CODI module 16

66 genes, 31 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 3.68	
Category	Term	PValue
GOTERM_CC_FAT	GO:0031981~nuclear lumen	9.84E-06
GOTERM_CC_FAT	GO:0005730~nucleolus	1.31E-05
GOTERM_CC_FAT	GO:0070013~intracellular organelle lumen	1.61E-05
GOTERM_CC_FAT	GO:0043233~organelle lumen	2.17E-05
GOTERM_CC_FAT	GO:0031974~membrane-enclosed lumen	3.05E-05
SP_PIR_KEYWORDS	nucleus	0.001569641
GOTERM_CC_FAT	GO:0043232~intracellular non-membrane-bounded organelle	0.037376461
GOTERM_CC_FAT	GO:0043228~non-membrane-bounded organelle	0.037376461
Annotation Cluster 2	Enrichment Score: 1.72	
Category	Term	PValue
GOTERM_BP_FAT	GO:0034660~ncRNA metabolic process	0.003014102
GOTERM_BP_FAT	GO:0034470~ncRNA processing	0.010516674
GOTERM_BP_FAT	GO:0006399~tRNA metabolic process	0.012784712
GOTERM_BP_FAT	GO:0009451~RNA modification	0.017050849
GOTERM_BP_FAT	GO:0006396~RNA processing	0.035325317
UP_SEQ_FEATURE	active site:Nucleophile	0.036743114
GOTERM_BP_FAT	GO:0008033~tRNA processing	0.040385229
SP_PIR_KEYWORDS	tRNA processing	0.047902076

Drug annotation:

Annotation type	Enriched term	q-value
Drug target	HRH1; histamine receptor H1	3.87E-03
Drug target	KCNH2; potassium voltage-gated channel, subfamily H (eag-related), member 2	7.12E-03
Drug target	CYP2D6; cytochrome P450, family 2, subfamily D, polypeptide 6	1.45E-02
Drug target	CALM1; calmodulin 1 (phosphorylase kinase, delta)	3.80E-02

Drug target	CYP3A4; cytochrome P450, family 3, subfamily A, polypeptide 4	4.67E-02
Drug target	HTR2A;5-hydroxytryptamine (serotonin) receptor 2A	4.77E-02
Drug target	ABCB1; ATP-binding cassette, sub-family B (MDR/TAP), member 1	6.47E-02
Side effect	paralytic ileus	3.12E-03
Side effect	galactorrhea	3.96E-02
Chemical Fragment	C=C(NC)NCC	2.34E-05
Chemical Fragment	C(=NCCCC)N	7.00E-05
Chemical Fragment	C(=NCCCCC)N	1.13E-04
Chemical Fragment	C(=NCCCC)N	3.02E-04
Chemical Fragment	c1ccc(cc1)CC	4.40E-04
Chemical Fragment	C(=NCCCC)N	4.63E-04
Chemical Fragment	C(=C(NC1cnc(nc1(N))C)C)S	6.77E-04
Chemical Fragment	C(=NOC(C)C)c1nc(N)sc1	2.42E-03
Chemical Fragment	C(=NOC(C)C)c1nc(N)sc1	3.11E-03
Chemical Fragment	C=C1CCCC2(C)(C(CC)CCC12)	6.56E-03
Chemical Fragment	Cc1c(ccc1Cl)Cl	6.56E-03

Drugs	# of cell lines	Drug annotation	Literature evidence
diphenhydramine	2	antihistamine (ATC: D04AA32) possessing anticholinergic, antitussive, antiemetic, and sedative properties	
LY-294002	2	PI3Ks inhibitor	(Maira <i>et al</i> , 2009)
sirolimus	2	inhibit proliferation; immunosuppressant (ATC:L04AA10)	(Wang <i>et al</i> , 2007)
benzamil	1	ENaC channel blocker	(Chalfant <i>et al</i> , 1996)
viomycin	1	antibiotics exhibiting anti-tuberculosis	
amantadine	1	antiviral and an antiparkinsonian drug (ATC: N04BB01)	
cefadroxil	1	bactericidal antibiotic (ATC:J01DB05)	
ciclopirox	1	cell cycle blocker; antifungal (ATC: D01AE14)	(Zhou <i>et al</i> , 2010)
cloxacillin	1	antibiotic (ATC: J01CF02)	
finasteride	1	5-alpha-reductase inhibitor (ATC: G04CB01)	
glimepiride	1	sulfonylurea antidiabetic (ATC: A10BB12)	
hydroflumethiazide	1	diuretic (ATC:C03AA02)	
latamoxef	1	oxacephem antibiotic (ATC: J01DD06)	
loperamide	1	opioid drug used against diarrhea (ATC: A07DA03)	
lovastatin	1	lowering cholesterol (ATC:C10AA02)	
lycorine	1	toxic alkaloid	
maprotiline	1	N06 Psychoanaleptics	
metitepine	1	antipsychotic	(Monachon <i>et al</i> , 1972)
methylbenzethonium chloride	1	induce apoptosis	(Yip <i>et al</i> , 2006)
metixene	1	N04 Anti-parkinson drugs	
naftidrofuryl	1	spasmolytic (ATC:C04AX21)	
perhexiline	1	antianginal agent (ATC: C08EX02)	
phenazopyridine	1	local analgesic effect (ATC:G04BX06)	
syrosingopine	1		
thiethylperazine	1	antiemetic (ATC: R06AD03); potential antipsychotic activity	(Rotrosen <i>et al</i> , 1978)
trimipramine	1	N06 Psychoanaleptics	
triprolidine	1	antihistamine with anticholinergic properties (ATC:R06AX07)	
troglitazone	1	antidiabetic (ATC:A10BG01); peroxisome proliferator-activated receptor activator	
lactobionic acid	1	antioxidant	
rosiglitazone	1	antidiabetic drug (ATC: A10BG02); peroxisome proliferator-activated receptor activator	
norcyclobenzaprine	1	structurally similar to tricyclic antidepressants	(Van Hoey)

CODI module 17

37 genes, 9 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 1.84	
Category	Term	PValue
UP_SEQ_FEATURE	repeat:WD 4	4.60E-03
UP_SEQ_FEATURE	repeat:WD 3	5.78E-03
UP_SEQ_FEATURE	repeat:WD 1	6.25E-03
UP_SEQ_FEATURE	repeat:WD 2	6.25E-03
SP_PIR_KEYWORDS	wd repeat	6.35E-03
INTERPRO	IPR019775:WD40 repeat, conserved site	6.78E-03
INTERPRO	IPR019782:WD40 repeat 2	2.45E-02
INTERPRO	IPR017986:WD40 repeat, region	2.71E-02
INTERPRO	IPR019781:WD40 repeat, subgroup	2.94E-02
INTERPRO	IPR001680:WD40 repeat	3.70E-02
SMART	SM00320:WD40	4.78E-02
INTERPRO	IPR015943:WD40/YVTN repeat-like	4.78E-02

Drug annotation:

Annotation type	Enriched term	q-value
ATC code (2nd level)	C01; Cardiac therapy	8.01E-02

Drugs	# of cell lines	Drug annotation	Literature evidence
digoxigenin	2	Na+/K+-ATPase inhibition	(Yoda, 1974)
helveticoside	2	Na+/K+-ATPase inhibition	(Yoda, 1974)
digoxin	2	Na+/K+-ATPase inhibition; cardiac glycoside (ATC: C01AA05)	
lanatoside C	2	Na+/K+-ATPase inhibition; cardiac glycoside (ATC: C01AA06)	
ouabain	2	Na+/K+-ATPase inhibition; cardiac glycoside (ATC: C01AC01)	
strophanthidin	2	Na+/K+-ATPase inhibition	(Deitmer & Ellis, 1978)
digitoxigenin	2	Na+/K+-ATPase inhibition	(Erenkamp <i>et al</i> , 1998)
bisacodyl	1	Na+/K+-ATPase inhibition; stimulant laxative drug (ATC: A06AB02)	(Schreiner <i>et al</i> , 1980)
ellipticine	1	antineoplastic agent, uncoupling agent	

CODI module 18

86 genes, 285 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 3.41	
Category	Term	PValue
SP_PIR_KEYWORDS	membrane	4.04E-05
UP_SEQ_FEATURE	transmembrane region	1.03E-04
SP_PIR_KEYWORDS	transmembrane	1.13E-04
UP_SEQ_FEATURE	glycosylation site:N-linked (GlcNAc...)	1.35E-04
UP_SEQ_FEATURE	topological domain:Extracellular	3.06E-04
SP_PIR_KEYWORDS	glycoprotein	3.93E-04
UP_SEQ_FEATURE	topological domain:Cytoplasmic	0.001852536
GOTERM_CC_FAT	GO:0016021~integral to membrane	0.002694147
GOTERM_CC_FAT	GO:0031224~intrinsic to membrane	0.004878841
Annotation Cluster 2	Enrichment Score: 2.90	
Category	Term	PValue
SP_PIR_KEYWORDS	signal	4.48E-05
UP_SEQ_FEATURE	signal peptide	4.57E-05
UP_SEQ_FEATURE	glycosylation site:N-linked (GlcNAc...)	1.35E-04
SP_PIR_KEYWORDS	glycoprotein	3.93E-04
SP_PIR_KEYWORDS	disulfide bond	0.002047932
SP_PIR_KEYWORDS	Secreted	0.007258047

UP_SEQ_FEATURE	disulfide bond	0.034776624
GOTERM_CC_FAT	GO:0005576~extracellular region	0.109053733

Drug annotation:

No enriched terms found.

CODI module 19

162 genes, 27 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 2.41	
Category	Term	PValue
GOTERM_CC_FAT	GO:0005783~endoplasmic reticulum	0.001041882
SP_PIR_KEYWORDS	endoplasmic reticulum	0.001620378
GOTERM_CC_FAT	GO:0044432~endoplasmic reticulum part	0.033999285

Drug annotation:

No enriched terms found.

CODI module 20

165 genes, 18 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 2.09	
Category	Term	PValue
GOTERM_CC_FAT	GO:0043228~non-membrane-bounded organelle	0.004337048
GOTERM_CC_FAT	GO:0043232~intracellular non-membrane-bounded organelle	0.004337048
GOTERM_CC_FAT	GO:0005856~cytoskeleton	0.026841081
Annotation Cluster 2	Enrichment Score: 2.06	
Category	Term	PValue
GOTERM_BP_FAT	GO:0016192~vesicle-mediated transport	4.95E-04
GOTERM_BP_FAT	GO:0046907~intracellular transport	0.001693696
SP_PIR_KEYWORDS	protein transport	0.002182699
GOTERM_BP_FAT	GO:0008104~protein localization	0.003850693
GOTERM_BP_FAT	GO:0015031~protein transport	0.009329004
GOTERM_BP_FAT	GO:0045184~establishment of protein localization	0.01024802
SP_PIR_KEYWORDS	transport	0.029596983
GOTERM_BP_FAT	GO:0034613~cellular protein localization	0.042971308
GOTERM_BP_FAT	GO:0070727~cellular macromolecule localization	0.045534093
GOTERM_BP_FAT	GO:0006886~intracellular protein transport	0.053601216

Drug annotation:

No enriched terms found.

CODI module 21

602 genes, 26 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 4.14	
Category	Term	PValue
GOTERM_BP_FAT	GO:0006952~defense response	1.27E-06
GOTERM_BP_FAT	GO:0009611~response to wounding	3.34E-04
GOTERM_BP_FAT	GO:0006954~inflammatory response	8.45E-04
Annotation Cluster 2	Enrichment Score: 3.28	
Category	Term	PValue
GOTERM_BP_FAT	GO:0007155~cell adhesion	7.55E-05
GOTERM_BP_FAT	GO:0022610~biological adhesion	7.59E-05
SP_PIR_KEYWORDS	cell adhesion	2.44E-04
GOTERM_BP_FAT	GO:0016337~cell-cell adhesion	0.053463483
Annotation Cluster 3	Enrichment Score: 3.21	
Category	Term	PValue
INTERPRO	IPR011993:Pleckstrin homology-type	1.36E-04

UP_SEQ_FEATURE	domain:PH	3.85E-04
INTERPRO	IPR001849:Pleckstrin homology	6.84E-04
SMART	SM00233:PH	0.00373482

Drug annotation:

No enriched terms found.

CODI module 22

836 genes, 14 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 5.03	
Category	Term	PValue
UP_SEQ_FEATURE	topological domain:Extracellular	1.25E-08
UP_SEQ_FEATURE	topological domain:Cytoplasmic	5.29E-07
SP_PIR_KEYWORDS	disulfide bond	2.15E-06
UP_SEQ_FEATURE	glycosylation site:N-linked (GlcNAc...)	3.66E-06
UP_SEQ_FEATURE	disulfide bond	6.43E-06
SP_PIR_KEYWORDS	transmembrane	9.26E-06
UP_SEQ_FEATURE	transmembrane region	9.46E-06
SP_PIR_KEYWORDS	glycoprotein	2.47E-05
SP_PIR_KEYWORDS	signal	3.10E-05
UP_SEQ_FEATURE	signal peptide	3.36E-05
SP_PIR_KEYWORDS	membrane	4.05E-05
GOTERM_CC_FAT	GO:0016021~integral to membrane	3.19E-04
GOTERM_CC_FAT	GO:0031224~intrinsic to membrane	3.92E-04
Annotation Cluster 2	Enrichment Score: 4.15	
Category	Term	PValue
UP_SEQ_FEATURE	topological domain:Extracellular	1.25E-08
UP_SEQ_FEATURE	topological domain:Cytoplasmic	5.29E-07
SP_PIR_KEYWORDS	receptor	8.87E-06
GOTERM_CC_FAT	GO:0005886~plasma membrane	6.35E-04
GOTERM_CC_FAT	GO:0031226~intrinsic to plasma membrane	7.13E-04
GOTERM_CC_FAT	GO:0005887~integral to plasma membrane	7.38E-04
SP_PIR_KEYWORDS	cell membrane	0.003911328
GOTERM_CC_FAT	GO:0044459~plasma membrane part	0.007741016
Annotation Cluster 3	Enrichment Score: 3.14	
Category	Term	PValue
GOTERM_MF_FAT	GO:0005543~phospholipid binding	4.71E-04
GOTERM_MF_FAT	GO:0035091~phosphoinositide binding	5.71E-04
UP_SEQ_FEATURE	domain:PX	7.39E-04
SMART	SM00312:PX	8.21E-04
GOTERM_MF_FAT	GO:0008289~lipid binding	8.65E-04
INTERPRO	IPR001683:Phox-like	9.70E-04

Drug annotation:

No enriched terms found.

CODI module 23

102 genes, 58 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 3.98	
Category	Term	PValue
INTERPRO	IPR001909:Krueppel-associated box	1.78E-08
UP_SEQ_FEATURE	domain:KRAB	2.02E-08
UP_SEQ_FEATURE	zinc finger region:C2H2-type 6	6.22E-08
SMART	SM00349:KRAB	6.96E-08
UP_SEQ_FEATURE	zinc finger region:C2H2-type 7	2.26E-07
UP_SEQ_FEATURE	zinc finger region:C2H2-type 5	3.24E-07
UP_SEQ_FEATURE	zinc finger region:C2H2-type 8	5.20E-07
INTERPRO	IPR013087:Zinc finger, C2H2-type/integrase, DNA-binding	5.45E-07

INTERPRO	IPR015880:Zinc finger, C2H2-like	7.43E-07
UP_SEQ_FEATURE	zinc finger region:C2H2-type 3	1.21E-06
UP_SEQ_FEATURE	zinc finger region:C2H2-type 11	1.25E-06
INTERPRO	IPR007087:Zinc finger, C2H2-type	3.30E-06
SMART	SM00355:ZnF_C2H2	3.57E-06
UP_SEQ_FEATURE	zinc finger region:C2H2-type 4	3.60E-06
UP_SEQ_FEATURE	zinc finger region:C2H2-type 10	3.64E-06
UP_SEQ_FEATURE	zinc finger region:C2H2-type 12	4.06E-06
UP_SEQ_FEATURE	zinc finger region:C2H2-type 2	5.18E-06
UP_SEQ_FEATURE	zinc finger region:C2H2-type 13	1.20E-05
UP_SEQ_FEATURE	zinc finger region:C2H2-type 17	2.24E-05
SP_PIR_KEYWORDS	zinc-finger	4.03E-05
UP_SEQ_FEATURE	zinc finger region:C2H2-type 16	7.44E-05
UP_SEQ_FEATURE	zinc finger region:C2H2-type 9	8.57E-05
UP_SEQ_FEATURE	zinc finger region:C2H2-type 15	1.73E-04
PIR_SUPERFAMILY	PIRSF005559:zinc finger protein ZFP-36	3.33E-04
UP_SEQ_FEATURE	zinc finger region:C2H2-type 1	4.16E-04
GOTERM_MF_FAT	GO:0008270~zinc ion binding	6.82E-04
GOTERM_MF_FAT	GO:0003677~DNA binding	7.01E-04
SP_PIR_KEYWORDS	zinc	7.02E-04
GOTERM_BP_FAT	GO:0006350~transcription	0.001896131
UP_SEQ_FEATURE	zinc finger region:C2H2-type 18	0.002231138
SP_PIR_KEYWORDS	dna-binding	0.002515738
SP_PIR_KEYWORDS	metal-binding	0.003244845
GOTERM_BP_FAT	GO:0006355~regulation of transcription, DNA-dependent	0.0033329
GOTERM_BP_FAT	GO:0051252~regulation of RNA metabolic process	0.00458636
GOTERM_MF_FAT	GO:0046914~transition metal ion binding	0.00532855
GOTERM_BP_FAT	GO:0045449~regulation of transcription	0.009425629
GOTERM_MF_FAT	GO:0046872~metal ion binding	0.011965016
GOTERM_MF_FAT	GO:0043169~cation binding	0.013365187
GOTERM_MF_FAT	GO:0043167~ion binding	0.016002071
SP_PIR_KEYWORDS	Transcription	0.018692939
UP_SEQ_FEATURE	zinc finger region:C2H2-type 14	0.022267624
SP_PIR_KEYWORDS	zinc finger	0.027265456
UP_SEQ_FEATURE	zinc finger region:C2H2-type 1; degenerate	0.042265807
SP_PIR_KEYWORDS	transcription regulation	0.048200293
SP_PIR_KEYWORDS	nucleus	0.078299633
SP_PIR_KEYWORDS	DNA binding	0.093466428

Drug annotation:

No enriched terms found.

MCF7 Dataset:

Drug-induced transcriptional module: MCF7-9

49 genes, 37 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 1.61	
Category	Term	PValue
GOTERM_BP_FAT	GO:0007186~G-protein coupled receptor protein signaling pathway	3.33E-03
GOTERM_BP_FAT	GO:0032103~positive regulation of response to external stimulus	2.30E-02
GOTERM_BP_FAT	GO:0048584~positive regulation of response to stimulus	5.37E-02
GOTERM_BP_FAT	GO:0032101~regulation of response to external stimulus	8.80E-02
Annotation Cluster 2	Enrichment Score: 1.56	
Category	Term	PValue
GOTERM_BP_FAT	GO:0060429~epithelium development	5.43E-03
GOTERM_BP_FAT	GO:0035295~tube development	7.90E-03
GOTERM_BP_FAT	GO:0048729~tissue morphogenesis	2.44E-02

GOTERM_BP_FAT	GO:0016331~morphogenesis of embryonic epithelium	2.53E-02
GOTERM_BP_FAT	GO:0001822~kidney development	4.26E-02
GOTERM_BP_FAT	GO:0002009~morphogenesis of an epithelium	5.64E-02
GOTERM_BP_FAT	GO:0001655~urogenital system development	5.80E-02
GOTERM_BP_FAT	GO:0048598~embryonic morphogenesis	7.99E-02

Drug annotation:

Annotation type	Enriched term	q-value
Drug target	ESR1; estrogen receptor 1	2.98E-04
ATC code (2nd level)	G03; Sex hormones and modulators of the genital system	3.33E-08
ATC code (2nd level)	L02; Endocrine therapy	7.76E-04
Side effect	vulvovaginitis	4.87E-03
Side effect	pelvic pain	7.53E-03
Side effect	endometriosis	9.59E-03
Side effect	pneumonia	9.76E-03
Side effect	varicose vein	1.53E-02
Side effect	Endocrine Disorders	2.10E-02
Side effect	uterine fibroids	2.53E-02
Side effect	breast neoplasm	5.98E-02
Side effect	breast pain	7.08E-02
Chemical Fragment	<chem>c1ccc(cc1)CC</chem>	5.49E-07
Chemical Fragment	<chem>C=C1CCCC2(C)(C(CC)CCC12)</chem>	7.95E-06
Chemical Fragment	<chem>Cc1c(ccc1Cl)Cl</chem>	7.95E-06
Chemical Fragment	<chem>C(C)CCCC(C)C</chem>	5.47E-05
Chemical Fragment	<chem>c1c(cc(cc1))I</chem>	7.20E-05
Chemical Fragment	<chem>C(C)CCCC(C)C</chem>	1.21E-04
Chemical Fragment	<chem>C(=NCCCCC)N</chem>	4.91E-04
Chemical Fragment	<chem>C(=NCCCC)N</chem>	4.91E-04
Chemical Fragment	<chem>C(c1ccccc1)CC</chem>	5.16E-04
Chemical Fragment	<chem>C(=C(NCc1cnc(nc1(N))C)C)S</chem>	9.45E-04
Chemical Fragment	<chem>c1c(cc(cc1))I</chem>	3.78E-03
Chemical Fragment	<chem>C(=NCCCCCN=CN)N</chem>	3.78E-03

Drugs	Drug annotation	Literature evidence
pregnenolone	GABAA antagonist and increases neurogenesis in the hippocampus	(Mayo <i>et al</i> , 2005)
fulvestrant	estrogen receptor antagonist(ATC: L02BA03)	
butyl hydroxybenzoate	Oestrogenic activity	(Charles & Darbre, 2009)
epiandrosterone	steroid hormone with weak androgenic activity	
bendroflumethiazide	thiazide diuretic used to treat hypertension (ATC:C03AA01)	
estropipate	a form of estrogen	
pentoxifyverine	selective agonist at the sigma-1 receptor (ATC: R05DB05)	
diethylstilbestrol	inhibit proliferation of human prostate cancer cell lines; nonsteroidal estrogen (ATC: G03CB02)	(Koike <i>et al</i> , 2005)
dilazep	adenosine reuptake inhibitor (ATC: C01DX10)	
dimethadione	anticonvulsant	
epitiostanol	steroidal antiestrogen	(Konishi <i>et al</i> , 1988)
equilin	Equilin results in increased activity of ESR1 protein	(Davis <i>et al</i> , 2011)
estriol	one of the three main estrogens	
ethisterone	progestogen hormone (ATC:G03DC04)	
etynodiol	hormonal contraceptive (ATC:G03DC06)	
hexestrol		
ketorolac	Cyclooxygenase Inhibitors (ATC: M01AB15)	
lorglumide	cholecystokinin antagonist	(Makovec <i>et al</i> , 1987)
mestranol	estrogen	
nitrendipine	calcium channel blocker (ATC: C08CA08)	
estradiol	estrogen receptor agonist (ATC: G03CA03)	PubChem ID:450
alpha-estradiol	estrogen receptor agonist (ATC: G03CA03)	PubChem ID:450

noretynodrel	synthetic progestogen (ATC: G03FA09)	
levonorgestrel	synthetic progestogen (ATC: G03AC03)	
raloxifene	selective estrogen receptor modulator (ATC: G03XC01)	
Ribavirin	anti-viral drug (ATC: J05AB04)	
solasodine	glycoalkaloid	
Genistein	estrogen receptor agonist	
tamoxifen	estrogen receptor antagonist (ATC: L02BA01)	
testosterone	steroid hormone from the androgen group	
theobromine	vasodilator and diuretic (ATC: C03BD01)	
corticosterone	corticosteroid (steroid hormone)	
lynestrenol	progestagen hormone (ATC: G03AC02)	
estrone	estrogenic hormone	
prasterone	conversion to produce the androgen testosterone and the estrogens	(Mo <i>et al.</i> , 2006)
naringenin	flavanon; antioxidant, anti-inflammatory	
aminophylline	nonselective phosphodiesterase inhibitor (ATC:R03DA05)	

PC3 Dataset:

Drug-induced transcriptional module: PC3-3

38 genes, 25 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 3.96	
Category	Term	PValue
SP_PIR_KEYWORDS	signal	3.44E-06
UP_SEQ_FEATURE	signal peptide	3.49E-06
UP_SEQ_FEATURE	disulfide bond	3.79E-05
SP_PIR_KEYWORDS	disulfide bond	6.34E-05
SP_PIR_KEYWORDS	Secreted	4.68E-03
GOTERM_CC_FAT	GO:0005576~extracellular region	1.22E-02
Annotation Cluster 2	Enrichment Score: 2.10	
Category	Term	PValue
SP_PIR_KEYWORDS	unfolded protein response	1.55E-03
GOTERM_BP_FAT	GO:0051789~response to protein stimulus	4.08E-03
GOTERM_BP_FAT	GO:0006986~response to unfolded protein	1.70E-02
GOTERM_BP_FAT	GO:0010033~response to organic substance	3.67E-02
Annotation Cluster 3	Enrichment Score: 1.68	
Category	Term	PValue
UP_SEQ_FEATURE	short sequence motif:Prevents secretion from ER	8.92E-04
GOTERM_CC_FAT	GO:0005788~endoplasmic reticulum lumen	2.38E-03
SP_PIR_KEYWORDS	endoplasmic reticulum	2.61E-03
GOTERM_CC_FAT	GO:0044432~endoplasmic reticulum part	4.88E-03
GOTERM_CC_FAT	GO:0005783~endoplasmic reticulum	7.13E-03
INTERPRO	IPR000886:Endoplasmic reticulum, targeting sequence	8.92E-03
GOTERM_CC_FAT	GO:0043233~organelle lumen	6.97E-01
GOTERM_CC_FAT	GO:0031974~membrane-enclosed lumen	7.17E-01
GOTERM_CC_FAT	GO:0070013~intracellular organelle lumen	8.25E-01

Drug annotation:

Annotation type	Enrichment term	q-value
Drug target	HRH1;histamine receptor H1	1.00E-05
Drug target	HTR2A;5-hydroxytryptamine (serotonin) receptor 2A	2.96E-05
Drug target	DRD2;dopamine receptor D2	3.78E-05

Drug target	DRD1;dopamine receptor D1	1.03E-04
Drug target	ADRA1A;adrenergic, alpha-1A-, receptor	2.60E-04
Drug target	DRD3;dopamine receptor D3	2.60E-04
Drug target	CHRM2;cholinergic receptor, muscarinic 2	4.15E-04
Drug target	CHRM4;cholinergic receptor, muscarinic 4	1.33E-03
Drug target	HTR2C;5-hydroxytryptamine (serotonin) receptor 2C	1.40E-03
Drug target	SLC6A2;solute carrier family 6 (neurotransmitter transporter, noradrenalin), member 2	1.45E-03
Drug target	CHRM5;cholinergic receptor, muscarinic 5	1.55E-03
Drug target	CHRM1;cholinergic receptor, muscarinic 1	1.77E-03
Drug target	ADCY1;adenylate cyclase 1 (brain)	8.41E-03
Drug target	CHRM3;cholinergic receptor, muscarinic 3	9.84E-03
Drug target	SLC6A4;solute carrier family 6 (neurotransmitter transporter, serotonin), member 4	1.08E-02
Drug target	HTR6;5-hydroxytryptamine (serotonin) receptor 6	1.28E-02
Drug target	HTR1A;5-hydroxytryptamine (serotonin) receptor 1A	1.81E-02
Drug target	HRH4;histamine receptor H4	3.71E-02
Drug target	DRD4;dopamine receptor D4	5.10E-02
ATC code (2nd level)	R06; Antihistamines for systemic use	1.89E-02
Side effect	paralytic ileus	3.85E-04
Side effect	galactorrhea	8.97E-03
Side effect	gynecomastia	2.77E-02
Side effect	breast enlargement	7.46E-02
Side effect	urinary retention	9.40E-02

Drugs	Drug annotation	Literature evidence
depropine	antihistamine with anticholinergic properties (ATC: R06AX16)	
promazine	N05 Psycholeptics	
homochlorcyclizine	antihistamine	(Haraguchi <i>et al</i> , 1997)
cyproheptadine	antihistamine (ATC: R06AX02)	
thioridazine	cytogenetic damage; inhibit cell proliferation; antipsychotic drug (ATC: N05AC02)	(Strobl <i>et al</i> , 1990)
pizotifen	prevention of vascular headache (ATC: N02CX01)	
clomipramine	tricyclic antidepressant (ATC: N06AA04)	
chlorpromazine	N05 Psycholeptics	
trimipramine	N06 Psychoanaleptics	
quinisocaine	antipruritic (ATC: D04AB05)	
alimemazine	antihistamine (ATC: R06AD01)	
cyclobenzaprine	muscle relaxant medication (ATC: M03BX08)	
amitriptyline	tricyclic antidepressant (ATC: N06AA09)	
imipramine	tricyclic antidepressant (ATC: N06AA02)	
promethazine	antihistamine (ATC: R06AD02)	
profenamine	antiparkinsonian agent; antihistamine action (ATC: N04AA05)	
chloropyramine	antihistamine (ATC: R06AC03)	
triprolidine	antihistamine with anticholinergic properties (ATC:R06AX07)	
vinburnine	vasodilator (ATC: C04AX17)	
loxapine	treatment of schizophrenia (ATC: N05AH01)	
mianserin	psychoactive drug (ATC: N06AX03)	
nisoxetine	selective norepinephrine reuptake inhibitor	(Graham & Langer, 1992)
metixene	N04 Anti-parkinson drugs	
domperidone	antidopaminergic drug (ATC: A03FA03)	
dicycloverine	muscarinic receptor antagonist (ATC: A03AA07)	

Drug-induced transcriptional module: PC3-9

39 genes, 17 chemicals

Functional enrichment of genes:

No significant annotation clusters found.

Drug Annotation:

Annotation type	Enrichment term	q-value
Drug target	SERPINE1;serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	1.08E-02
Drug target	LPL;lipoprotein lipase	1.08E-02
Drug target	PPARG;peroxisome proliferator-activated receptor gamma	1.08E-02
Drug target	SLCO1B1;solute carrier organic anion transporter family, member 1B1	1.81E-02
Drug target	ABCC8;ATP-binding cassette, sub-family C (CFTR/MRP), member 8	2.86E-02
ATC code (2nd level)	A10; Drugs used in diabetes	1.70E-04

Drugs	Drug annotation	Literature evidence
trogliptazone	antidiabetic (ATC:A10BG01); peroxisome proliferator-activated receptor gamma activator	
rosiglitazone	antidiabetic drug (ATC: A10BG02); peroxisome proliferator-activated receptor gamma activator	
15-delta prostaglandin J2	NSAID; inhibition of cell proliferation	(Kim <i>et al</i> , 2007; Forman <i>et al</i> , 1995)
gliquidone	sulfonylurea antidiabetic (ATC: A10BB08); peroxisome proliferator-activated receptor gamma activator	(Scarsi <i>et al</i> , 2007)
glibenclamide	sulfonylurea antidiabetic (ATC: A10BB01); peroxisome proliferator-activated receptor gamma activator	(Fukuen <i>et al</i> , 2005)
mifepristone	progesterone receptor antagonist	
glimepiride	sulfonylurea antidiabetic (ATC: A10BB12); peroxisome proliferator-activated receptor gamma activator	(Scarsi <i>et al</i> , 2007; Fukuen <i>et al</i> , 2005)
tiratricol	thyroid hormone analogue (ATC: H03AA04 D11AX08)	
tretinoin	acid form of vitamin A; treat acne vulgaris and keratosis pilaris; antineoplastic (ATC: L01XX14); all-trans retinoic acid, peroxisome proliferator-activated receptor gamma activator	
3-acetylcoumarin		
acemetacin	non-steroidal anti-inflammatory drug (ATC: M01AB11)	
clemizole	Antihistamine	
rilmenidine	treatment of hypertension	
bezafibrate	fibrate drug against hyperlipidaemia; peroxisome proliferator-activated receptor gamma activator	
zaprinast	phosphodiesterase inhibitor	(Choi <i>et al</i> , 2002)
racecadotril	antidiarrheal (ATC: A07XA04); enkephalinase inhibitor	(Matheson & Noble, 2000)
raubasine	Antihypertensive and antidiabetic	

Drug-induced transcriptional module: PC3-11

73 genes, 22 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 5.14	
Category	Term	PValue
UP_SEQ_FEATURE	glycosylation site:N-linked (GlcNAc...)	3.03E-09
SP_PIR_KEYWORDS	glycoprotein	1.56E-08
SP_PIR_KEYWORDS	Secreted	8.60E-08
SP_PIR_KEYWORDS	signal	1.01E-06
UP_SEQ_FEATURE	signal peptide	1.04E-06
GOTERM_CC_FAT	GO:0005576~extracellular region	3.30E-06
GOTERM_CC_FAT	GO:0044421~extracellular region part	4.39E-04
SP_PIR_KEYWORDS	disulfide bond	1.16E-03
UP_SEQ_FEATURE	disulfide bond	4.98E-03
GOTERM_CC_FAT	GO:0005615~extracellular space	1.09E-02
Annotation Cluster 2	Enrichment Score: 2.39	
Category	Term	PValue
GOTERM_MF_FAT	GO:0030414~peptidase inhibitor activity	9.73E-05

GOTERM_MF_FAT	GO:0004866~endopeptidase inhibitor activity	9.73E-05
GOTERM_BP_FAT	GO:0042060~wound healing	1.44E-03
KEGG_PATHWAY	hsa04610:Complement and coagulation cascades	2.02E-03
GOTERM_BP_FAT	GO:0050878~regulation of body fluid levels	2.81E-03
GOTERM_MF_FAT	GO:0004867~serine-type endopeptidase inhibitor activity	2.82E-03
GOTERM_MF_FAT	GO:0004857~enzyme inhibitor activity	4.55E-03
SP_PIR_KEYWORDS	serine proteinase inhibitor	5.76E-03
INTERPRO	IPR000215:Protease inhibitor I4, serpin	6.31E-03
SMART	SM00093:SERPIN	7.02E-03
GOTERM_BP_FAT	GO:0050817~coagulation	8.81E-03
GOTERM_BP_FAT	GO:0007596~blood coagulation	8.81E-03
PIR_SUPERFAMILY	PIRSF001630:serpin	9.34E-03
GOTERM_BP_FAT	GO:0007599~hemostasis	1.08E-02
UP_SEQ_FEATURE	site:Reactive bond	1.17E-02
SP_PIR_KEYWORDS	Serine protease inhibitor	2.22E-02
SP_PIR_KEYWORDS	protease inhibitor	3.55E-02

Drug annotation:

Annotation type	Enriched term	q-value
Drug target	ADRB2; adrenergic, beta-2-, receptor, surface	6.55E-08
Drug target	ADRB1; adrenergic, beta-1-, receptor	2.60E-04
Drug target	ADRB3; adrenergic, beta-3-, receptor	3.75E-03
Drug target	ADCY10; adenylate cyclase 10	1.81E-02
ATC code (2nd level)	R03; Drugs for obstructive airway diseases	3.19E-06
ATC code (2nd level)	C01; Cardiac therapy	7.91E-02
Side effect	tachycardia	7.88E-02
Chemical Fragment	C(=NCCCC)N	2.35E-12
Chemical Fragment	C(C)c1cccc1	1.02E-08
Chemical Fragment	C(=C(NCc1cnc(nc1(N))C)C)S	6.44E-08
Chemical Fragment	C(c1cccc1)c2cccc2	1.14E-07
Chemical Fragment	C(=NCCCCCN=CN)N	1.14E-07
Chemical Fragment	C(C)(C)CC(C)(C)C	1.46E-07
Chemical Fragment	C(=NCCCCCN=CN)N	5.86E-07
Chemical Fragment	C(C)=C(NCc1cnc(nc1(N))C)C	7.36E-07
Chemical Fragment	C(=NCCCCCN=CN)N	7.36E-07
Chemical Fragment	C(=NCCCC)N	1.92E-06
Chemical Fragment	C(=NCCCC)N	3.12E-06
Chemical Fragment	C(=NCCCCCN=CN)N	7.95E-06
Chemical Fragment	C(C)(C)CC(C)(C)C	1.34E-05
Chemical Fragment	C(=NCCCC)N	1.41E-05
Chemical Fragment	C(=NCCCC)N	2.00E-05
Chemical Fragment	C(=NCCCC)N	2.19E-05
Chemical Fragment	C(=NOC)c1nc(N)sc1	9.31E-05
Chemical Fragment	C(=NCCCC)N	1.32E-04
Chemical Fragment	C(=C(NCc1cnc(nc1(N))C)C)S	1.89E-04
Chemical Fragment	c1ccc(C)cc1	1.99E-04
Chemical Fragment	C=CNCCSC	1.99E-04
Chemical Fragment	C1=Nc3cccc3(Oc2ccc(cc12)Cl)	3.87E-04
Chemical Fragment	C(=C(NCc1cnc(nc1(N))C)C)S	3.87E-04
Chemical Fragment	C(=NCCCCCN=CN)N	7.64E-04
Chemical Fragment	C(=NOC(C)C)c1nc(N)sc1	8.41E-04
Chemical Fragment	C(C)CCCC(C)C	1.09E-03
Chemical Fragment	C(=NOC(C)C)c1nc(N)sc1	2.13E-03
Chemical Fragment	C(=NOC)c1nc(N)sc1	2.93E-03
Chemical Fragment	C(=NCCCC)N	6.81E-03

Drugs	Drug annotation	Literature evidence
salbutamol	ADRB2 agonist (ATC: R03AC02) (ADRB2 : adrenergic, beta-2-, receptor)	
metanephrine	metabolite of epinephrine (that is ADRB2 agonist)	(Thomas & Friedland, 1998)
alprostadil	prostaglandin; treatment of erectile dysfunction (ATC: G04BE01); Alprostadil results in increased phosphorylation of ADRB2 protein	(Davis <i>et al.</i> , 2011)

adenosine phosphate	can also exist as a cyclic structure known as cyclic AMP	
butamben	local anesthetic	
clenbuterol	ADRB2 agonist (ATC: R03AC14)	
dipivefrine	ADRB2 agonist	
dipyridamole	inhibits thrombus formation (ATC:B01AC07)	
ritodrine	ADRB2 agonist	
ethaverine	Vasodilator and antispasmodic	
etilefrine	ADRB2 agonist	(Nusser <i>et al</i> , 1965)
fenoterol	ADRB2 agonist	
dobutamine	ADRB2 agonist	
isoetarine	ADRB2 agonist	
(+)- isoprenaline	ADRB2 agonist	PubChem ID: 3779
(-)- isoprenaline	ADRB2 agonist	PubChem ID: 3779
isoxsuprine	ADRB2 agonist	(Falkay & Kovács, 1986)
corbadrine	metabolite of methyl dopa (alpha-2-adrenergic receptor agonist)	
orciprenaline	ADRB2 agonist	
papaverine	antispasmodic (ATC: A03AD01); inhibition of the enzyme phosphodiesterase causing elevation of cyclic AMP	
terbutaline	ADRB2 agonist (ATC: R03AC03)	
zardaverine	phosphodiesterases (PDE III/IV) inhibition	

HL60 Dataset:

Drug-induced transcriptional module: HL60-17

21 genes, 27 chemicals

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 1.88	
Category	Term	PValue
GOTERM_BP_FAT	GO:0051249~regulation of lymphocyte activation	1.15E-02
GOTERM_BP_FAT	GO:0002694~regulation of leukocyte activation	1.32E-02
GOTERM_BP_FAT	GO:0050865~regulation of cell activation	1.46E-02

Drug annotation:

Annotation type	Enriched term	q-value
Drug target	ADRB2; adrenergic, beta-2-, receptor, surface	4.54E-03
ATC code (2nd level)	R03; Drugs for obstructive airway diseases	1.46E-03
ATC code (2nd level)	G02; Other gynecologicals	4.72E-02
Chemical Fragment	C(=C(NCc1cnc(nc1(N))C)C)S	7.92E-07
Chemical Fragment	C(=NCCCC)N	1.51E-05
Chemical Fragment	C(=NCCCC)N	1.71E-05
Chemical Fragment	C(=NCCCC)N	1.72E-05
Chemical Fragment	C(=NCCCC)N	2.10E-05
Chemical Fragment	C(=C(NCc1cnc(nc1(N))C)C)S	1.41E-04
Chemical Fragment	C(=NCCCCCN=CN)N	2.39E-04
Chemical Fragment	C(=NCCCC)N	4.50E-04
Chemical Fragment	C(=NCCCC)N	5.25E-04
Chemical Fragment	C(=NCCCC)N	7.79E-04
Chemical Fragment	C(=NCCCCCN=CN)N	1.14E-03
Chemical Fragment	C(=NCCCC)N	1.24E-03
Chemical Fragment	C(C)c1cccc1	1.24E-03
Chemical Fragment	C(=C(NCc1cnc(nc1(N))C)C)S	1.83E-03
Chemical Fragment	C(=NCCCC)N	1.83E-03
Chemical Fragment	C1c3ccccc3(C=Cc2ccccc12)	1.83E-03
Chemical Fragment	C(c1cccc1)c2ccccc2	1.83E-03
Chemical Fragment	C(=C(NCc1cnc(nc1(N))C)C)S	1.83E-03

Chemical Fragment	C(=NCCCCCN=CN)N	1.83E-03
Chemical Fragment	C1=Ne3cccc3(Oc2ccc(cc12)Cl)	2.61E-03
Chemical Fragment	C(=C(NCc1cnc(nc1(N))C)C)S	2.61E-03
Chemical Fragment	C(C)c1cccc1	4.05E-03
Chemical Fragment	C(C)=C(NCc1cnc(nc1(N))C)C	6.83E-03
Chemical Fragment	C(=NCCCCCN=CN)N	6.83E-03
Chemical Fragment	C(=NOC)c1nc(N)sc1	7.33E-03
Chemical Fragment	C(C)(C)CC(C)(C)C	9.17E-03
Chemical Fragment	C(C)(C)CC(C)(C)C	9.55E-03

Drugs	Drug annotation	Literature evidence
(+)-chelidone	cell cycle blocker	(Panzer <i>et al</i> , 2001)
co-dergocrine mesilate	alpha-adrenergic receptor antagonist	(Kitamura, 1980)
dinoprost	abortifacient (ATC: G02AD01)	
salbutamol	ADRB2 agonist (ATC: R03AC02) (ADRB2 : adrenergic, beta-2-, receptor)	
alprostadil	prostaglandin; treatment of erectile dysfunction (ATC: G04BE01); Alprostadil results in increased phosphorylation of ADRB2 protein	
bromocriptine	alpha-2 adrenergic agonist	(De Leeuw van Weenen <i>et al</i> , 2010)
clonidine	centrally acting alpha-2 adrenergic agonist (ATC:N02CX02)	
dihydroergocristine	treat dementia and age-related cognitive impairment (ATC:C04AE01)	
dihydroergotamine	Alpha 2-adrenergic agonist and alpha 1-adrenergic antagonist	(Nusser <i>et al</i> , 1965)
dipivefrine	ADRB2 agonist	
ethaverine	Vasodilator and antispasmodic	
etilefrine	ADRB2 agonist	(Ruffolo <i>et al</i> , 1987)
fenoterol	ADRB2 agonist	
hexetidine	anti-bacterial and anti-fungal (ATC: A01AB12)	
isoetarine	ADRB2 agonist	
(+)-isoprenaline	ADRB2 agonist	PubChem ID: 3779
(-)-isoprenaline	ADRB2 agonist	PubChem ID: 3779
corbadrine	metabolite of methyl dopa (alpha-2-adrenergic receptor agonist)	
orciprenaline	ADRB2 agonist(ATC: R03AB03)	
methylergometrine	vessel constrictor and smooth muscle agonist (ATC:G02AB01)	
nimodipine	dihydropyridine calcium channel blocker (ATC: C08CA06)	
papaverine	antispasmodic (ATC: A03AD01); inhibition of the enzyme phosphodiesterase causing elevation of cyclic AMP	
pergolide	alpha-2 adrenergic agonist	(Reid <i>et al</i> , 1997)
podophyllotoxin	purgative, vesicant, antirheumatic, antiviral, and antitumor agents (ATC: D06BB04)	
terbutaline	ADRB2 agonist (ATC: R03AC03)	
vigabatrin	inhibiting GABA transaminase (ATC: N03AG04)	
zardaverine	phosphodiesterases (PDE III/IV) inhibition	

Rat Liver Dataset:

Drug-induced transcriptional module: RatLiver-2

54 genes, 49 experiments

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 2.19	
Category	Term	PValue
KEGG_PATHWAY	rno04210:Apoptosis	3.54E-04
GOTERM_BP_FAT	GO:0009617~response to bacterium	4.67E-03
GOTERM_BP_FAT	GO:0032496~response to lipopolysaccharide	6.26E-03
GOTERM_BP_FAT	GO:0002237~response to molecule of bacterial origin	8.02E-03
GOTERM_BP_FAT	GO:0019221~cytokine-mediated signaling pathway	1.80E-02

KEGG_PATHWAY	rno04060:Cytokine-cytokine receptor interaction	4.55E-02
Annotation Cluster 2	Enrichment Score: 1.99	
Category	Term	PValue
GOTERM_BP_FAT	GO:0009611~response to wounding	5.06E-05
GOTERM_BP_FAT	GO:0006954~inflammatory response	6.20E-05
GOTERM_BP_FAT	GO:0006952~defense response	2.49E-04
GOTERM_BP_FAT	GO:0050900~leukocyte migration	8.05E-04
GOTERM_BP_FAT	GO:0002526~acute inflammatory response	3.00E-03
GOTERM_BP_FAT	GO:0030595~leukocyte chemotaxis	6.29E-03
GOTERM_BP_FAT	GO:0060326~cell chemotaxis	7.32E-03
GOTERM_BP_FAT	GO:0016477~cell migration	9.39E-03
SP_PIR_KEYWORDS	inflammatory response	1.04E-02
GOTERM_BP_FAT	GO:0042060~wound healing	1.83E-02
GOTERM_BP_FAT	GO:0051674~localization of cell	2.05E-02
GOTERM_BP_FAT	GO:0048870~cell motility	2.05E-02
GOTERM_BP_FAT	GO:0007626~locomotory behavior	2.91E-02
GOTERM_BP_FAT	GO:0042330~taxis	2.93E-02
GOTERM_BP_FAT	GO:0006935~chemotaxis	2.93E-02
GOTERM_CC_FAT	GO:0005615~extracellular space	4.12E-02
GOTERM_BP_FAT	GO:0006928~cell motion	4.40E-02
SP_PIR_KEYWORDS	Secreted	5.58E-02
GOTERM_CC_FAT	GO:0044421~extracellular region part	1.30E-01
GOTERM_BP_FAT	GO:0007610~behavior	1.56E-01
GOTERM_BP_FAT	GO:0006955~immune response	3.88E-01
Annotation Cluster 3	Enrichment Score: 1.79	
Category	Term	PValue
GOTERM_BP_FAT	GO:0042493~response to drug	3.80E-03
GOTERM_BP_FAT	GO:0042981~regulation of apoptosis	5.35E-03
GOTERM_BP_FAT	GO:0043067~regulation of programmed cell death	5.75E-03
GOTERM_BP_FAT	GO:0010941~regulation of cell death	5.89E-03
GOTERM_BP_FAT	GO:0006916~anti-apoptosis	1.13E-02
GOTERM_BP_FAT	GO:0043066~negative regulation of apoptosis	2.18E-02
GOTERM_BP_FAT	GO:0043069~negative regulation of programmed cell death	2.29E-02
GOTERM_BP_FAT	GO:0060548~negative regulation of cell death	2.31E-02
GOTERM_BP_FAT	GO:0045449~regulation of transcription	7.81E-01

Drug annotation:

Drugs	Experiments	Drug annotation	Literature evidence
benoxaprofen	3days; exp6406 5days; exp6408	NSAID (ATC: M01AE06)	
benzethonium chloride	1days; exp6427 3days; exp6431 5days; exp6435	surfactant,antiseptic, and anti-infective properties	
benzothiazyl disulfide	5days; exp5588	Vulcanizing accelerant	
bupropion	1days; exp6052	atypical antidepressant and smoking cessation aid (ATC: N06AX12)	
celecoxib	5days; exp6368	NSAID; COX-2 inhibitor (ATC: M01AH01)	
cholecalciferol	3days; exp5040	a form of vitamin D similar to steroids	
diclofenac	3days; exp3352 5days; exp3348	NSAID (ATC: M01AB05)	
etodolac	3days; exp5659 5days; exp5668	NSAID (ATC: M01AB08)	
ibuprofen	.25days; exp2691 3days; exp2703 3days; exp6535 5days; exp2697	NSAID (ATC: M01AE01)	
indomethacin	1days; exp6550	NSAID (ATC: M01AB01)	

	5days; exp3317 3days; exp3322 3days; exp3524 3days; exp6534 3days; exp6544 4days; exp7029 5days; exp3523		
interleukin-1 beta (rat)	3days; exp6494		
ketorolac	5days; exp6055	NSAID (ATC: M01AB15)	
Lipopolysaccharide, E. coli O55:B5	3days; exp4704 3days; exp4940 3days; exp5237 5days; exp4820 5days; exp5099	endotoxins and elicit strong immune responses	(Hertz <i>et al</i> , 1956)
meloxicam	1days; exp3370	NSAID (ATC: M01AC06)	
methotrexate	3days; exp3294	cell cycle blocker; antimetabolite (ATC: L01BA01)	(Moe <i>et al</i> , 2008; Zold <i>et al</i> , 2011)
naproxen	1days; exp3256	NSAID (ATC: M01AE02)	
nimesulide	3days; exp2804	NSAID (ATC: M01AX17)	
nystatin	1days; exp5550 5days; exp5543	antifungal (ATC: D01AA01)	
oxiconazole	3days; exp5270 5days; exp5253	antifungal (ATC: D01AC11)	
pramoxine	1days; exp5561	PDE-4 inhibitor (ATC: R03DX07)	
roflumilast	3days; exp7317 4days; exp7328	topical anesthetic; antipruritic (ATC: D04AB07)	
sildenafil	5days; exp3528	treat erectile dysfunction and pulmonary arterial hypertension (ATC: G04BE03)	
sulindac	1days; exp3055 3days; exp2735 5days; exp2747	NSAID (ATC: M01AB02)	
tnf alpha (rat)	.25days; exp7532		
trichloroacetic acid	5days; exp5568		

Drug-induced transcriptional module: RatLiver-7

52 genes, 18 experiments

Functional enrichment of genes:

No significant annotation clusters found.

Drug annotation:

Drugs	Experiments	Drug annotation	Literature evidence
alfacalcidol	3days; exp6300	analogue of vitamin D; effects on parathyroid hormone levels and immune system, including regulatory T cells	(Reid <i>et al</i> , 1997)
allyl alcohol	1days; exp6029		
amiodarone	3days; exp6206	antiarrhythmic agent (ATC: C01BD01)	
betamethasone	1days; exp6208	glucocorticoid steroid with anti-inflammatory and immunosuppressive properties (ATC: D07AC01)	
cerivastatin	5days; exp5449	statins; HMG-CoA reductase inhibitor (ATC: C10AA06)	
chlorpromazine	1days; exp2860	typical antipsychotic (ATC: N05AA01)	
cholecalciferol	3days; exp5040	a form of vitamin D similar to steroids	
ethinylestradiol	.25days; exp2867	a derivative of estradiol (ATC: L02AA03)	
fludrocortisone acetate	1days; exp6265	synthetic corticosteroid (ATC: H02AA02)	
fluocinolone acetonide	1days; exp6589	corticosteroid (ATC: D07AC04)	
hydralazine	1days; exp4380	smooth muscle relaxant; vasodilator (ATC: C02DB02)	
hydrocortisone	1days; exp6434	glucocorticoid (ATC: D07AA02)	
ketoconazole	1days; exp3255	antifungal drug (ATC: D01AC08)	
Lipopolysaccharide, E. coli O55:B5	3days; exp4704 3days; exp4940 5days; exp4820	endotoxins and elicit strong immune responses	(Seifert <i>et al</i> , 1994; Liu <i>et al</i> , 1993)
prednisolone	1days; exp4938	corticosteroid (ATC: D07AA03)	
primidone	3days; exp5667	anticonvulsant (ATC: N03AA03)	

Drug-induced transcriptional module: RatLiver-12

59 genes, 24 experiments

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 9.92	
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Category	Term	PValue
SP_PIR_KEYWORDS	lipid synthesis	2.04E-16
GOTERM_BP_FAT	GO:0008610~lipid biosynthetic process	2.80E-16
GOTERM_BP_FAT	GO:0016126~sterol biosynthetic process	3.12E-16
GOTERM_BP_FAT	GO:0006695~cholesterol biosynthetic process	8.72E-15
GOTERM_BP_FAT	GO:0016125~sterol metabolic process	6.55E-14
GOTERM_BP_FAT	GO:0008203~cholesterol metabolic process	1.69E-12
GOTERM_BP_FAT	GO:0006694~steroid biosynthetic process	2.18E-12
SP_PIR_KEYWORDS	Steroid biosynthesis	3.41E-12
GOTERM_BP_FAT	GO:0008202~steroid metabolic process	1.58E-10
KEGG_PATHWAY	mo00100: Steroid biosynthesis	3.10E-10
SP_PIR_KEYWORDS	sterol biosynthesis	4.12E-10
KEGG_PATHWAY	rno00900: Terpenoid backbone biosynthesis	1.01E-08
SP_PIR_KEYWORDS	Cholesterol biosynthesis	1.05E-08
GOTERM_BP_FAT	GO:0008299~isoprenoid biosynthetic process	2.20E-06
GOTERM_BP_FAT	GO:0006720~isoprenoid metabolic process	4.23E-05
SP_PIR_KEYWORDS	Isoprene biosynthesis	3.64E-04
SP_PIR_KEYWORDS	magnesium	2.28E-02
Annotation Cluster 2	Enrichment Score: 3.62	
Category	Term	PValue
KEGG_PATHWAY	mo00100: Steroid biosynthesis	3.10E-10
GOTERM_CC_FAT	GO:0005789~endoplasmic reticulum membrane	1.42E-06
GOTERM_CC_FAT	GO:0042175~nuclear envelope-endoplasmic reticulum network	2.23E-06
GOTERM_BP_FAT	GO:0055114~oxidation reduction	4.01E-06
GOTERM_CC_FAT	GO:0005783~endoplasmic reticulum	5.85E-06
GOTERM_CC_FAT	GO:0044432~endoplasmic reticulum part	7.61E-06
SP_PIR_KEYWORDS	oxidoreductase	1.17E-04
GOTERM_CC_FAT	GO:0012505~endomembrane system	1.61E-04
SP_PIR_KEYWORDS	endoplasmic reticulum	1.65E-04
GOTERM_CC_FAT	GO:0031090~organelle membrane	2.20E-04
SP_PIR_KEYWORDS	membrane	1.37E-02
SP_PIR_KEYWORDS	transmembrane	2.42E-02
UP_SEQ_FEATURE	transmembrane region	2.64E-02
GOTERM_CC_FAT	GO:0016021~integral to membrane	3.51E-01
GOTERM_CC_FAT	GO:0031224~intrinsic to membrane	4.14E-01
UP_SEQ_FEATURE	topological domain: Cytoplasmic	6.37E-01
Annotation Cluster 3	Enrichment Score: 2.91	
Category	Term	PValue
GOTERM_BP_FAT	GO:0006633~fatty acid biosynthetic process	1.22E-04
GOTERM_BP_FAT	GO:0006631~fatty acid metabolic process	4.10E-04
UP_SEQ_FEATURE	short sequence motif: Histidine box-1	6.32E-04
UP_SEQ_FEATURE	short sequence motif: Histidine box-3	6.32E-04
UP_SEQ_FEATURE	short sequence motif: Histidine box-2	6.32E-04
GOTERM_BP_FAT	GO:0046394~carboxylic acid biosynthetic process	1.61E-03
GOTERM_BP_FAT	GO:0016053~organic acid biosynthetic process	1.61E-03
GOTERM_MF_FAT	GO:0005506~iron ion binding	2.33E-03
KEGG_PATHWAY	mo01040: Biosynthesis of unsaturated fatty acids	8.60E-03
SP_PIR_KEYWORDS	Fatty acid biosynthesis	1.04E-02

Drug annotation:

Drugs	Experiments	Drug annotation	Literature evidence
atorvastatin	1days; exp2848 3days; exp2834 5days; exp2856	statins; HMG-CoA reductase inhibitor (ATC: C10AA05)	

cerivastatin	1days; exp4378 3days; exp4359 5days; exp5449	statins; HMG-CoA reductase inhibitor (ATC: C10AA06)	
doxycycline	1days; exp4388	tetracycline antibiotics (ATC: J01AA02)	
fluvastatin	1days; exp3382 3days; exp3415 3days; exp3470 5days; exp3408 5days; exp3409	statins; HMG-CoA reductase inhibitor (ATC: C10AA04)	
gemfibrozil	7days; exp2878	fibrates;used to lower lipid levels (ATC: C10AB04)	
lovastatin	1days; exp2966 1days; exp2977 3days; exp2971 3days; exp3000 5days; exp2967 5days; exp2992	statins; HMG-CoA reductase inhibitor (ATC: C10AA02)	
pravastatin	3days; exp5212 5days; exp5182	statins; HMG-CoA reductase inhibitor (ATC: C10AA03)	
simvastatin	1days; exp2824 3days; exp2813	statins; HMG-CoA reductase inhibitor (ATC: C10AA01)	
troglitazone	1days; exp6883	antidiabetic (ATC:A10BG01); peroxisome proliferator-activated receptor activator	

Drug-induced transcriptional module: RatLiver-22

88 genes, 16 experiments

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 2.71	
Category	Term	PValue
GOTERM_BP_FAT	GO:0042330~taxis	1.03E-05
GOTERM_BP_FAT	GO:0006935~chemotaxis	1.03E-05
GOTERM_BP_FAT	GO:0050900~leukocyte migration	3.79E-04
GOTERM_BP_FAT	GO:0030595~leukocyte chemotaxis	1.42E-03
GOTERM_BP_FAT	GO:0007626~locomotory behavior	1.57E-03
GOTERM_BP_FAT	GO:0060326~cell chemotaxis	1.78E-03
GOTERM_BP_FAT	GO:0007610~behavior	3.92E-03
GOTERM_BP_FAT	GO:0016477~cell migration	4.68E-03
GOTERM_BP_FAT	GO:0006954~inflammatory response	9.94E-03
GOTERM_BP_FAT	GO:0051674~localization of cell	1.39E-02
GOTERM_BP_FAT	GO:0048870~cell motility	1.39E-02
GOTERM_MF_FAT	GO:0005125~cytokine activity	2.19E-02
GOTERM_BP_FAT	GO:0006928~cell motion	3.94E-02
Annotation Cluster 2	Enrichment Score: 2.53	
Category	Term	PValue
GOTERM_BP_FAT	GO:0051240~positive regulation of multicellular organismal process	1.22E-04
KEGG_PATHWAY	mo04623:Cytosolic DNA-sensing pathway	3.58E-04
KEGG_PATHWAY	mo04621:NOD-like receptor signaling pathway	1.12E-03
GOTERM_BP_FAT	GO:0001817~regulation of cytokine production	2.42E-03
GOTERM_BP_FAT	GO:0001819~positive regulation of cytokine production	1.04E-02
GOTERM_BP_FAT	GO:0051046~regulation of secretion	1.61E-02
GOTERM_BP_FAT	GO:0060341~regulation of cellular localization	8.62E-02
Annotation Cluster 3	Enrichment Score: 2.45	
Category	Term	PValue
GOTERM_BP_FAT	GO:0006955~immune response	1.43E-07
GOTERM_BP_FAT	GO:0045321~leukocyte activation	5.50E-07
GOTERM_BP_FAT	GO:0002684~positive regulation of immune system process	1.20E-06
GOTERM_BP_FAT	GO:0001775~cell activation	1.76E-06
GOTERM_BP_FAT	GO:0050870~positive regulation of T cell activation	4.86E-06

GOTERM_BP_FAT	GO:0046649~lymphocyte activation	7.33E-06
GOTERM_BP_FAT	GO:0051094~positive regulation of developmental process	1.62E-05
GOTERM_BP_FAT	GO:0051251~positive regulation of lymphocyte activation	2.52E-05
GOTERM_BP_FAT	GO:0002696~positive regulation of leukocyte activation	4.16E-05
GOTERM_BP_FAT	GO:0050867~positive regulation of cell activation	5.13E-05
GOTERM_BP_FAT	GO:0042110~T cell activation	5.67E-05
GOTERM_BP_FAT	GO:0050863~regulation of T cell activation	5.67E-05
GOTERM_BP_FAT	GO:0051249~regulation of lymphocyte activation	2.27E-04
GOTERM_BP_FAT	GO:0002694~regulation of leukocyte activation	4.14E-04
GOTERM_BP_FAT	GO:0050865~regulation of cell activation	5.19E-04
GOTERM_CC_FAT	GO:0009897~external side of plasma membrane	5.33E-04
GOTERM_BP_FAT	GO:0045582~positive regulation of T cell differentiation	1.10E-03
GOTERM_BP_FAT	GO:0045621~positive regulation of lymphocyte differentiation	1.31E-03
GOTERM_BP_FAT	GO:0030098~lymphocyte differentiation	2.57E-03
GOTERM_BP_FAT	GO:0045580~regulation of T cell differentiation	3.01E-03
GOTERM_BP_FAT	GO:0045597~positive regulation of cell differentiation	4.10E-03
GOTERM_BP_FAT	GO:0045619~regulation of lymphocyte differentiation	4.89E-03
GOTERM_BP_FAT	GO:0045058~T cell selection	5.17E-03
GOTERM_BP_FAT	GO:0002521~leukocyte differentiation	6.65E-03
GOTERM_BP_FAT	GO:0030217~T cell differentiation	7.36E-03
KEGG_PATHWAY	mo05340:Primary immunodeficiency	2.66E-02
GOTERM_BP_FAT	GO:0030097~hemopoiesis	4.76E-02
GOTERM_BP_FAT	GO:0050671~positive regulation of lymphocyte proliferation	4.93E-02
GOTERM_BP_FAT	GO:0032946~positive regulation of mononuclear cell proliferation	5.08E-02
GOTERM_BP_FAT	GO:0070665~positive regulation of leukocyte proliferation	5.39E-02
GOTERM_CC_FAT	GO:0005768~endosome	5.57E-02
GOTERM_BP_FAT	GO:0048534~hemopoietic or lymphoid organ development	6.43E-02
GOTERM_BP_FAT	GO:0002520~immune system development	7.36E-02
GOTERM_BP_FAT	GO:0044093~positive regulation of molecular function	8.52E-02
GOTERM_BP_FAT	GO:0050670~regulation of lymphocyte proliferation	9.88E-02
GOTERM_BP_FAT	GO:0032944~regulation of mononuclear cell proliferation	1.01E-01
GOTERM_BP_FAT	GO:0070663~regulation of leukocyte proliferation	1.05E-01
GOTERM_BP_FAT	GO:0043085~positive regulation of catalytic activity	1.30E-01
SP_PIR_KEYWORDS	immune response	1.47E-01
GOTERM_BP_FAT	GO:0042325~regulation of phosphorylation	2.21E-01
GOTERM_BP_FAT	GO:0051174~regulation of phosphorus metabolic process	2.41E-01
GOTERM_BP_FAT	GO:0019220~regulation of phosphate metabolic process	2.41E-01
GOTERM_BP_FAT	GO:0045860~positive regulation of protein kinase activity	3.21E-01
GOTERM_BP_FAT	GO:0033674~positive regulation of kinase activity	3.39E-01
GOTERM_BP_FAT	GO:0051347~positive regulation of transferase activity	3.58E-01
GOTERM_BP_FAT	GO:0045859~regulation of protein kinase activity	4.90E-01
GOTERM_BP_FAT	GO:0043549~regulation of kinase activity	5.16E-01
GOTERM_BP_FAT	GO:0051338~regulation of transferase activity	5.42E-01

Drug annotation:

Drugs	Experiments	Drug annotation	Literature evidence
carbon tetrachloride	5days; exp7327	affect the central nervous system, degenerate the liver and kidneys	(Reid <i>et al</i> , 1997)
doxapram	3days; exp5223 5days; exp5230	respiratory stimulant (ATC: R07AB01)	
lead(ii) acetate	1days; exp3323 5days; exp3440	causes lead poisoning	
Lipopolysaccharide, <i>E. coli</i> O55:B5	.25days; exp4446 1days; exp7363 1days; exp7617 3days; exp5237 3days; exp5239 3days; exp5347 5days; exp5099 5days; exp5182	endotoxins and elicit strong immune responses	(Moe <i>et al</i> , 2008; Zold <i>et al</i> , 2011)
n-nitrosodimethylamine	5days; exp6945	highly toxicand suspected carcinogen	
pralidoxime chloride	5days; exp6260	against organophosphate poisoning (ATC: V03AB04)	
rofecoxib	1days; exp3088	NSAID (ATC: M01AH02)	

Drug-induced transcriptional module: RatLiver-23

45 genes, 25 experiments

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 3.03	
Category	Term	PValue
GOTERM_BP_FAT	GO:0010557~positive regulation of macromolecule biosynthetic process	3.72E-07
GOTERM_BP_FAT	GO:0031328~positive regulation of cellular biosynthetic process	6.65E-07
GOTERM_BP_FAT	GO:0009891~positive regulation of biosynthetic process	8.06E-07
GOTERM_BP_FAT	GO:0006350~transcription	9.27E-07
SP_PIR_KEYWORDS	dna-binding	1.38E-06
UP_SEQ_FEATURE	domain:Leucine-zipper	2.92E-06
GOTERM_BP_FAT	GO:0045449~regulation of transcription	3.28E-06
GOTERM_BP_FAT	GO:0010604~positive regulation of macromolecule metabolic process	6.59E-06
GOTERM_MF_FAT	GO:0030528~transcription regulator activity	8.53E-06
INTERPRO	IPR004827:Basic-leucine zipper (bZIP) transcription factor	1.64E-05
UP_SEQ_FEATURE	DNA-binding region:Basic motif	1.76E-05
GOTERM_MF_FAT	GO:0003677~DNA binding	1.97E-05
GOTERM_BP_FAT	GO:0010033~response to organic substance	2.18E-05
GOTERM_MF_FAT	GO:0003700~transcription factor activity	3.29E-05
GOTERM_BP_FAT	GO:0045941~positive regulation of transcription	3.86E-05
GOTERM_MF_FAT	GO:0043565~sequence-specific DNA binding	3.92E-05
GOTERM_BP_FAT	GO:0010628~positive regulation of gene expression	4.66E-05
SMART	SM00338:BRLZ	4.79E-05
SP_PIR_KEYWORDS	transcription regulation	6.55E-05
GOTERM_BP_FAT	GO:0006355~regulation of transcription, DNA-dependent	7.20E-05
GOTERM_BP_FAT	GO:0045893~positive regulation of transcription, DNA-dependent	8.44E-05
INTERPRO	IPR011616:bZIP transcription factor, bZIP-1	8.58E-05
KEGG_PATHWAY	mo04010:MAPK signaling pathway	8.71E-05
GOTERM_MF_FAT	GO:0016563~transcription activator activity	8.80E-05
GOTERM_BP_FAT	GO:0051254~positive regulation of RNA metabolic process	8.97E-05
GOTERM_BP_FAT	GO:0051252~regulation of RNA metabolic process	9.26E-05
SP_PIR_KEYWORDS	DNA binding	9.52E-05
GOTERM_BP_FAT	GO:0045935~positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	1.06E-04
SP_PIR_KEYWORDS	Transcription	1.23E-04
GOTERM_MF_FAT	GO:0003690~double-stranded DNA binding	1.28E-04
GOTERM_BP_FAT	GO:0051173~positive regulation of nitrogen compound metabolic process	1.32E-04
SP_PIR_KEYWORDS	nucleus	1.74E-04
GOTERM_MF_FAT	GO:0043566~structure-specific DNA binding	5.57E-04
GOTERM_BP_FAT	GO:0006357~regulation of transcription from RNA polymerase II promoter	5.75E-04
GOTERM_BP_FAT	GO:0006351~transcription, DNA-dependent	1.06E-03
GOTERM_BP_FAT	GO:0032774~RNA biosynthetic process	1.15E-03
GOTERM_BP_FAT	GO:0009612~response to mechanical stimulus	1.92E-03
GOTERM_MF_FAT	GO:0046983~protein dimerization activity	2.44E-03
GOTERM_CC_FAT	GO:0031981~nuclear lumen	2.45E-03
GOTERM_BP_FAT	GO:0006366~transcription from RNA polymerase II promoter	3.60E-03
GOTERM_BP_FAT	GO:0045944~positive regulation of transcription from RNA polymerase II promoter	7.45E-03
GOTERM_BP_FAT	GO:0051726~regulation of cell cycle	7.98E-03
GOTERM_BP_FAT	GO:0009628~response to abiotic stimulus	8.72E-03
GOTERM_CC_FAT	GO:0070013~intracellular organelle lumen	9.29E-03
SP_PIR_KEYWORDS	Proto-oncogene	1.01E-02
GOTERM_CC_FAT	GO:0043233~organelle lumen	1.13E-02
GOTERM_CC_FAT	GO:0031974~membrane-enclosed lumen	1.30E-02
KEGG_PATHWAY	mo05200:Pathways in cancer	1.34E-02
GOTERM_CC_FAT	GO:0005654~nucleoplasm	1.40E-02
GOTERM_BP_FAT	GO:0051591~response to cAMP	1.80E-02
GOTERM_BP_FAT	GO:0031668~cellular response to extracellular stimulus	1.86E-02
GOTERM_MF_FAT	GO:0046982~protein heterodimerization activity	2.23E-02

GOTERM_BP_FAT	GO:0009314~response to radiation	2.34E-02
KEGG_PATHWAY	mo05210:Colorectal cancer	2.45E-02
GOTERM_BP_FAT	GO:0014070~response to organic cyclic substance	3.02E-02
GOTERM_BP_FAT	GO:0034097~response to cytokine stimulus	5.05E-02
GOTERM_CC_FAT	GO:0044451~nucleoplasm part	6.19E-02
GOTERM_BP_FAT	GO:0007611~learning or memory	6.74E-02
GOTERM_CC_FAT	GO:0043232~intracellular non-membrane-bounded organelle	7.98E-02
GOTERM_CC_FAT	GO:0043228~non-membrane-bounded organelle	7.98E-02
GOTERM_CC_FAT	GO:0005730~nucleolus	1.14E-01
GOTERM_CC_FAT	GO:0044427~chromosomal part	1.40E-01
GOTERM_CC_FAT	GO:0005694~chromosome	1.71E-01
GOTERM_BP_FAT	GO:0042493~response to drug	2.85E-01
GOTERM_CC_FAT	GO:0005856~cytoskeleton	3.25E-01
GOTERM_BP_FAT	GO:0007610~behavior	3.99E-01
GOTERM_CC_FAT	GO:0044430~cytoskeletal part	4.42E-01
GOTERM_BP_FAT	GO:0050877~neurological system process	8.68E-01
GOTERM_BP_FAT	GO:0050890~cognition	9.08E-01
Annotation Cluster 2	Enrichment Score: 2.18	
Category	Term	PValue
GOTERM_BP_FAT	GO:0042127~regulation of cell proliferation	1.08E-03
GOTERM_BP_FAT	GO:0009968~negative regulation of signal transduction	3.80E-03
GOTERM_BP_FAT	GO:0010648~negative regulation of cell communication	6.22E-03
GOTERM_BP_FAT	GO:0008285~negative regulation of cell proliferation	1.00E-02
GOTERM_MF_FAT	GO:0008134~transcription factor binding	4.88E-02
Annotation Cluster 3	Enrichment Score: 2.00	
Category	Term	PValue
GOTERM_BP_FAT	GO:0010962~regulation of glucan biosynthetic process	1.67E-03
GOTERM_BP_FAT	GO:0005979~regulation of glycogen biosynthetic process	1.67E-03
GOTERM_BP_FAT	GO:0032885~regulation of polysaccharide biosynthetic process	1.67E-03
GOTERM_BP_FAT	GO:0032881~regulation of polysaccharide metabolic process	2.25E-03
GOTERM_BP_FAT	GO:0043467~regulation of generation of precursor metabolites and energy	4.73E-03
GOTERM_BP_FAT	GO:0043255~regulation of carbohydrate biosynthetic process	4.73E-03
GOTERM_BP_FAT	GO:0010906~regulation of glucose metabolic process	8.42E-03
GOTERM_BP_FAT	GO:0010675~regulation of cellular carbohydrate metabolic process	1.04E-02
GOTERM_BP_FAT	GO:0006109~regulation of carbohydrate metabolic process	1.13E-02
GOTERM_BP_FAT	GO:0031329~regulation of cellular catabolic process	2.02E-02
GOTERM_BP_FAT	GO:0009894~regulation of catabolic process	4.12E-02
GOTERM_CC_FAT	GO:0000267~cell fraction	4.97E-02
KEGG_PATHWAY	mo04910:Insulin signaling pathway	5.97E-02
GOTERM_MF_FAT	GO:0019899~enzyme binding	1.43E-01

Drug annotation:

Drugs	Experiments	Drug annotation	Literature evidence
alfacalcidol	3days; exp6300 5days; exp6297	analogue of vitamin D; effects on parathyroid hormone levels and immune system, including regulatory T cells	(Koike <i>et al.</i> , 2005)
amoxicillin	3days; exp6032	beta-lactam antibiotic (ATC: J01CA04)	
cetaxate	5days; exp5732	cytoprotective effect	
chloroxylenol	3days; exp5394	antimicrobial chemical compound	
clomipramine	3days; exp5101	tricyclic antidepressant (ATC: N06AA04)	
closantel	3days; exp5044 5days; exp5206	Anthelmintic, insecticide (ATCvet: QP54AA51)	
daunorubicin	3days; exp6882	chemotherapeutic (ATC: L01DB02)	
epirubicin	5days; exp6491	anthracycline drug used for chemotherapy (ATC: L01DB03)	
ethanol	.25days; exp2686	psychoactive (ATC: D08AX08)	
flucinolone acetonide	3days; exp6583	corticosteroid (ATC: D07AC04)	
geraniol	5days; exp5105	used in perfumery	

ipriflavone	3days; exp4950	synthetic isoflavone; prevent osteoporosis (ATC: M05BX01)	
isoeugenol	3days; exp5524		
methocarbamol	3days; exp4750	central muscle relaxant (ATC: M03BA03)	
mevastatin	3days; exp5187	statins; HMG-CoA reductase inhibitor (ATC: C10AA01)	
oxfendazole	5days; exp4943	benzimidazole anthelmintic	
prednisolone	5days; exp4945	corticosteroid (ATC: D07AA03)	
sertraline	5days; exp4988	antidepressant of the selective serotonin reuptake inhibitor (ATC: N06AB06)	
streptozotocin	3days; exp5560	antineoplastic agent (ATC: L01AD04)	
tamoxifen	5days; exp6054	estrogen receptor antagonist (ATC: L02BA01)	
tretinoin	5days; exp5328	acid form of vitamin A; treat acne vulgaris and keratosis pilaris; antineoplastic (ATC: L01XX14)	
troglitazone	3days; exp6905	antidiabetic (ATC:A10BG01); peroxisome proliferator-activated receptor activator	
vecuronium bromide	3days; exp6278	muscle relaxant; non-depolarizing blocking agents (ATC: M03AC03)	

Drug-induced transcriptional module: RatLiver-36

88 genes, 37 experiments

Functional enrichment of genes:

Annotation Cluster 1	Enrichment Score: 10.92	
Category	Term	PValue
GOTERM_CC_FAT	GO:0043232~intracellular non-membrane-bounded organelle	1.44E-14
GOTERM_CC_FAT	GO:0043228~non-membrane-bounded organelle	1.44E-14
GOTERM_CC_FAT	GO:0015630~microtubule cytoskeleton	4.30E-13
GOTERM_CC_FAT	GO:0044430~cytoskeletal part	1.17E-08
GOTERM_CC_FAT	GO:0005856~cytoskeleton	2.21E-07
Annotation Cluster 2	Enrichment Score: 10.30	
Category	Term	PValue
GOTERM_BP_FAT	GO:0007049~cell cycle	1.36E-19
GOTERM_BP_FAT	GO:0022402~cell cycle process	2.43E-17
GOTERM_BP_FAT	GO:0022403~cell cycle phase	3.14E-17
GOTERM_BP_FAT	GO:0000279~M phase	2.15E-15
GOTERM_BP_FAT	GO:0000278~mitotic cell cycle	3.06E-11
GOTERM_BP_FAT	GO:0000087~M phase of mitotic cell cycle	4.05E-10
GOTERM_BP_FAT	GO:0051301~cell division	1.10E-08
SP_PIR_KEYWORDS	cell division	1.93E-08
GOTERM_BP_FAT	GO:0000280~nuclear division	1.10E-07
GOTERM_BP_FAT	GO:0007067~mitosis	1.10E-07
SP_PIR_KEYWORDS	cell cycle	1.53E-07
GOTERM_BP_FAT	GO:0048285~organelle fission	1.73E-07
SP_PIR_KEYWORDS	mitosis	5.26E-05
Annotation Cluster 3	Enrichment Score: 7.50	
Category	Term	PValue
GOTERM_CC_FAT	GO:0005694~chromosome	1.44E-13
GOTERM_CC_FAT	GO:0044427~chromosomal part	2.64E-13
GOTERM_CC_FAT	GO:0031981~nuclear lumen	1.77E-07
GOTERM_CC_FAT	GO:0031974~membrane-enclosed lumen	4.26E-06
GOTERM_CC_FAT	GO:0070013~intracellular organelle lumen	6.84E-06
GOTERM_CC_FAT	GO:0043233~organelle lumen	1.15E-05
GOTERM_CC_FAT	GO:0005654~nucleoplasm	1.34E-05

Drug annotation:

Drugs	Experiments	Drug annotation	Literature evidence
1-naphthylisothiocyanate	3days; exp2675	an isothiocyanate derivative of naphthalene	

acetaminophen	3days; exp2915 3days; exp6042	analgesic and antipyretic (ATC: N02BE01)	
allyl alcohol	3days; exp6041		
Anastrozole	1days; exp5123	aromatase-inhibiting drug against breast cancer(ATC: L02BG03)	
Artemisinin	1days; exp4789	antimalarial (ATC: P01BE01)	
benoxaprofen	1days; exp6369	NSAID (ATC: M01AE06)	
beta-Estradiol	1days; exp3134	estrogen receptor agonist (ATC: G03CA03)	PubChem ID:450
Clotrimazole	1days; exp2748 1days; exp3062	antifungal (ATC: D01AC01)	
crotamiton	1days; exp5195	antipruritic and scabicial (ATCvet: QP53AX04)	
cyproterone acetate	1days; exp4628	antiandrogen (ATC: G03HA01)	
diethylstilbestrol	1days; exp2861	inhibit proliferation of human prostate cancer cell lines; nonsteroidal estrogen (ATC: G03CB02)	(Cvek & Dvorak, 2008)
dipyron	1days; exp6092	analgesic and antipyretic (ATC: N02BB02)	
disulfiram	1days; exp4338	treatment of chronic alcoholism; proteasome inhibitor	(Cvek & Dvorak, 2008)
ethinylestradiol	1days; exp2779	a derivative of estradiol (ATC: L02AA03)	
ethylestrenol	1days; exp6370	anabolic steroid with some progesterone-like activity (ATC:A14AB02)	
geraniol	3days; exp5139	used in perfumery	
granisetron	1days; exp4521	serotonin 5-HT3 receptor antagonist (ATC: A04AA02)	
ketoconazole	1days; exp2952	antifungal drug (ATC: D01AC08)	
methapyrilene	1days; exp6099 3days; exp6104	antihistamine and anticholinergic (ATC: R06AC05)	
methimazole	1days; exp4306	antithyroid drug (ATC: H03BB02)	
n,n-dimethylformamide	1days; exp3157 3days; exp3164	linked to cancer and birth defects	
nafenopin	1days; exp6622	hypolipidemic agent	
norethindrone	1days; exp2827	progestogen (ATC: G03AC01)	
pantoprazole	1days; exp5043	proton pump inhibitor (ATC:A02BC02)	
pirinixic acid	1days; exp6031	hypolipidemic, peroxisome proliferator-activated receptor	
praziquantel	1days; exp5428	anthelmintic (ATC: P02BA01)	
pyrogallol	1days; exp5628	antiseptic properties	
rofecoxib	1days; exp6367	NSAID (ATC: M01AH02)	
sildenafil	1days; exp3482	treat erectile dysfunction and pulmonary arterial hypertension (ATC: G04BE03)	
testosterone	1days; exp6361	steroid hormone from the androgen group	
ticlopidine	1days; exp5469	antiplatelet drug (ATC:B01AC05)	
ticrynafen	1days; exp6130	uric acid-lowering (uricosuric) action (ATC: C03CC02)	
vinblastine	3days; exp6136	antimicrotubule drug against certain types of cancer (ATC: L01CA01)	