

Gene symbol	DPS /CON	
	Microarray	RT-qPCR
ANKRD1	217	470 ± 1.6
TGFβ2	17.5	10.7 ± 0.2
GLIPR1	15.3	29.5 ± 0.9
FHL2	5.0	4.4 ± 0.1
GADD45A	4.7	4.2 ± 0.3
SERPINE1	3.4	4.7 ± 4.1
FAM176A	3.0	3.3 ± 0.7

Suppl Data 4A. RT-qPCR validation of microarray data. HI-LAPC-4 cells were treated with DPS under normoxia as in microarray assay (3 μM, 4 hr), and processed for RT-qPCR measurement as described in Suppl Data 11. The primer sequences used are also presented at Suppl Data 11. The table provides the fold-changes of DPS-treated cells over untreated controls, and the corresponding microarray data. The tested genes were in the dataset of DPS/CON (4 hr, Suppl Data 1), and have high- (ANKRD1), medium- (TGFβ2 and GLIPR1), and low- (FHL2, GADD45A, SERPINE1, and FAM176A) fold changes.

Gene symbol	RIGHT PRIMER	LEFT PRIMER
ANKRD1	gcagccttcagaaacgtagg	gaaacaacgagaggcagagc
TGFβ	tgccttctgctcttgtttt	ttgacgtctcagcaatggag
GLIPR1	atctgccaaacaacctgag	agctgcacccaaacttact
FHL2	ctcatagcagggcacacaga	ctcatccaagtgccaggaat
GADD45A	cttcggctcttctgctctcc	gaggaattctcggctgga
SERPINE1	ggatcatgttgctttccagt	gacatcctggaactgccta
FAM176A	gctgctgctctctgtctct	tcctagcggcctattcctt
VEGFα	cacacaggatggcttgaaga	ctacctccaccatgccaagt
HK2	ccacaccactgtcactttg	tagggcttgagagcacctgt
HIF2α	ggaacctgctcttgctgttc	ttgatgtggaaacggatgaa
TBP	ctcatgattaccgcagcaaa	ttcggagagttctgggattg

Suppl Table 4B. qRT-PCR analysis and primers sequences. For qRT-PCR assays, total RNA was treated with DNase I (Invitrogen), and reverse transcribed with Superscript III reverse transcriptase (Invitrogen). The cDNA product was mixed with Power SYBR® Green PCR Master Mix (ABI) and primers of choice in the subsequent qPCR using a 7900HT PCR system (MJ Research). Transcript levels of TATA box binding protein (TBP) were assayed simultaneously with each of the genes selected for validation as an internal control to normalize the transcript levels.

Suppl Data 4C. Ingenuity Pathway Analysis of Biological Functions and Canonical Pathways

	DPS/CON NO			AIO/CON NO			DPS/ATO NO			DPS/CON HO				
	Biological function	p-value	Canonical Pathway	p-value	Biological function	p-value	Canonical Pathway	p-value	Biological function	p-value	Canonical Pathway	p-value		
1	neoplasia	1.39E-30	Hepatic Fibrosis / Hepatic Stellate Cell Activation	3.98E-11	rheumatic disease (Connective Tissue Disorders)	5.61E-15	Hepatic Fibrosis / Hepatic Stellate Cell Activation	1.86E-06	tissue development	5.80E-11	Hepatic Fibrosis / Hepatic Stellate Cell Activation	4.05E-08	Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	1.07E-04
2	tumorigenesis	1.61E-30	LXR/RXR Activation	5.25E-07	rheumatic disease (Inflammatory Disease)	5.61E-15	Gα12/13 Signaling	3.98E-06	development of epithelial tissue	2.69E-09	Human Embryonic Stem Cell Pluripotency	7.55E-07	Hepatic Fibrosis / Hepatic Stellate Cell Activation	3.65E-04
3	tumorigenesis of malignant tumor	8.22E-06	Atherosclerosis Signaling	5.25E-07	rheumatic disease (Skeletal and Muscular Disorders)	5.61E-15	Differential Regulation of Cytokine Production in Macrophages and T Helper Cells by IL-17A and IL-17F	3.31E-05	development of organ	1.09E-07	Glucocorticoid Receptor Signaling	1.07E-05	Axonal Guidance Signaling	1.32E-03
4	tumorigenesis of cells	2.37E-05	Acute Phase Response Signaling	7.76E-06	rheumatoid arthritis (Connective Tissue Disorders)	6.38E-15	Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	5.25E-05	development of endothelial tissue	1.30E-07	Cenamide Signaling	1.29E-06	Airway Pathology in Chronic Obstructive Pulmonary Disease	2.82E-03
5	cancer	7.97E-29	Gα12/13 Signaling	2.34E-05	rheumatoid arthritis (Inflammatory Disease)	6.38E-15	Colorectal Cancer Metastasis Signaling	1.95E-04	endothelial cell development	1.33E-07	Oncostatin M Signaling	3.21E-05	Role of IL-17A in Psoriasis	5.90E-03
6	carcinoma	1.91E-25	Hepatic Cholestasis	1.00E-04	rheumatoid arthritis (Skeletal and Muscular Disorders)	6.38E-15	Role of Hyperyokemia/hypercholesterolemia in the Pathogenesis of Influenza	6.76E-04	development of cardiovascular tissue	3.10E-07	Sphingosine-1-phosphate Signaling	1.85E-04	Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	5.89E-03
7	solid tumor	6.77E-25	VDR/RXR Activation	1.74E-04	rheumatoid arthritis (Immunological Disease)	6.38E-15	Role of Tissue Factor in Cancer	9.12E-04	development of connective tissue	4.60E-07	cAMP-mediated signaling	3.15E-04	IL-6 Signaling	1.41E-02
8	digestive organ tumor	3.98E-15	Glucocorticoid Receptor Signaling	2.09E-04	Athritis (Connective Tissue Disorders)	8.59E-15	Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	9.33E-04	development of gland	1.29E-05	Granzyme A Signaling	5.48E-04	Role of IL-17A in Athritis	1.55E-02
9	metastatic colorectal cancer	5.53E-15	Regulation of Cytokine Production by Macrophages and T Helper Cells by IL-17A and IL-17F	3.98E-04	Athritis (Inflammatory Disease)	8.59E-15	Communication Between Innate and Adaptive Immune Cells	9.77E-04	development of embryonic tissue	1.87E-05	BRK5 Signaling	4.51E-03	IL-17A Signaling in Gastric Cells	1.95E-02
10	genital tumor	1.27E-14	MIF-mediated Glucocorticoid Regulation	4.17E-04	Athritis (Skeletal and Muscular Disorders)	8.59E-15	Atherosclerosis Signaling	1.32E-03	lung development	2.88E-05	Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	5.48E-03	Atherosclerosis Signaling	2.00E-02
11	metastasis	2.11E-14	Communication Between Innate and Adaptive Immune Cells	6.17E-04	autoimmune disease	3.20E-14	Molecular Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-17A and IL-17F	1.74E-03	development of bone	4.02E-05	Aldosterone Signaling in Epithelial Cells	6.53E-03	LXR/RXR Activation	2.14E-02
12	metastasis of tumor	3.37E-06	Pathogenesis of Multiple Sclerosis	6.31E-04	tumorigenesis	4.77E-13	TREML Signaling	2.04E-03	development of uterus	1.30E-04	Coagulation System	1.03E-02	Colorectal Cancer Metastasis Signaling	2.75E-02
13	colorectal tumor	9.55E-14	Coagulation System	6.46E-04	neoplasia	1.18E-12	IL-6 Signaling	3.24E-03	development of endoblast	1.49E-04	Protein Ubiquitination Pathway	1.03E-02	Crosstalk between Bending Cells and Endothelial Cells in Rheumatoid Arthritis	3.09E-02
14	colorectal cancer	2.63E-13	Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	8.31E-04	cancer	2.39E-12	Hepatic Cholestasis	3.24E-03	development of endocrine gland	1.83E-04	HIF1α Signaling	2.93E-06	Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	3.16E-02
15	gastrointestinal tract cancer	3.21E-13	Hypercytokemia/hypercholesterolemia in the Pathogenesis of Influenza	9.55E-04	metastatic colorectal cancer	1.09E-11	Leukocyte Extravasation Signaling	3.39E-03	development of endocrine region of pancreas	2.78E-04	Expression in Activated and Anergic T Lymphocytes	3.23E-05	O-Glycan Biosynthesis	3.39E-02
16	prostate cancer	4.95E-12	MIF Regulation of Innate Immunity	1.20E-03	metastatic colorectal cancer	1.09E-11	Pathogenesis of Multiple Sclerosis	3.80E-03	development of skeletal system	4.29E-04	Protein Kinase A Signaling	5.29E-05	Human Embryonic Stem Cell Pluripotency	3.47E-02
17	adenocarcinoma	3.59E-11	LPSTL-1 Mediated Inhibition of RXR Function	1.78E-03	solid tumor	6.69E-11	LPSTL-1 Mediated Inhibition of RXR Function	4.27E-03	development of muscle	6.41E-04	Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	5.65E-03	Oncostatin M Signaling	4.27E-02
18	breast cancer	4.34E-10	Factors Promoting Carcinogenesis in Vertebrates	1.91E-03	cell death	1.04E-10	Receptor Signaling	5.62E-03	development of ventricular septum	7.80E-04	p38 MAPK Signaling	7.19E-03	Bladder Cancer Signaling	4.79E-02
19	head and neck cancer	1.24E-09	Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	2.00E-03	carcinoma	1.76E-10	PPARα/RXRα Activation	7.08E-03	development of pancreas	9.64E-04	Hypoxia Signaling in the Cardiovascular System	1.03E-02	Hepatic Cholestasis	4.90E-02
20	mammary tumor	1.41E-09	Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	3.09E-03	apoptosis	2.11E-10	LXR/RXR Activation	7.24E-03	development of pericardium	9.66E-04	Neuregulin Signaling	1.03E-02	Thyroid Cancer Signaling	5.25E-02

	Normoxia						Hypoxia	
adjP rank	DPS/CON		ATO/CON		DPS/ATO		DPS/CON	
1	NFAT	$3.7 * e^{-24}$	AACTTT [§]	$2.1 * e^{-18}$	SP1	$5.5 * e^{-21}$	E12	$1.6 * e^{-18}$
2	E12	$6.2 * e^{-21}$	NFAT	$6.3 * e^{-15}$	E12	$1.7 * e^{-20}$	NFAT	$5.2 * e^{-15}$
3	TATA	$4.8 * e^{-20}$	E12	$3.1 * e^{-12}$	AACTTT [§]	$2.2 * e^{-14}$	MYOD	$1.6 * e^{-11}$
4	FOXO4	$2.0 * e^{-19}$	TATA	$6.9 * e^{-12}$	MAZ	$1.2 * e^{-12}$	FOXO4	$3.1 * e^{-11}$
5	AACTTT [§]	$4.1 * e^{-19}$	MAZ	$1.8 * e^{-10}$	NFAT	$1.3 * e^{-10}$	LEF1	$8.2 * e^{-10}$
6	AP1	$7.6 * e^{-15}$	HNF3	$28 * e^{-8}$	LEF1	$4.2 * e^{-10}$	MAZ	$3.8 * e^{-9}$
7	LEF1	$2.9 * e^{-13}$	TTANTCA [§]	$3.7 * e^{-8}$	NF1	$6.4 * e^{-10}$	TATA	$6.4 * e^{-9}$
8	MAZ	$8.9 * e^{-13}$	FOXO4	$4.3 * e^{-8}$	FOXO4	$1.1 * e^{-9}$	MEF2	$9.0 * e^{-9}$
9	FREAC2	$1.8 * e^{-12}$	NF1	$1.1 * e^{-7}$	AP4	$1.3 * e^{-9}$	AML	$7.6 * e^{-9}$
10	AREB6	$1.8 * e^{-9}$	AP1	$1.4 * e^{-7}$	NFY	$3.0 * e^{-9}$	CTGCAGY [§]	$1.3 * e^{-8}$

Suppl Data 4D: The top 10 DPS- or ATO-modified transcription factors obtained from Transcription Factor Enrichment analysis and ordered by adjP (p values by hypergeometric test and adjusted by the multiple test adjustment). §, Entrz genes with unknown ID.

Suppl Data 4E. DPS and ATO Connectivity Map (CMAP) analysis. The analysis was carried out using microarray datasets DPS/CON and ATO/CON (Suppl Data 1) to query established drug gene expression signatures. The table A and B list the top 20 identified molecules with positive or negative correlations/connectivities with DAR or ATO, respectively, ordered by the significance level.

Mean: arithmetic mean of the scores for all the instances in the database; n, number of instances; enrichment, measure of enrichment of those instances related to each agent.

A high positive connectivity score indicated that the corresponding perturbagen induced the expression of the query signature, whereas a high negative connectivity score indicated reversal of expression of the query signature by the perturbagen. A permuted analysis was performed to estimate the likelihood that the enrichment of all instances of each perturbagen in the list would be observed by chance, and a *P* value was derived.

The specificity value is defined as the frequency at which the enrichment of a set of instances equals or exceeds that of the same set of instances in queries executed on published, experimentally derived signatures using the Molecular Signatures Database. Lower values are associated with a greater specificity. The non-null percentage represents a measure of the support for the connection between a set of instances and a signature of interest based on the behavior of the individual instances in that set.

Table A (DPS/CON)

DPS/CON rank	CMAP name	mean	n	enrichment	p	specificity	percent non-null
1	phenoxybenzamine	0.927	4	0.996	0	0.005	100
2	withaferin A	0.804	4	0.982	0	0.0211	100
3	parthenolide	0.699	4	0.957	0	0.024	100
4	semustine	0.691	4	0.945	0	0.017	100
5	15-delta prostaglandin J2	0.548	15	0.615	0	0.1062	86
6	tanespimycin	0.366	62	0.402	0	0.171	62
7	wortmannin	-0.482	18	-0.553	0.00002	0.0637	66
8	azacitidine	0.769	3	0.974	0.00004	0.024	100
9	GW-8510	0.627	4	0.919	0.00004	0.0829	100
10	daunorubicin	0.642	4	0.91	0.00006	0.0354	100
11	MG-262	0.792	3	0.964	0.00008	0.0649	100
12	camptothecin	0.729	3	0.962	0.00008	0.1429	100
13	apigenin	0.663	4	0.908	0.00008	0.0234	100
14	thiostrepton	0.694	4	0.907	0.00008	0.0196	100
15	chrysin	0.628	3	0.946	0.0002	0.0088	100
16	geldanamycin	0.321	15	0.528	0.00026	0.1522	66
17	resveratrol	0.527	9	0.652	0.0003	0.1226	88
18	alvespimycin	0.425	12	0.561	0.0004	0.046	75
19	helveticoside	0.511	6	0.767	0.00042	0.0681	100
20	lanatoside C	0.579	6	0.762	0.00046	0.0872	100

Table B (ATO/CON)

ATO/CON rank	CMAP name	mean	n	enrichment	p	specificity	percent non-null
1	thiamine	- 0.755	3	-0.98	0.00004	0	100
2	monensin	- 0.403	6	-0.786	0.00018	0	50
3	ethotoin	0.257	6	0.762	0.00046	0	50
4	tracazolate	0.395	4	0.84	0.00103	0.0084	50
5	aminophenazone	0.513	5	0.782	0.00104	0	80
6	talampicillin	0.328	4	0.835	0.00113	0	50
7	cefamandole	- 0.471	4	-0.836	0.00127	0	75
8	Prestwick-857	- 0.396	4	-0.822	0.00189	0	75
9	solanine	0.269	4	0.813	0.00237	0.0078	50
10	mestranol	0.519	4	0.804	0.00277	0	75
11	quinpirole	- 0.372	4	-0.803	0.00288	0	50
12	flucytosine	0.488	4	0.801	0.00296	0	75
13	meteneprost	- 0.337	4	-0.795	0.00352	0.0078	50
14	sulfadimidine	0.281	6	0.67	0.00362	0	50
15	amantadine	- 0.266	4	-0.786	0.00422	0.0261	50
16	cefalonium	0.375	3	0.847	0.00681	0.0078	66
17	methazolamide	0.316	4	0.754	0.00704	0	50
18	bumetanide	- 0.271	4	-0.752	0.00758	0.0541	50
19	roxithromycin	0.336	4	0.744	0.00816	0.0152	50
20	11-deoxy-16,16-dimethylprostaglandin E2	0.28	4	0.742	0.00843	0.0245	50