



















Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
IL32		cytokine		0.58	0.00635	BBC3,CXCL1,CXCL3,CXCL8,EIF2AK2,FAS,MCL1,PTGS2	424 (17)
retinoid		chemical drug		0.579	0.00102	CEACAM1,DUSP1,EDN1,HBEGF,LIMA1,MUC2,PLAAT4,PTGS2	478 (24)
miR-145-5p (and other miRNAs w/seed UCCAGUU)		mature microRNA		0.578	0.00578	ACSS2,CCNA2,KLF4,KRT7,PADI1,PARP8,RASA1,RTKN,SWAP70	
TET2		enzyme		0.577	0.0224	ADAM8,BCL3,CEBPA,CYP2S1,GRK5,IFIT3,IFITM3,KCNE3,MAFF,MTSS1,RND3,SH2B3,SORL1	
BHLHE40		transcription regulator		0.577	0.0131	ANXA1,ATP1B1,CRABP2,CXCL3,ECM1,IFITM2,IL1R2,MYB,PHLDA1,PLAC8,RND3,TXK	
PRDX1		enzyme		0.577	0.00387	ECM1,EGLN1,PTGS2,REL	217 (7)
lipoarabinomannan		chemical - endogenous non-mammalian		0.577	0.0241	CXCL2,CXCL8,CXCR4,IRF1	
CNN2		growth factor		0.574	0.0371	CD44,EGR1,FLNB,IGF2,JUN,KITLG,LTBP3,MIA3,SDC4,SOX4	
mir-223		microRNA		0.573	0.0113	ALCAM,CAMKK1,EMP1,GASK1B,ID2,IL1RN,MSMO1,MT1E,MUC13,MYOF,NDRG2,SCARB1,STMN1,TOB1	
NR3C1		ligand-dependent nuclear receptor		0.57	6.41E-15	ISP1,DUSP16,EDN1,EFNA1,EGR1,EMP1,ERN1,ERRF1,F2R,F2RL1,FOS,GAB1,GADD45A,GADD45B,GLCCI1,HGD,HMGCS2,HSPA6,IFIH1,IL15RA,IRF1,ITGB6,JUN,JUND,KLF9,LIF,I	562 (21)
SHH		peptidase		0.57	0.00274	AMD1,ANGPT1,AQP5,BMP4,CAV1,CCNG2,CD25A,DDC,FGF19,GATA2,GLI1,GLI2,IGF2,PPARG,RUNX2,SOSTDC1,TGFB2,TJP1,TSC22D3	463 (22)
fish oils		chemical drug		0.57	0.000131	ACSL1,CEBPA,CPT1A,CYP1A1,CYP2B6,EDN1,NR1P1,NUC2,PIK3R1,PTGS2	362 (10)
Tc7		transcription regulator		0.566	0.0000362	6,ARRDC4,ECM1,FAAH,FYN,ID2,IL15RA,KLF6,LRIG1,MBOAT1,MSMO1,MXD1,NCOA7,NR5A2,NTN4,OSBPL5,PHLDA1,PPARG,RARG,REL,SC5D,SH3BGR2,SOX12,SQLE,TBL1X,T	343 (11)
INSIG1		other		0.566	0.00000547	ACSS2,CD68,CXCL2,CXCL3,CXCR4,ELOVL6,HMGCR,HMGCS2,IDI1,IRS2,LCN2,LIPG,LSS,NFKBIZ,PLD1,PPARG,SCARB1,SQLE,STEAP2	422 (16)
SQSTM1		transcription regulator		0.563	0.000866	CXCL2,CYP2B6,EDN1,HBEGF,IL15RA,IRF1,JUN,MAP1L3B,TSC22D1	
UCLH1		peptidase		0.563	0.0346	CGAS,HDAC9,HERC6,ITPRIP,LPP,PFKM,PSME1,SLC39A8	
WNT3A		cytokine		0.567	9.21E-09	IN2,BBC3,BGN,BMP4,CCN1,CD44,CD68,CEBPA,CYP24A1,DDIT4,DKK1,DVL1,EDN1,ENG,FHL2,GLI1,IRS2,JD2,JUN,KITLG,KLF4,LCN2,MCL1,MT1X,NR5A2,PLD1,PPARG,PTGS2,I	461 (22)
4-nitroquinoline-1-oxide		chemical toxicant		0.555	0.000778	DLRKA,CCNA2,CDK6,EGR1,PTGS2	367 (7)
POMC		other		0.547	0.0263	CXCR4,DUSP1,FOS,FOSL1,IGF2,JUN,PCSK5,REN,SCARB1,SMAD3	
EGFR		kinase		0.539	8.93E-13	F2RL1,FOS,FOSL1,GADD45A,GCNT2,HBEGF,HMGA2,HSPB1,IGF2,IQGAP2,IRF1,ITGB6,JUN,JUND,LAMC2,LCN2,LRP8,MACF1,MCL1,MGAT1,NOX1,NT5E,NUDC,PTGS2,RHOB,RU	530 (22)
plicamycin		chemical drug		0.537	0.00000412	BBC3,CA9,CD25A,CXCL1,FYN,GJB2,GPD1,HMGR,MAOA,MUC2,PAI1,PPP1R1B,ROR1,SEMA7A,SERPINE2,STAR1D,STX1A,TGFB2,UBC,VDR	481 (19)
EHF		transcription regulator		0.535	0.000238	BMP4,CRABP2,CYP1A1,EHF,EREG,GATA2,GRHL3,IL1RN,CLK6,SECL,SERPINA3,SPDEF,TFPI,ZFP36L1	
phenylbutazone		chemical drug		0.532	0.00000528	ABCC2,ANXA1,CD44,CLU,LAMC2,LCN2,LGALS3,PSMB8,PTGS2,RCN1,S100A10,TNFRSF12A,TSPAN8	328 (11)
CDK8		kinase		0.528	0.00295	CD44,CXCL1,CXCL2,CXCL8,CXCR4	368 (11)
ADM		other		0.526	0.0443	CXCL2,EDN1,FOS,PPARG,PTGS2,REN	
CIP2A		other		0.525	0.000893	CDKN2B,GADD45A,PKD4,PDLM7,PTPRB,RHOD,S100A16,SAT1,SERPINE2,SLC16A3,SLC22A18,TUBA4A	349 (8)
deferoxamine		chemical drug		0.508	0.00000102	3A5,DUSP1,DUSP16,DUSP5,ECM1,EGLN1,ERRF1,FOS,GADD45A,GADD45B,GDF15,HSPA1A/HSPA1B,IGFBP2,JAG2,JUN,LCN2,LDHA,MAP1LC3B,ME1,PMAIP1,PPARG,PRKCA,S	452 (18)
TFAP4		transcription regulator		0.508	0.000133	CASP9,CCNG2,CD44,CLDN1,EGR1,ETV1,FOS,GDF15,LIF,STEAP3	368 (7)
AR		ligand-dependent nuclear receptor		0.507	1.56E-12	11,IFIH1,IGF2,KITLG,LAMA5,LRIG1,LRKK1,MAOA,MSMO1,MT1X,MYB,MYO1B,NPC1,NR5A2,PDE9A,PDIA5,PMAIP1,PRKCA,PROS1,PSCA,RARRS1,REN,RHOB,SECL,SEC61B,SE	547 (26)
NR1I2		ligand-dependent nuclear receptor		0.504	0.00000158	10,ABCC2,ALDH1A1,CEBPA,CPT1A,CYP1A1,CYP24A1,CYP2B6,CYP3A5,EGR1,ELOVL6,ENTPD5,FGF19,HMGCS2,HNF4A,INSIG1,JUN,LCN2,MYB,NR0B2,PPARG,SCARB1,TCN2	651 (24)
SP1		transcription regulator		0.494	7.54E-16	3R1,EIF2AK2,ENG,ENTPD5,EREG,F2R,FAS,FOS,FOSL1,FYN,GDF15,HBEGF,HMGCR,HNF4A,IFIH1,IGF2,IRF1,JUN,KLF4,KLF6,LTBP3,MAOA,MOB,MAT2A,MCL1,MUC2,NCOA3,I	537 (20)
EGR2		transcription regulator		0.493	0.00102	ABCC1,ACVR1,ASS1,BCL6,CBL8,EGR1,FOS,HMGCR,ID2,IGF2,IL1R2,JUN,KITLG,LTBP3,MYB,NCPA,SLC16A1,SQLE	476 (20)
KAT2B		transcription regulator		0.491	0.0346	B2M,FOSB,GLI1,HLA-B,PTGS2,TGFB2	
3-methyladenine		chemical toxicant		0.489	0.00221	AGR2,CXCL2,CXCL8,MAP1LC3B,PTGS2,RCAN1,RUNX2	401 (21)
MTPN		transcription regulator		0.487	0.000168	ANXA1,CASP7,CASP9,CCNA2,CEBPA,DDC,EDN1,ENG,FAS,FOS,JUN,S100A10,TGFB2	370 (11)
LGALS1		other		0.481	0.0281	CXCL16,CXCL2,GLI1,GPCPD1,HBEGF,IFNGR2,INSIG1,LGALS3	
HSD17B4		enzyme		0.478	0.000147	ACAA1,ACSL1,GLI1,GLI2,PKK4,PEX11A,PTGS2	481 (7)
Growth hormone		group		0.474	3.42E-09	3PD,CLU,COL18A1,CXCL1,CXCL2,DYRK2,EGR1,FOS,GDF15,IGF2,IGFBP2,IGFBP6,IRF1,JUN,NDRG2,NEED9,NR1D1,PKK4,PLAAT3,PPARG,PPP1R15A,S100A4,SCARB1,SGK1,TE	540 (23)
gemfibrozil		chemical drug		0.472	0.000042	CASP9,CD25A,CPT1A,CXCL8,CXCR4,CYP3A5,EGR1,FAS,FOSL1,MDK,NT5E,PTGS2,SLC28A3	451 (24)
AGT		growth factor		0.471	6.16E-16	1,GLI2,GRK5,HBEGF,HMGR,HSPA1A/HSPA1B,HSPA1L,HSPB1,HSPG2,IDI1,IGFBP2,IRS2,ITPR2,JUN,KITLG,LATS2,LCN2,LGALS3,LIF,LIPG,LOXL4,LPP,LRP8,LSS,LTBP3,LTBP4	635 (23)
IRF2		transcription regulator		0.47	6.47E-10	A13,B2M,CEACAM1,CFTR,CLDN2,CTSS,DST,ITPR2,IRF1,IRF7,KLF4,LCN2,MMP7,PSMB10,PSMB8,PSME1,PSME2,PTGS2,RARRS1,TAP2,TBP3,TR1	293 (18)
daunorubicin		chemical drug		0.464	0.000188	ABCA2,ABCC1,CFTR,DMT1,MCL1,PFKM,TAP2,UQCRFS1	428 (17)
3,4,5,3',4'-pentachlorobiphenyl		chemical toxicant		0.461	0.0232	BMP4,CAPN9,CD44,CYP1A1,GADD45A,HSPA1A/HSPA1B,JUN,NR0B2,TIPARP	
mir-130		microRNA		0.454	0.0333	CD68,HXA5,KLF4,LCN2,PTGS2	
BMP2		growth factor		0.453	0.00345	AOC1,BMP4,DKK1,ETS1,FGFR2,FOS,FOSB,GADD45B,ID2,JUN,KLF4,KLF9,NFYA,PCSK6,PPARG,PTGS2,RUNX2,SOSTDC1,TGM2,TOB1,VDR	544 (25)
AGER		transmembrane receptor		0.45	0.0281	CXCL2,CXCL3,CXCL8,EGR1,FAS,PTGS2,TJP1,TXNIP	
YY1		transcription regulator		0.449	0.000475	P4,CASP7,CCNA2,CDKN2B,CFTR,CLU,CXCR4,CYP24A1,DNAJB4,DNMT3A,EDN1,EGR1,FAS,FOS,GRIN2D,HMGCR,ID2,IL1R2,INCEP,KLF4,MAT2A,NFKBIZ,PPP1R15A,RND3,SC	506 (23)
ibrutinib		chemical drug		0.447	0.00656	CD44,CDK6,FAS,MCL1,UGCG	319 (17)
THRA		ligand-dependent nuclear receptor		0.447	0.00653	BMP4,CD44,CEBPA,CIRBP,CPT1A,CXCL2,CXCL3,ENG,FOS,IRF1,JUN,KLF9,MMP7,PPARG	463 (26)
SELP		transmembrane receptor		0.447	0.0212	CLK1,CXCL2,CXCL8,CXCR4,IL1R2	
SFN		other		0.447	0.0107	BCL6,PKK4,PPP1R1B,SGK1,TJP1	
hymecromone		chemical drug		0.447	0.000763	CASP9,CAV1,CD44,CXCL8,CXCR4,FAS,MCL1	433 (20)
romidepsin		biologic drug		0.44	0.0079	CDKN2B,CXCL8,DUSP1,EGR1,FOS,GSN,JUN,MCL1,PTGS2,RHOB	458 (24)
lenalidomide		chemical drug		0.437	0.000803	V1,CAV2,CD68,CEBPA,DEPP1,DKK1,DVL1,ELF3,ERN1,HIPK2,IFIH1,IFIT3,KLF4,LIMA1,MYB,NFKBIZ,NMI,PPIF,PROS1,RCAN3,REL,RNF213,ROR1,S100A16,SIPA1L2,SMAD3,WNT	465 (13)
FAS		transmembrane receptor		0.431	0.00000225	CXCL2,CXCL3,CXCL8,EFNA1,EGR1,F2RL1,F5,FAS,FOS,FOSB,GRK5,IL15RA,IQGAP2,IRF1,JUN,JUND,LGALS3,MAP4K4,MBOAT7,PDLM7,PLD1,PLD2,PPFBP2,PPP1R15A,RASA1	421 (17)
isobutylmethylxanthine		chemical toxicant		0.429	0.000244	1,ATP5MC1,CAV1,CAV2,CD44,CEBPA,CEBP,CRABP2,CXCR4,DGAT2,DHRS3,EGR1,ELOVL6,FOS,GNPAT,IFIT3,IRF7,JUN,KLF4,LDHA,PKK4,PLAAT3,PPARG,SCARB1,SGK1,ZC	415 (19)
PIM1		kinase		0.426	0.00193	BBC3,CAV2,CD44,CD25A,EPHA2,FOSL1,ID2,PIM1,PROS1	461 (18)
tetrachlorodibenzodioxin		chemical toxicant		0.421	0.0000435	YP2S1,EDN1,FAS,FOS,GLI2,HDAC9,HSPA1A/HSPA1B,IGF2,IRF1,JCAD,JUN,JUND,KCNE3,KRT7,MMP15,MYB,NEED9,NR0B2,PJA1,PRKCA,PTGS2,S100A4,SAT1,SERPINH1,SER	545 (22)
SRA1		transcription regulator		0.418	0.00295	CAV1,PPARG,SLC22A12,TBL1X,TGFB2	331 (13)
MED1		transcription regulator		0.415	0.000104	ACAA1,AOC1,AURKA,BCL3,BCL6,CEBPA,CYP1A1,CYP24A1,CYP2B6,CYP3A5,GADD45A,ID2,KLF4,LIF,MCL1,PKK4,PEX11A,PIM1,PPARG,VDR	456 (21)
PTK2		kinase		0.415	0.0247	BIRC3,CCN1,CSPG4,FOS,LPP,MMP7,TJP1	
WNT1		cytokine		0.406	0.0000266	AXIN2,BMP4,CALB2,CEBPA,DKK1,EDN1,EGR1,FOS,HNF4A,IGF2,JUN,PPARG,PTGS2,RARG,RHO,UNX2,SERPINE2,STRA6,TJP1	498 (24)
gossypol		chemical drug		0.404	7.02E-08	ATF3,CXCL1,CXCL8,MCL1,NCOA3,PMAIP1,SAT1	398 (11)
AFP		transporter		0.404	0.00144	EGR1,FOS,TNFRSF12A,TSC22D1	
BCL2		transporter		0.396	0.00714	ABCC1,BBC3,CXCL1,CXCL8,FAS,FOS,GADD45A,IGFBP6,MCAM,MCL1,TGFB2,VDAC1	487 (21)
1,25-dihydroxyvitamin D		chemical drug		0.396	0.0158	CCNG2,CXCL8,CYP24A1,EGR1,IGF2,REN,VDR	
nicotinic acid		chemical - endogenous mammalian		0.391	0.0299	ANGPT1,CD68,CEACAM1,ELOVL6,SCARB1	
MMP14		peptidase		0.391	0.00485	ATF3,BCAM,CSPG4,DAPK1,PTGS2,SMARCA1	259 (7)
SRSF3		other		0.391	0.000387	CD44,CXCL8,E2F7,HIPK2,JUN	359 (12)
carboplatin		chemical drug		0.389	0.0003	ABCC2,CD44,CLU,ELF3,LAMC2,LCN2,LGALS3,NT5E,PMAIP1,TNFRSF12A	197 (7)
beta-carotene		chemical - endogenous mammalian		0.389	0.0000504	ACSS2,APOL6,ARRDC3,DGAT2,ELOVL6,HSPA1A/HSPA1B,ME1,NR1D1,PPARG,PTGS2,SCARB1	370 (13)
GF11		transcription regulator		0.385	0.000000301	BBC3,BCL3,CARD6,CEBPA,CEP95,CXCL8,CXCR4,EIF2AK2,ETS1,F2R,ID2,IRF1,JUN,MAFF,MMP7,NT5E,REL,SERPINA1,SERPINA3,SGK1,SMAD3,TFF3,TKN2,VDR	453 (17)
paclitaxel		chemical drug		0.382	3.69E-12	(CL2,CXCL8,CYP1A1,CYP3A5,DUSP5,EGR1,EMP1,EPHA2,EREG,ETV1,FAS,FOSL1,GADD45B,GDF15,HBEGF,JUN,JUND,KDM6B,MACF1,MCL1,MUC2,NT5E,PHLDA1,PTGS2,REN,	510 (20)
CDKN1A		kinase		0.382	0.00734	RKA,BBC3,CCN1,CCNA2,CD44,CD25A,CDKN2B,CXCL2,CXCL3,DUSP1,E2F7,FAS,GADD45A,GNAI1,HJURP,HSPA1A/HSPA1B,IFIH1,IFITM3,LGALS3,LGALS3BP,LIMA1,MUC2,STMN1,TC	453 (17)
NLRP12		other		0.381	7.59E-08	BCL3,CXCL2,CXCL8,CXCR4,HLA-B,HLA-C,HLA-E,HLA-J,IL1RN,JUN,MAP3K14,PSMB8	449 (14)
CDH11		other		0.378	0.000319	LAMA5,MMP15,MMP7,PIK3R1,SERPINA1,TJP1,TKN2	290 (7)
ARHGAP31		other		0.378	0.000928	GADD45B,GDF15,ID2,ITGB6,JUN,SERTAD2,TGFB2	
BACH1		transcription regulator		0.378	0.0105	AIFM3,ATP5MC1,ATP5MC3,CXCR4,DUSP1,ME1,PKK4,PPARG	
PAK2		kinase		0.378	0.00221	ASS1,BMP4,CKB,DUSP1,ETS1,GADD45A,HBEGF	477 (18)
SAHM1		chemical reagent		0.378	0.00399	ABLIM1,CD44,DDIT4,DOCK5,PPARG,RHO,TRC1D4	
CCN5		growth factor		0.377	0.0000118	AXIN2,CD44,CEBPA,CLDN1,JUN,KLF4,LAMC2,PPARG,PROCR,SDC4,SMAD3,TFF3,TGFB2	427 (17)
caffeine		chemical drug		0.372	0.00188	CAV1,CD25A,CEBPA,CXCL8,EGR1,FOS,FOSB,PPARG,PRKCA,PTGS2	460 (21)
Hsp27		group		0.371	0.029	CASP9,CXCL8,FBXO32,FOS,PPP1R1B,PTGS2	
BRAF		kinase		0.359	0.00022	CVR1,B3GNT5,BCAM,BIRC3,CASP9,CXCL8,EGR1,GCNT2,HSPG2,LAMC2,MCL1,MSLN,NPC1,NT5E,PSMB10,PSMB8,RND3,SERPINE2,SLC22A5,ST3GAL2,TSC22D1,TSPAN13,UGT	431 (22)
cyclophosphamide		chemical drug		0.342	0.00000258	ATF3,B2M,CD44,CLU,CYP2B6,ELF3,FAS,FOS,HLA-E,IL1R2,KITLG,LAMC2,LGALS3,PSMB8,SLC22A5,TNFRSF12A,TSPAN8,UGCG	523 (21)
CDX1		transcription regulator		0.342	0.00358	CLDN1,CLDN2,CLU,CTSE,DDC,FXDY3,HEPH,PTGS2	
FGF10		growth factor		0.342	0.0174	ANXA1,BMP4,FGFR2,LMO7,LSS,PTGS2,TSPAN8	
conjugated linoleic acid		chemical drug		0.342	0.000134	CEBPA,CXCL8,CXCR4,DUSP1,FOS,GDF15,IL1RN,PPARG,PTGS2	476 (19)
flutamide		chemical drug		0.34	0.00787	CCN1,CXCL2,CYP1A1,CYP3A5,FOS,GPD1,KITLG,ME1,PSCA,REN,SERPINA5	385 (7)
butylated hydroxyanisol		chemical toxicant		0.337	0.0165	FOS,IRF1,IRF7,JUN,NOX1	
EZH2		transcription regulator		0.337	0.0000411	ISPLD2,CXCL1,CXCL2,CXCL8,CXCR4,DKK1,DUSP5,EFNA1,EGR1,EPC1,GATA6,GDF15,KLF4,LAMC2,LATS2,LCN2,MMP7,MYOEV,NCOA7,PARP12,PLAAT4,PPARG,PTGS2,RAP1C	527 (23)
napabucasin		chemical drug		0.333	0.00384	ALCAM,ALDH1A1,B2M,CD44,CXCL8,ENG,FGFR2,KITLG,KLF4	
MAPK11		kinase		0.314	0.0188	CAV1,FAS,FOS,PTGS2,VDR	
fulvestrant		chemical drug		0.313	4.53E-09	NA2,CD25A,CEBP,CLK1,DDIT4,EGR1,F2R,FOS,GAB2,GADD45A,GJB2,ID2,IRF1,JUN,LRP8,MYB,MYO1B,NCOA3,NRP1,PMAIP1,PPARG,PTGS2,RNF126,SAPCD2,SEMA7A,SLC	532 (24)
miR-124-3p (and other miRNAs w/seed AAGGCAC)		mature microRNA		0.313	0.00103	AK2,ARHGAP29,CAV1,CD44,CDK6,CEBPA,EGR1,ENDOD1,ERN1,GSN,ITPRID2,KANK1,KHLH24,NME4,PDLM7,PGM1,RARG,SLC16A1,SLC22A5,SMCO4,SWAP70,TJP2,TRIM29	
buccladesine		chemical toxicant		0.313	4.47E-10	3A5,DUSP1,EGR1,ERRF1,FAAH,FOS,FOSL1,FRRS1,FSTL3,GADD45B,GDF15,HMGCR,IGF2,IGFBP6,IRS2,JUN,KITLG,LIF,LPCAT1,MACROD1,MAT2A,MCAM,NOX1,PTGS2,PTPN2	515 (21)
BIRC3		enzyme		0.311	0.00108	BIRC3,CXCL1,CXCL8,MAP3K14,MCL1,REL	439 (16)
IGF1		growth factor		0.31	1.82E-10	O32,FOS,FOSB,GADD45A,GATA2,GPD1,HMGR,HXA5,ID2,IFITM3,IFNGR2,IGF2,IGFBP2,IGFBP6,IRS2,JD2,JUN,KLF6,KLHL24,CLK6,LCN2,LDHA,MCL1,MDK,MYB,NOX1,PKC2,F	

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TMPRSS2-ERG		fusion gene/product		0.293	3.23E-09	RDC4,BBC3,CALB2,CARD6,CHAC1,DDIT4,DHRS3,DNAJA4,EREG,GDF15,HCAAR1,IFI44,IGFBP6,KLF9,MEGF6,MSLN,MYEOV,PCK2,PHLDA1,PIM1,PPARG,PSPH,ROR1,SAMD9,USF	
TRPV4		ion channel		0.283	0.0319	AQP5,CXCL2,FAS,FOS	
mevalonic acid		chemical - endogenous mammalian		0.279	0.00221	CD55,CYP2B6,GNAI1,HMGCR,PTGS2,SCARB1,SMAD3	438 (15)
PHLPP1	0.446	enzyme		0.277	0.00183	CEBPD,CXCL2,CXCL3,MCL1,PRKCA	471 (24)
BAP1		peptidase		0.277	0.00183	ATF3,CCN1,CXCL2,LATS2,LIF	
AZGP1	-0.672	transporter		0.277	0.0078	AZGP1,BMP4,EGR1,FBXO32,PNPLA2	216 (7)
KRAS		enzyme		0.275	6.87E-25	IF2,IGFBP2,IQGAP2,IRF1,ITGB6,ITM2B,JUN,KLF6,LAMA5,LAMC2,LCN2,LDHA,LGALS3,LIF,LIPG,LMO7,LRP8,LTBP4,MACC1,MAP1LC3B,MCAM,MPMP7,MSLN,MUC20,NOX1,1	470 (25)
INS		other		0.271	0.000135	AMOTL2,CCN1,CPT1A,CRABP2,DUSP1,EDN1,EGR1,ERRF1,FAS,FOS,FOSB,FOSL1,HMGCR,IGFBP2,IRS2,JUN,JUND,PPARG,PTGS2,UGCG	457 (22)
S-nitrosoglutathione		chemical toxicant		0.266	0.0158	BIRC3,IRS2,LIF,PPARG,PTGS2,S100A10	
2-bromoethylamine		chemical reagent		0.266	0.0000195	ABCC2,ANXA1,CD44,CLUJ,ELF3,LAMC2,LCN2,LGALS3,S100A10,TNFRSF12A,TSPAN8	
SPP1		cytokine		0.266	0.0000132	ANGPT1,AURKA,CCL15,CD44,CDC25A,CXCL1,CXCL2,CXCL3,CXCL8,FGFR2,FOS,HMGCR,INSIG1,KRT20,LIF,MMP7,NDRG2,PIK3R1,PPARG,PTGS2,RUNX2,S100A4,SC5D,TGFBF	427 (19)
IL2RG		transmembrane receptor		0.263	0.0051	BCL6,CXXC5,ETS1,FOS,IRF7,JUN,NEDD4L,TKX	451 (23)
phosphate		chemical - endogenous mammalian		0.262	0.00131	ACAT1,AMBP,CYP24A1,DNMT3A,ECM1,EGR1,F2R,FGFR2,FOSL1,LDHA,RUNX2,SDF2L1,ZFHX3	197 (13)
allopurinol		chemical drug		0.261	0.00000115	ABCC2,ANXA1,BIRC3,CD44,CLU,ELF3,LAMC2,LCN2,LGALS3,PSMB8,PTGS2,RCN1,REN,S100A10,TNFRSF12A,TSPAN8,TXNIP	463 (21)
OGA		enzyme		0.258	9.67E-14	5,CXCL16,CXCL8,CYP2B6,DPEP1,DST,EPHB6,FAS,FLNB,GADD45A,GALNT6,GFOD1,GNE,GSN,HIPK2,HIVEP2,HMGCR,HPGD,IFIT3,IFNGR2,IGF2,JD2,JUN,LIF,LRIG1,LSS,MCAM	460 (19)
GATA4		transcription regulator		0.256	0.00019	KN2B,CLDN1,CLDN2,CRABP2,CXCL2,CXCR4,EDN1,FOS,GATA6,GRHL3,HK1,IGFBP6,JUN,KRT7,LCN2,LDHA,NR5A2,OVOL1,PML,PPL,PTGS2,PTPRB,S100A4,SERPINA3,SERPIN	179 (7)
PTAHR		G-protein coupled receptor		0.249	0.0207	CXCL2,CXCL8,MCAM,PTGS2	
PTHLH		other		0.248	0.00215	ANGPT1,CDKN2B,CXCL8,ECM1,FOS,HSPA1A/HSPA1B,PTGS2,RGS2,RUNX2,SMPD3,VDR	419 (24)
SP3		transcription regulator		0.247	0.000000079	AMOTL2,CCN1,SGK1,STMN1,TJP1	503 (18)
1L-6-hydroxymethyl-chiro-inositol 2-(R)-2-O-methyl-3-O-octadecylcarbonate		chemical - kinase inhibitor		0.246	0.000101	CXCL16,GDF15,MT2A,PPARG,PTGS2	427 (17)
EHMT1		transcription regulator		0.243	0.0000249	ACSL1,ALDH2,CEBPD,EFNA1,GFOD1,ITPRIP,LCN2,LOC102724788/PRODH,MSLN,PCSK6,PPL,PRR15L,RARRS1,SAT1,SLC7A7,STRA6,TJP3	
clenbuterol		chemical drug		0.243	0.00106	CXCL1,FBXO32,IL1RN,SLC16A1,VDR	
TCF7L1		transcription regulator		0.243	0.00295	ATF3,AXIN2,JUN,KLF4,NR5A2,PPARG	321 (9)
levodopa		chemical - endogenous mammalian		0.241	0.0000475	HBEGF,IGFBP2,ITPKA,KLF6,KLF9,LAT2,LPP,MAT2A,MEIS2,MPP6,MSMO1,MXD1,MYO1B,MYORG,NEDD4L,NT5E,ONECUT2,PADI2,PGM2L1,PGPEP1,PIK3R1,PITPNM3,PLEKHA2,I	222 (12)
TSC22D3	0.927	transcription regulator		0.239	0.000748	ANXA1,BBC3,CEBPA,CXCL8,DUSP1,PPARG,PTGS2,RUNX2,SGK1	473 (25)
ZBTB17		transcription regulator		0.235	0.0475	CCNA2,CDKN2B,EGR1,JUN,KDM8,PMAIP1,TNFAIP2,ZFP36	
PARP1		enzyme		0.224	0.0392	CASP4,CXCL1,CXCL3,FAS,FOS,GDF15,HRH1,JUN,LGALS3BP,LIF,PTGS2	
MAPK7		kinase		0.22	3.02E-08	ACSS2,CXCL2,CXCL3,CXCL8,DUSP1,EDN1,ELOVL6,IDI1,INSIG1,JUN,KLF4,LSS,MCL1,MSMO1,PTGS2,SQLE,STEAP4,TRAF4	426 (22)
ETS1	0.464	transcription regulator		0.22	0.0000586	BMP4,CAV1,CD44,CDK6,CYP24A1,EGR1,ETS1,FBXL19-AS1,HPGD,HSPA1A/HSPA1B,HSPA1A,HSPA6,IDI2,INSIG1,ITGB6,MCAM,MCL1,MMP7,MYB,PML,REN,RUNX2,SP100,TBXA1	508 (22)
C3AR1		G-protein coupled receptor		0.218	0.0264	CASP4,CD55,CXCL8,DYRK2,TGFB2,TGFB2	
chlorpromazine		chemical drug		0.218	0.0000393	CYP2B6,DEPP1,FOS,HMGCR,IDI1,LSS,MSMO1,SC5D,SERPINA3,SQLE,TSC22D3	
indirubin		chemical drug		0.218	0.0101	BIRC3,CCN1,CYP1A1,JUN	
miR-21-5p (and other miRNAs w/seed AGCUUAAU)		mature microRNA		0.213	0.0208	CDC25A,CDK6,FAS,GLCC1,PIK3R1,PRRG4,TGFB2,TGFB2	
HTT		transcription regulator		0.211	0.0177	31,DNAJC3,DUSP5,EGR1,ETV1,FOS,FOSL1,GRIN2D,GRK5,GSN,HBEGF,HIVEP2,HMGCR,IGF2,JUN,KLF4,KLF9,LDHA,MCAM,MEIS2,NR1D2,PFKM,PPARG,PPP1R1B,PSMB8,PSMI	
miR-204-5p (and other miRNAs w/seed UCCUUUUU)		mature microRNA		0.21	0.0000403	ACVR1,ATP2B1,HMGA2,IDI2,PIK3R1,PPARG,SMAD3,SOX4,SPDEF,STX1A,TGFB2,TRPS1	
ORMDL3		other		0.2	0.00367	ADAM8,CASP9,CXCL8,MAP1LC3B,OAS3	
ROR1	0.776	kinase		0.2	0.0188	AMOTL2,CCN1,SGK1,STMN1,TJP1	
daporinad		chemical drug		0.194	0.000234	ALDH1A1,CD44,FAM111B,LIF,LRIG1,RCAN1,VDR,ZNF488	319 (7)
NGFR		transmembrane receptor		0.192	0.00655	CCNA2,FGFR2,FOS,JUN,NR0B2,RHOB	416 (19)
cyclopamine		chemical reagent		0.187	0.00457	ANGPT1,FAS,GLI1,GLI2,PTGS2,SMPD3,TJP1	332 (10)
ALDH1A2		enzyme		0.186	0.00414	ALDH1A1,ALDH1A3,ATF3,BGN,CCN1,CD44	290 (7)
NR4A2		ligand-dependent nuclear receptor		0.184	0.0265	CXCL8,DDC,ETV1,KITLG,PTGS2,SLC39A8,SMAD3,TSC22D3,TSM	
CNR1		G-protein coupled receptor		0.18	0.0141	BMP4,CA9,CEACAM1,DKK1,DYRK2,ERRF1,FOS,MDK,PLD1,PLSCR1,PTGS2,SCARB1,SMURF1,TJP1	404 (15)
glucocorticoid		chemical drug		0.17	0.0000777	'D,CLIP2,CLU,CXCL1,CXCL2,CXCL8,CXCR4,CYP24A1,CYP2B6,CYP3A5,DUSP1,EDN1,FAS,GABRP,GPR158,IL1R2,IL1RN,LAT2,MAOA,MT2A,PPARG,PTGS2,SERPINA3,SGK1,TGF	404 (19)
MMP2		peptidase		0.168	0.00839	CD44,COL18A1,HMGCR,IL1RN,INSIG1,IRF7,PK4,SCARB1,TJP1	474 (19)
STK11		kinase		0.167	0.0000217	'TP5MC1,ATP5MC3,CAMKK1,CCNA2,CEBPA,CYP2B6,EREG,FGFR2,FOSL1,GADD45A,GADD45B,GALM,GLI1,KLF12,LDHA,MCAM,NEDD9,NR1D1,NT5E,PAPSS1,PCK2,PGM1,PPAF	521 (22)
ERG		transcription regulator		0.166	0.000253	AXIN2,BIRC3,CCNA2,CXCL1,CXCL8,CXCR4,ETS1,F2R,FAM174B,FLNB,FOSB,FYN,HPGD,IRS2,LAMA5,PIM1,PLPPP3,SLC24A1,SOX4,SVIL,TGFB2,TSC22D3,WNT11	457 (18)
panobinostat		chemical drug		0.155	0.013	BBC3,CDK6,CEBPD,MCL1,PMAIP1,PPP1R1B,PTGS2	
budesonide		chemical drug		0.154	0.0000413	CASP9,CXCL2,CXCL8,CYP3A5,FYN,GNA14,GNAI1,JUN,KLF9,NMI,PDLIM1,PRKCA,RAP1GAP,TSC22D3	280 (11)
BCL2L1		other		0.154	0.0138	CD44,CXCL1,CXCL3,CXCL8,ECM1,FAS,MCL1,PRAP1	
GW501516		chemical drug		0.154	0.00491	ACSL1,CPT1A,CYP24A1,GPD1,IGFBP2,IGFBP6,KLK6,LIPG,PK4,PPL,SNCG,SULT2B1	198 (9)
SLC51A		transporter		0.152	0.00144	ABCC2,CYP2B6,CYP3A5,NR0B2	
PMP22		other		0.152	0.00651	CSPG4,FLOT1,HMGCR,JUN	
LATS2	0.349	kinase		0.152	0.0488	ALDH1A3,BBC3,CCN1,CYP24A1,LATS2	
ACSL5		enzyme		0.152	0.00818	ADAMTS6,GPRC5A,MCAM,MDK	
DCAF1		kinase		0.152	0.0363	PIIF,TGM2,TOB1,TXNIP	
let-7a-5p (and other miRNAs w/seed GAGGUAG)		mature microRNA		0.146	0.00613	AGO4,ATAD3B,CDC25A,CDK6,DOCK5,EDN1,HMGA2,CLK10,LOXL4,OTULINL,PTGS2,RHOB,S100A4,SIGMAR1,SNAP23,SPCS3,TGFB2,UGT8	
ABCA1		transporter		0.142	0.00213	ANXA1,CPT1A,CXCL3,DGAT2,HMGCR,PPARG,PTGS2,SCARB1	530 (25)
mir-33		microRNA		0.139	0.000672	CDK6,CEBPA,CPT1A,HMGA2,IRS2,PPARG	79 (4)
CCNC		other		0.131	0.041	CEBPA,FAS,PNPLA2,PPARG	
ADRB		group		0.129	0.0000591	ATF3,BCL10,CASP4,CCNA2,CD68,CDK6,CXCL2,DDIT4,ENDOD1,FAS,FOS,GADD45A,GDF15,IFIT3,INSIG1,JUN,KLF4,LSS,MSMO1,PTGS2,SLCO4A1	496 (23)
PCDH11Y		other		0.128	0.000393	AXIN2,BMP4,CD44,FOSL1,JUN,PTGS2	289 (7)
mir-22		microRNA		0.128	0.0158	CCN1,CLIP2,FOSL1,MALAT1,RGS2,TGFB2	
ATF3	1.18	transcription regulator		0.128	0.000182	ATF3,AURKA,BBC3,BIRC3,CDC25A,CHAC1,CXCL1,CXCL16,GSN,HSPB1,JUN,MT2A,NFKBIZ,PPP1R15A,SRI	511 (20)
ATF6		transcription regulator		0.113	0.00118	AURKA,CPT1A,DAPK1,DNAJC3,FOS,MAP1LC3B,MCL1,NR0B2,NUCB2,RCAN1	428 (17)
CNTF		cytokine		0.105	0.00727	CEBPD,CXCL8,EGR1,FOS,IRF1,LIF,PPP1R1B,SERPINA3,SLC16A1,ZFP36	492 (21)
ANXA2		other		0.104	0.00112	CDK6,FAS,GADD45A,JUN,PTGS2,S100A10,SESN2	452 (20)
Calcineurin protein(s)		complex		0.103	0.000814	AQP5,CBLB,CXCL3,CXCL8,DUSP1,EGR1,FOS,PTGS2,RCAN1,RGS2,RNF128	436 (21)
CYP19A1		enzyme		0.103	0.0279	B3GNT5,CD44,CLCF1,HLA-E,JUN,NR5A2,PPARG,S100A10,SCARB1,STEAP4	
MLX		transcription regulator		0.094	0.000293	ARRDC4,ELOVL6,IGF2,IL1RN,LGALS3BP,TXNIP	
ETV5		transcription regulator		0.093	0.00000287	ALCAM,AQP5,CAV1,CLDN1,CLIC5,CXCR4,KRT13,KRT7,KRT80,LCN2,LGALS3,LMOT,MYB,S100A14,SCARB1,TINAGL1,TJP1,TJP2,TJP3	153 (6)
SLC9A3R1		other		0.092	0.0207	ABCC2,CFTR,S100A4,SCARB1	
rifampin		chemical drug		0.086	1.71E-09	,ALDH1A1,ATP2B1,AXIN2,CEACAM5,CEACAM6,CEP135,CEP70,CYP1A1,CYP24A1,CYP2B6,CYP3A5,ELOVL6,GATA6,MAOB,ME1,MYB,NR0B2,PADI2,PCK2,SLC39A10,TBC1D9,TM	480 (18)
PAX3-FOXO1		fusion gene/product		0.084	0.00509	XA1,ARHGDI8,AURKA,CCN1,CDKN2B,CEP41,CXCR4,DAPK1,DUSP1,FGFR2,FOSL1,GPRC5A,HSPA1A/HSPA1B,IGF2,IGFBP2,MCAM,MT1X,SDCCAG8,SLC16A1,SMAD3,SPHK2,SI	394 (7)
RBPJ		transcription regulator		0.083	0.00139	AXIN2,CD44,DUSP1,ETS1,FOS,GNAI1,IGF2,JUN,KITLG,LIF,MDK,MI2,MUC2,PRKAR2A,REN,SOX4,TGFB2	451 (22)
SOX11		transcription regulator		0.081	0.00141	ADAM9,BMP4,BTNL9,CAV1,CD58,CXCR4,EGR1,FAS,IFIH1,KLK6,LGALS9,MYO1B,PAG1,RUNX2,SKAP2,SMAD3	
cinnamaldehyde		chemical toxicant		0.075	0.00000515	CPT1A,CXCL8,DDIT4,EGR1,FGFR2,FOS,HSPA1A/HSPA1B,INSIG1,JUN,PK4,PNPLA2,PPARG,PPP1R10,PTGS2,SLC2A12,TXNIP	497 (20)
benzyl isothiocyanate		chemical - endogenous non-mammalian		0.07	0.0488	FOS,MCL1,PTGS2,ZBTB10,ZBTB4	
tacrolimus		chemical drug		0.069	0.000637	ABLIM1,ANGPT1,CALB2,CASP7,CEBPA,CXCL2,CXCL8,CXCR4,DAPK1,EDN1,EGR1,ETV1,F5,FOS,FOSB,IL1R2,JUN,MARF1,NRP1,NT5E,PTGS2,RCN1,RUNX2,TJP1,TNFRSF12A	444 (19)
lovastatin		chemical drug		0.066	0.00218	ATF3,CCNA2,COTL1,GNPAT,HMGCR,IRF1,KLF4,LIF,MCL1,MPP6,PTGS2,RHOB,RHOV,SDC4,SMAD3,TFPI	493 (19)
RARA		ligand-dependent nuclear receptor		0.065	9.22E-14	:2F7,EGR1,EIF5A2,FOS,FUT4,GDF15,GLI1,GPR158,HLA-B,HLA-C,HLA-D,HOXA3,HOXA5,IFI44,IGFBP6,IRF1,JUN,KLF4,KRT20,LGALS3BP,MAOB,MUC20,MXD4,NCOA3,NEDD9,NRF	444 (22)
brefeldin A		chemical - endogenous non-mammalian		0.063	0.000185	BBC3,CD44,CXCL3,GADD45B,HLA-B,HLA-C,KLF4,PTGS2,SESN2,SLC38A5	479 (22)
NANOG		transcription regulator		0.061	0.00437	AMER1,CDC25A,CDK6,EGR1,FOS,FOSB,GATA6,GLI1,HSPA1A/HSPA1B,IERSL,KLF4,NRP1,TOB1,ZFHX3	401 (10)
dexamethasone		chemical drug		0.06	3.66E-33	DEPP1,DEXI,DGAT2,DNAJC3,DST,DUSP1,DUSP16,DUSP5,DYRK2,EDN1,EFNA1,EGR1,EHF,ELOVL6,EREG,ERRF1,F2RL1,F5,FBXO32,FLNB,FOS,FOSB,FOSL1,FSTL3,GAB1,GA	559 (23)
CD28		transmembrane receptor		0.058	0.00148	.B,CDK6,CLK1,CXCL2,CXCL8,CXCR4,FOS,FYN,GLI1,HSPA1A/HSPA1B,IGFBP6,IL15RA,IRF1,JUN,LDHA,MSLN,PRDX4,PTGS2,REL,RNF128,SEC61B,SLC16A3,SRPRB,STEAP2,TA	363 (17)
MAP3K7		kinase		0.057	0.000444	BIRC3,CXCL2,CXCL8,IFI44,IFIH1,IFIT3,IRF1,IRF7,JUN,MUC2,PTGS2,RGS2	293 (18)
dextran sulfate		chemical drug		0.051	0.000217	(A,BMP4,CCNA2,CCNF,COL18A1,CXCL2,CXCL3,CXCL8,E2F7,ENG,ERCC8L,FANCF,FIGLN1,HUJRP,IFITM3,IRF7,NOX1,NRP1,PTGS2,REN,SOX12,STEAP3,STMN1,TGFB2,TGFBF	464 (18)
beta-estradiol		chemical - endogenous mammalian		0.035	8.45E-46	ECE2,EDN1,EFNA1,EGR1,ELF3,EMP1,EREG,ERRF1,ETS1,ETV1,F2R,F2RL1,F5,FAAH,FAM182A,FAM3D,FAS,FEZ2,FGFR2,FHL2,FLNB,FLOT1,FOS,FOSB,FOSL1,FRMD4B,FUT8,F	636 (22)
CEBPA	-0.415	transcription regulator		0.028	8.68E-11	CXCR4,CYP2B6,CYP3A5,DGAT2,EEF1A2,FOS,GADD45A,GATA2,GATA6,GLI1,GRHL3,H1-10,HLA-B,HMGCR,HPGD,IDI2,IL1RN,IRS2,JUN,KLF4,KRT7,LCN2,MT2A,NR5A2,NRP1,OV	516 (22)
cyclosporin A		biologic drug		0.027	1.32E-09	XCR4,CYP3A5,DDIT4,DEXI,EDN1,EGR1,ELF3,F5,FAS,FOS,FOSB,FYN,HMGCR,HNF4A,IQGAP2,ITGB6,ITPR2,JUN,LAMC2,LCN2,LGALS3,MARF1,MUC2,PRKCA,PSMB10,PSMB8,P1	503 (19)
MEN1		transcription regulator		0.027	0.00846	CDKN2B,FOS,GLI1,IGFBP2,IRS2,RUNX2,TGFB2	426 (19)
cobalt chloride		chemical reagent		0.021	0.0000147	ABCB10,BBC3,CA9,CLU,COL18A1,CXCL8,CXCR4,CYP1A1,DDIT4,DUSP1,MCL1,PTGS2,SORL1,TJP1,VDAC1	430 (18)
TO-901317		chemical reagent		0.019	0.000017	2,ASS1,CASP4,CASP7,CPT1A,CYP3A5,DDC,ELOVL6,GPD1,HMGCS2,LGALS3,LIPG,MRPS2,NR0B2,NR1D1,NR5A2,PPARG,PSMB8,PSME1,PTGS2,PSXMP2,SCARB1,SERPINA3,SI	497 (22)
miR-29b-3p (and other miRNAs w/seed AGCACCA)		mature microRNA		0.019	0.000119	CAV2,CDK6,DNMT3A,DUSP2,INSIG1,KLF4,LOXL4,MCL1,PIK3R1,TGFB2,TUBB2A,ZFP36L1	
RXRA		ligand-dependent nuclear receptor		0.014	9.54E-11	IA,CRABP2,CTSS,CYP24A1,CYP2B6,CYP3A5,ECM1,ENG,FGF19,FLRT3,FOS,GPD1,HBEGF,HMGCS2,HNF4A,IGFBP6,INSIG1,KLF9,LCN2,MAOB,NEDD9,NR0B2,NR1D1,NR5A2,PCI	571 (27)
medroxyprogesterone acetate		chemical drug		0	3.13E-09	368,CDK6,CDKN2B,CEBPA,CKB,CLDN1,CXCR4,CYP1A1,DKK1,ETS1,F2R,FAS,FLNB,FOSL1,FUT8,FYN,GLI1,GSN,HESE6,IDI2,IFI35,IGF2,IQGAP2,JUN,LGMN,LIF,MAOA,MAOB,MMP	553 (18)
puromycin		chemical - endogenous non-mammalian		0	0.0148	ABCC1,CYP1A1,CYP2B6,CYP3A5	
FKBP4		enzyme		0			



Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
lysophosphatidylcholine		chemical - other		-0.296	0.000488	CXCL1, CXCL8, EGR1, HBEGF, HMGCR, INSIG1, JUN, LSS, MSMO1, PPARG, RGS2, SCARB1, S100A4, SCEL, SDF2L1, SLC16A3, SLC39A8;	418 (19)
Gsk3		group		-0.296	0.00176	BBC3, CEBA, CXCL8, FOS, FOSB, GDF15, HMGCR, JUN, MYB, PPARG, PTGS2	497 (22)
CD38		enzyme		-0.299	0.00000309	ATP1B1, BCL6, CD44, EGN1, IL1R2, LGALS3, LMO7, MYADM, NABP1, NTSE, PDLIM1, PGM1, PIM1, PKIB, PRDX4, RAP1GAP, RBPMS, S100A4, SCEL, SDF2L1, SLC16A3, SLC39A8;	508 (26)
Y 27632		chemical drug		-0.306	0.00115	AMOTL2, BBC3, BMP4, CCN1, CD44, CDKN2B, CEBA, FOS, PPARG, PTGS2, TJP1	496 (20)
berberine		chemical drug		-0.31	0.0015	BIRC3, CASP7, CASP9, CPT1A, CXCL8, CYP1A1, CYP2B6, CYP3A5, HMGCR, MCL1, PPARG, PTGS2, SAT1, SCARB1	481 (23)
BMP7		growth factor		-0.31	0.0000254	ACVR1, BMP4, CAV2, CD44, CEBA, CECPD, CXCL8, DKK1, EDN1, EREG, ID2, IGFBP6, IL1RN, KLF4, PCSK6, PIK3R1, PPARG, RGS2, RUNX2, S100A4, SOSTDC1, WNT11	386 (16)
mir-148		microRNA		-0.312	0.041	ALCAM, EGR1, MMP15, TGFB2	489 (22)
CFTR	-0.375	ion channel		-0.323	0.000215	ACAA1, CFTR, CXCL3, CXCL8, CYP2B6, CYP3A5, FAAH, FAS, HPGD, ID1, NFKBIZ, PTGS2, S100A4, SOSTDC1, WNT11	489 (22)
S100A9		other		-0.325	0.00026	AKAP12, ALDH1A1, ATF3, BACE2, BCL3, CXCL3, CXCL8, DDC, DDIT4, EFNA1, FAS, FOSL1, GJB2, GPRC5A, LOC102724788/PRODH, PHLDA1, PLK3, SEMA3B, SGK1, TXNIP	489 (22)
STAT5A		transcription regulator		-0.328	2.97E-18	IS, FOSB, GADD45A, GASK1B, GRHL3, ID2, IFITM2, IRF1, KRT20, KRT80, LCN2, MCL1, MMP7, MUC13, MUC20, PIM1, PLAAT4, PPARG, PPF1BP2, PRR15L, PSMB8, QPCT, RAB27B, RUNX2, SBT	481 (21)
HIF1		complex		-0.329	0.0109	C9, CCNG2, CXCR4, DDIT4, EDN1, LDHA, SLC16A1, SLC16A3, TFF3	
SOX7		transcription regulator		-0.333	0.0015	CRABP2, EFNA1, ENG, GRHL3, HSPG2, KRT7, OVOL1, PPL, PRKCA, SOX4	
FLT1		kinase		-0.333	0.0202	DEPP1, FOS, HK1, HLA-B, MAT2A, NRP1, SNAP23, TGFB2, VDAC1	
CBFB		transcription regulator		-0.342	0.0302	CEBA, ITGB6, KCNK5, LGALS3BP, LGMN, NRP1, PPARG, RUNX2, TGFB2	
hemin		chemical - endogenous mammalian		-0.342	0.0457	ACO1, AKR1C1/AKR1C2, CD68, CXCL8, HDAC9, JUN, NFYA, PROCR, PTGS2	
RASSF1		other		-0.345	7.38E-12	ALDH1A1, CASP4, CAV1, CAV2, CCNA2, CLU, CRABP2, CXCR4, DKK1, EGR1, EMP1, FOS, FRMD4B, GDF15, GSN, HBEGF, KLF4, LIF, MDK, MTUS1, PROS1, PTGS2, TGM2, TUBB2A	446 (18)
tempol		chemical drug		-0.346	0.00984	BMP4, CXCL2, CXCL8, NOX1, PTGS2, SGK1	415 (24)
Insulin		group		-0.35	0.00000656	T4, DGAT2, DNAJB4, DUSP1, EDN1, EGR1, ELOVL6, ERRF1, FBXO32, FER, FOS, FOSB, HMGCR, HNF4A, IFIT3, IGFBP2, INSIG1, IRF7, IRS2, JUN, KLF4, LDHA, LGALS3BP, MAOA, MAOI	378 (21)
FOXA1		transcription regulator		-0.356	0.00352	AGR2, ANXA1, CD58, CFTR, COL18A1, CXCL8, DDC, DDIT4, HK1, HNF4A, HNF4G, MUC2, NR1P1, S100A2, SPDEF, TFF3, TNFRSF12A	357 (11)
TGFBR2	-0.513	kinase		-0.357	0.0000218	N, CD44, CDKN2B, CLU, CXCL2, DYRK2, GADD45B, GJB2, GLI1, GLI2, HPGD, IL1R2, JUN, MUC2, MYOF, NRP1, PTGS2, RUNX2, SLC12A4, SMAD3, TBXAS1, TGFB2, TGFB2, TNFRSF12A, TXI	470 (18)
ERBB2		kinase		-0.359	4.93E-17	iCR, HSPA1A/HSPA1B, HSPB1, ID2, IDI1, IGFBP2, ITGB6, ITPR2, JAG2, JUN, KLF4, KRT7, LAMC2, LCN2, LDHA, LGALS3, LPCAT1, LSS, LTBP3, MACE1, MAOA, MCL1, MMP7, MSLN, NEDI	344 (22)
FOSB	0.826	transcription regulator		-0.37	0.0000566	CEBA, FOS, FOSB, FOSL1, HPGD, MT2A, PPARG, RUNX2, SMAD3	347 (15)
cigitazone		chemical drug		-0.372	0.000872	CAV1, CAV2, CXCL1, CXCL8, GPD1, GSN, LCN2, MKD1, NOX1, PPARG, PTGS2, SULT2B1	427 (22)
PGR		ligand-dependent nuclear receptor		-0.373	1.22E-16	IST, EDN1, F2RL1, FOS, GPR160, GPRC5A, HBEGF, HPGD, IFI35, IFI44, IFI3, IRF7, IRS2, KLF4, KLF9, MAT2A, MBOAT7, MTS1, NEDD9, NPC1, NQO2, OAS3, PDLIM1, PHF21A, PPARG, PPIF, F	566 (24)
IgG		complex		-0.375	9.03E-11	, CRABP2, CXCL8, DUSP1, EDN1, EGR1, EMP1, FOSB, GPRC5A, GUK1, HLA-E, HSPB1, IFIH1, IFITM3, IL1RN, JUND, KLF6, KRT13, LCN2, LGALS3, PIM1, PPIF, PPL, PPP1R15A, PTGS2, RND3,	507 (22)
HDL-cholesterol		complex		-0.378	0.00189	CHAC1, EGR1, ID1, KHL24, MSMO1, SLC3A1, S100A4, SOSTDC1, WNT11	
PPARδ		ligand-dependent nuclear receptor		-0.382	0.000848	A1, ALDH2, ASS1, CD68, CPT1A, CYP2B6, GPD1, HMGCS2, IGFBP2, IGFBP6, KLF6, LDHA, LGALS4, LIPG, PCSK6, PDK4, PNPLA2, PPARG, PTGS2, RUNX2, SAT1, SORD, TFF3, TNFRSF12A, I	363 (19)
gefitinib		chemical drug		-0.387	0.000476	ALDH1A1, AURKA, CCNF, CECPD, CXCL2, CXCL8, EFN1, FGF2, FOSL1, GADD45B, GLI1, HSPB1, IL1R2, MAFF, MAP4K4, MMP15, PPARG, PTGS2, RHOB, S100A14	459 (23)
KN-62		chemical - kinase inhibitor		-0.396	0.0000232	AQP5, ATF3, CXCL8, CYP3A5, EGR1, HNF4A, PPARG, PPP1R15A, PTGS2	481 (21)
ADCYAP1		other		-0.401	0.0000488	, BCAM, CCNA2, CECPD, CLCF1, CXCL2, CXCL3, DNMT3A, EGR1, EPHA2, FGF2, FOS, FRRS1, GLI1, GRK5, HK1, IRF1, MCAM, PPP1R3B, RHOB, S100A10, SCARB1, SERPINE3, SERPINE2, I	561 (22)
NPPA		other		-0.401	0.0165	DUSP1, EDN1, EGR1, MCL1, PTGS2	
celecoxib		chemical drug		-0.405	0.00353	CD68, CYP3A5, DNAJB9, FAS, FOS, GADD45A, GDF15, MCL1, MUC2, PPARG, PTGS2, ST3GAL4, TGFB2, TRAF4	423 (18)
MYRF		transcription regulator		-0.427	0.00636	AKR1C3, AMOTL2, CEACAM1, GDF15, LOXL4, PARP10, PDK4, RASSF6, RHOU	
NCOR1		transcription regulator		-0.436	0.00000206	AZGP1, BCL3, CCNA2, CEBA, CYP3A5, DUSP1, FXYP3, HK1, ME1, MT1X, NR1D1, PDE9A, PDK4, PPARG, PTGS2, SORD, SPINK1, STEAP2, STK39	492 (20)
miR-291a-3p (and other miRNAs w/sead AAGUGCU)		mature microRNA		-0.438	0.0483	ADAM9, ANKRD13B, CD44, DKK1, GBP3, LATS2, TBC1D2, TGFB2, TRPS1	
interferon alfacon-1		biologic drug		-0.447	0.0268	CXCL8, HIPK2, IL1R2, MAFF, PARP14	
xanthohumol		chemical drug		-0.447	0.00863	ANXA1, BIRC3, DGAT2, FOS, GAB2, RUNX2	193 (7)
SETD2		enzyme		-0.447	0.0268	CAV1, CCN1, ENG, JUN, RHOB	
HOXD10		transcription regulator		-0.447	0.00092	CD44, CEACAM1, DAPP1, HBEGF, MAOB, RAB40B, REN, RHOB, TFF1, TJP1	
EED		transcription regulator		-0.447	0.00457	GATA6, IGFBP2, KLF4, MMP7, PTGS2, RUNX2, SLC26A6	
BGN	-1.301	other		-0.447	0.00919	AXIN2, CXCL3, CXCL8, RUNX2, SMAD3	481 (19)
MED13		transcription regulator		-0.447	0.024	ELOVL6, GPD1, HMGCR, KITLG, LIF, PPARG	
SGK1	-0.361	kinase		-0.447	0.0422	ASIC1, CDK6, CEBA, CFTR, HBEGF, LIF, PPARG	
amiodarone		chemical drug		-0.447	0.0016	AK4, CXCL8, CYP1A1, LSS, ME1, NDRG2, PPARG	
SB 290157		chemical reagent		-0.447	0.00546	BMP4, CASP4, CXCL2, CXCL3, PTGS2	
2-methoxyestradiol		chemical - endogenous mammalian		-0.452	0.00592	ATF3, CAV1, CXCR4, LOC102724788/PRODH, MCL1, PTGS2, SERPINE2	466 (17)
GW3965		chemical reagent		-0.453	0.00243	CAV1, CCNA2, CXCL8, DGAT2, DUSP1, GNAI1, IL1RN, NR1D1, NR5A2, PDK4, PKIB, PPP1R15A, PTGS2, SC5D	506 (24)
genistein		chemical drug		-0.456	0.00000126	CL3, CXCL8, CYP1A1, DKK1, DUSP1, EREG, FOS, GDF15, GJB2, GLI1, HMGCR, HPGD, HSPA1A/HSPA1B, ID2, IRF7, JUN, JUND, LGMN, MAOA, MUC2, MYB, NOX1, NPC1, PIK3R1, PIM1, PKIB, P	591 (20)
ACOX1		enzyme		-0.457	0.00000038	, ER2, ACSL1, CTSE, DPP4, GADD45A, IGFBP2, KLF6, LCN2, LGALS3, LGALS3BP, PDK4, PEX11A, PHLDA1, PLSCR1, PXMP2, QPCT, RGS2, SERPINA1, SGK1, SLC16A1, SLC4A4, TM4SF4, U	180 (7)
spironolactone		chemical drug		-0.458	0.0283	ABCC2, BMP4, CXCR4, CYP3A5, EDN1, LGALS3, PPARG, PTGS2, REN	
EIF4EBP1		transcription regulator		-0.462	0.0000607	BBC3, CEBA, CECPD, EGR1, IL1RN, IRF7, PHLPP1, PNPLA2, PPARG, PTGS2	400 (12)
indole-3-carbinol		chemical drug		-0.462	0.0268	ANXA1, CDK6, CYP3A5, FOS, GDF15	
tributyltin		chemical reagent		-0.463	0.000043	ACSL1, ASS1, ATP5MC1, CEBA, DGAT2, ELOVL6, F2RL1, GPRC5A, IFIT3, IRF7, KRT80, LDHA, PDK4, PPARG, PPL, SLC04A1, SNTB1, WNK4	387 (12)
tanepimycin		chemical drug		-0.473	0.00152	BIRC3, CAV1, CDK6, CDKN2B, CXCL8, DNAJB1, FAS, HMGCR, HRH1, HSPA1A/HSPA1B, JUN, LDHA, MCL1, POLR2L, SERPINH1	503 (22)
resveratrol		chemical drug		-0.475	0.0000678	1A, CXCL2, CXCL3, CXCL8, CYP1A1, DAPK1, EDN1, EGN1, EGR1, FAS, FOS, FOSL1, GDF15, GLI1, HMGCR, IGFBP2, JUN, JUND, KRT20, MALAT1, MCL1, NOX1, NR1P1, PDK4, PPARG, PPP1R15	463 (21)
GSTO1		enzyme		-0.48	0.00000424	CELSR1, CHAC1, FUT8, LAMA5, LMO7, MTUS1, NPDC1, OAS3, PKIB, SAMD9, SAT1, SEMA3A, SFLN5, SOX4, ZFP36L1	
FGFR2	0.626	kinase		-0.489	0.000812	BMP4, DKK1, FAS, FGF2, FLRT3, GASK1B, GATA6, ID2, IGFBP2, NOSTRIN, NR5A2, PLXNB2, RUNX2, SPINK1, TRPS1, TSPAN8	473 (12)
ursodeoxycholic acid		chemical - endogenous mammalian		-0.499	0.00427	ABCC2, CYP1A1, CYP2B6, ELF3, GLI1, LGALS3, PTGS2, TGFB2, VDR	496 (14)
mir-21		microRNA		-0.502	0.013	CARD6, CASP4, CCNA2, CDC25A, CDK6, CDKN2B, CLU, CXCL2, FAS, GBP3, GLCCI1, HMG2, IRF1, NPAS2, OAS3, PRRG4, PSME2, RHOB, SSR1, STMN1, TBC1D1, TGFB2, TRMT10C	
ADORA2A		G-protein coupled receptor		-0.508	0.00839	ATP2B1, CKB, CXCL2, DGAT2, DUSP1, FOS, GLI1, IFITM3, PMPCA, PPP1R1B, PTGS2, TJP1, TSC22D3, TUBB2A	363 (19)
SRC (family)		group		-0.518	0.00454	CYP1A1, EGR1, MAOA, MCL1, NOX1, PTGS2, S100A4, TJP1	464 (19)
caffeic acid phenethyl ester		chemical drug		-0.532	0.00241	ABCB10, BIRC3, CD44, CXCL3, CXCL8, EGR1, HSPB1, IGFBP6, KLF6, MUC2, PLD1, PTGS2, RHOB	441 (18)
ADIPOQ		other		-0.538	0.0124	ACSL1, BCL3, CEBA, CXCL1, CXCL2, CXCL3, CXCL8, DUSP1, EGR1, FOS, GPD1, HBEGF, HMGCS2, HNF4A, PPARG, PTGS2, RUNX2	
glucagon		biologic drug		-0.552	0.0017	ESAM, FOS, IRS2, LIMA1, NDRG2, PPP1R1B, RAP1GAP, SEC81B, TJP2	
DL-fructose		chemical - endogenous mammalian		-0.555	0.0241	BBC3, ELOVL6, GPD1, TXNIP	
SIAH2		transcription regulator		-0.562	0.0000888	AKR1C3, ANGPT1, CYP24A1, EGN1, FXYP3, MT1X, PDE9A, PLK3, STEAP2	422 (11)
CITED2		transcription regulator		-0.562	0.0196	CDKN2B, CXCL1, CXCL8, DUSP1, GATA6, TGM2	
GW7647		chemical drug		-0.57	0.000193	ABCC1, CPT1A, IGFBP2, IGFBP6, NPC1, PDK4, SLC22A5	211 (11)
EIF4EBP2		transcription regulator		-0.572	0.0000823	CEBA, CECPD, EGR1, IL1RN, IRF7, PNPLA2, PPARG, PTGS2	254 (7)
FGF21		growth factor		-0.577	0.000468	CPT1A, DGAT2, EGR1, ERN1, FGF2, FOS, HMGCS2, IRS2, ME1, PDK4	503 (24)
colistin		biologic drug		-0.577	0.00714	ALCAM, BMP4, DNAJB4, FOS, LGALS3, MYO1B, NPNT, NR1P1, SLC04A1, SMAD3, SOX4, TJP1	
BHLHA15		transcription regulator		-0.577	0.00651	ARRDC3, CLU, GJB2, RAB3D	
kanamycin A		chemical drug		-0.577	0.00822	ALCAM, BMP4, DNAJB4, FOS, LGALS3, MYO1B, NPNT, NR1P1, SLC04A1, SMAD3, SOX4, TJP1	
metronidazole		chemical drug		-0.577	0.0115	ALCAM, BMP4, DNAJB4, FOS, LGALS3, MYO1B, NPNT, NR1P1, SLC04A1, SMAD3, SOX4, TJP1	
IGF2BP1		transcription regulator		-0.577	0.00565	AXIN2, CD44, GADD45A, GLI1, IGFBP2, SERPINH1	
SOX9		transcription regulator		-0.581	0.00171	CEACAM5, CXCR4, FOS, MMP15, MUC2, PPARG, PRKCA, RUNX2, S100A4, SMPD3, SOSTDC1, SOX4, WNT11	478 (23)
ATG7		enzyme		-0.584	0.0000868	ACAT1, ACSL1, AGR2, CASP7, CD44, CXCL8, HK1, IFIH1, PDLIM1, RCAN1, S100A4, SCARB1, TGFB2	444 (16)
obeticholic acid		chemical drug		-0.588	0.000399	ABCC2, CD68, CEBA, CXCL2, CXCL3, FGF19, NR0B2, PPARG, PTGS2	541 (18)
KLF15		transcription regulator		-0.589	0.029	ACAT1, ACSL1, DGAT2, PDK4, PPARG, PXMP2	
PTPN1		phosphatase		-0.592	0.00454	CXCL2, CXCL3, DUSP1, DUSP2, IRS2, NOX1, PIK3R1, RASA1	435 (20)
CTNNB1		transcription regulator		-0.6	1.46E-15	IS, FOS, FOSL1, FSTL3, GADD45B, GDM, GATA2, GDF15, GJB2, GLI1, GLI2, HBEGF, HMGCR, HMGCS2, HNF4A, HOXA5, ID2, IDI1, IGFBP2, JUN, KITLG, KRT7, LAMC2, LGALS3, LIF, MAC	561 (20)
CREBZF		transcription regulator		-0.6	0.00183	DNAJB9, ERN1, HSPA1A/HSPA1B, INSIG1, PDK4	
IL4		cytokine		-0.604	1.14E-14	, HPGD, HRH1, HSPA1A/HSPA1B, IFI44, IFIH1, IFIT3, IFITM3, IFNGR2, IL15RA, IL1R2, IL1RN, IMPD1, IRF1, IRF7, JUN, JUND, KDM6B, KITLG, KLF6, LGALS3, LGALS3BP, LIF, LIPG, LMO7, MAC	509 (19)
IKZF3		transcription regulator		-0.607	0.0000438	CAV1, CAV2, CD68, DEPP1, DKK1, IFIT3, IRF7, KLF4, NFKBIZ, PROS1, RNFB2, S100A16, SIPA1L2, SMAD3	
estrogen receptor		group		-0.608	2.07E-11	, CXCL8, CXCR4, CYP1A1, CYP2B6, EDN1, EGR1, EREG, ETS1, FGF2, FOS, HBEGF, HSPA1A/HSPA1B, JUN, KRT7, LAMC2, MMP15, NEDD9, NR1P1, NTSE, PDK4, PMAIP1, PPARG, RGS2, SA	568 (19)
IRS1		enzyme		-0.615	0.00023	ATP2A3, CDKN2B, CEBA, CECPD, CRABP2, EGR1, FBXO32, FOS, HMGCR, ID2, IRS2, KLF4, NRP1, PIK3R1, PLPP3, PPARG, RHOU	476 (21)
WBP2		transcription regulator		-0.621	0.0000293	ADGRF1, AXIN2, BMP4, CASP7, CSPG4, CXCL1, CXCL2, CXCL3, CXCL8, CYP24A1, EGR1, GLCCI1, JDP2, JUN, LIPG, MAPRE3, MBOAT1, PTGS2, SIGMAR1, SLC16A3, SOX4	500 (17)
LRP5		transmembrane receptor		-0.625	0.00485	ALDH1A1, AXIN2, HNF4A, IGFBP2, IRS2, SLC38A5	433 (15)
KLF6	0.654	transcription regulator		-0.628	0.0000139	ATF3, BCL6, CXCL2, CXCL8, CYP1A1, ENG, GLI1, HNF4A, MCL1, MSLN, NR1D1, PMAIP1, PPARG, PTGS2, RARG, SERPINH1	413 (20)
PPARGC1A		transcription regulator		-0.628	0.0000016	I, EGN1, FBXO32, GDF15, HMGCS2, IGFBP6, IL1R2, IL1RN, INSIG1, IRS2, LDHA, MAOB, ME1, MMP15, MSMO1, NR5A2, PCK2, PCSK5, PDIA5, PDK4, PIK3R1, PMAIP1, PNPLA2, PTGS2, RUNX	372 (18)
curcumin		chemical drug		-0.631	0.00000487	CL1, CXCL3, CXCL8, CXCR4, CYP1A1, DAPK1, DNAJB1, EDN1, EGR1, ENTPD5, ETS1, FAS, FER, FOS, FOSB, FOSL1, FYN, HSPA1A/HSPA1B, JUN, JUND, KLF9, MCL1, NE01, PIM1, PNPLA2, I	496 (22)
EFNA5		kinase		-0.632	0.000156	CRABP2, EREG, FOSL1, IRF1, IRF7, ITGB6, KRT13, KRT7, NTSE, PTGS2	253 (7)
niacinamide		chemical - endogenous mammalian		-0.632	0.0117	CCNG2, CXCL8, IRP1, KLF4, MCL1, NFYA, PDK4, PMAIP1, PTGS2, RUNX2	
TAL1		transcription regulator		-0.636	0.000767	AZGP1, BCL6,	

Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
BTK		kinase		-0.68	0.000412	BBC3, CDC25A, CDK6, CEBPA, CXCL3, CXCL8, CXCR4, EMP1, ETS1, IFI35, IFIT3, IRF1, JUN, OAS3, PIM1	424 (19)
glutamine		chemical - endogenous mammalian		-0.682	0.0000429	AKR1C1/AKR1C2, ASS1, CXCL1, CXCL8, DUSP1, FOS, GADD45A, HK1, HSPA1A/HSPA1B, IGF2, IGF2BP2, JUN, KLF4, MCL1, PCK2, PTGS2, SLC16A1, WARS1	492 (24)
mir-9		microRNA		-0.689	0.0319	BCL6, CXCR4, ETS1, MEIS2	
PNPLA2	0.343	enzyme		-0.701	0.00473	ACSL1, CD68, CEBPA, CPT1A, DGAT2, PDK4, PNPLA2, PPARG, SLC16A1	393 (21)
KDM3B		enzyme		-0.707	0.00917	AXIN2, DAPK1, DEGS2, FRMD4B, GATA2, HUIRP, NEDD4L, SORL1, STMN1	
UBE2I		enzyme		-0.707	0.0000566	CEBPA, CEBPD, CPT1A, IRF1, NR0B2, PDK4, PML, PPARG, SGK1	469 (24)
EFNA2		kinase		-0.707	0.00635	CRABP2, FOSL1, FOXL1, IRF7, KRT13, KRT7, NEDD4L, NTSE	
selenomethylselenocysteine		chemical - endogenous mammalian		-0.707	0.0000561	ABCC1, ATP1B3, CLU, CXCL3, CYP3A5, EGR1, JUN, PSME1	170 (7)
CLOCK		transcription regulator		-0.711	0.0000779	:MIP, DNAJB9, ELOVL6, F2R, GADD45A, GADD45B, HES6, HMGC2, HSPH1, LRATD2, MMP7, MSMO1, NPAS2, NR0B2, NR1D1, NR1D2, OAS3, PPIF, RAP2B, SERINC5, ST6GALNAC4, TMED3	
FOS	0.547	transcription regulator		-0.72	4.51E-13	A-B, HPGD, IGF2BP6, IRS2, JUN, KITLG, KLF6, KRT13, LGALS3, LGALS3BP, LGALS4, LRP8, LTBP3, MALAT1, MADA, MAP4K4, MMP7, MSLN, MT2A, MXD1, NR5A2, NRIP1, PAR6B, PHLDA1, PI	477 (20)
CLDN7		other		-0.72	3.87E-11	DIB, ATP5MC1, CD68, CEACAM5, CEACAM6, CXCL8, DKK1, F5, FOSL1, HLA-B, IFI44, LGALS3, LGR4, LIMA1, MT1X, MT2A, MUC13, NCOA7, PLAAT3, SCEL, SOSTDC1, SYTL2, TEAD2, TINAGL	
prednisolone		chemical drug		-0.724	0.0000116	XC3, BTG1, CEBPD, CTSS, CXCR4, CYP1A1, DAPK1, DUSP1, EDN1, FAS, FBXO32, GAB1, GLI1, IRS2, KLF9, MAP1LC3B, MCL1, NQO2, PLAAT4, PTGS2, SGK1, SPHK2, TGM2, TMEM43, TSC22I	442 (19)
T3-TR-RXR		complex		-0.728	0.0142	AKR1C1/AKR1C2, AKR1C3, KLF9, ME1, SCARB1, SLC16A3	
8-bromoguanosine 3',5'-cyclic monophosphate		chemical - kinase inhibitor		-0.73	0.00754	CAV1, CYP3A5, EDN1, FOS, S100A10, SLC12A4	457 (23)
salicylic acid		chemical drug		-0.742	0.0144	BGN, CXCL8, GDF15, KITLG, MCL1, PTGS2, SCARB1	
testosterone		chemical - endogenous mammalian		-0.744	7.14E-09	:DDIT4, DNMT3A, EGR1, FAS, FBXO32, FGFR2, FOS, FOSB, FOSL1, GADD45A, HMGC2, HSPA1A/HSPA1B, IRS2, JUN, JUND, MAOA, MMP7, NR5A2, PIK3R1, PKIB, PPARG, PTGS2	615 (22)
propranolol		chemical drug		-0.749	0.0488	CYP1A1, DUSP1, FOS, MAOA, PTGS2	
ESR1		ligand-dependent nuclear receptor		-0.751	1.16E-21	C2, HLA-B, HLA-C, HLA-E, HLA-J, HMG2A, HMGC2, HSPH1, IFI44, IFITM2, IFITM3, IGF2, IGF2BP2, INCENP, IRF1, IRS2, JUN, JUND, KLHL24, KRT13, KRT7, LATS2, LCN2, LGALS3BP, LI	567 (21)
PI3K (family)		group		-0.752	2.57E-08	AKR1B10, AKR1C1/AKR1C2, BIRC3, CCNG2, CDKN2B, CLDN2, CXCL1, CXCL8, CXCR4, DDIT4, EGLN1, FBXO32, FOS, GLI1, HK1, MCL1, PTGS2, SCARB1, SOX4, TGM2, TJP1, TXNIP	553 (29)
silibinin		chemical drug		-0.756	0.0243	BBC3, CD44, CDK6, CXCL8, EGR1, KLF4, MCL1, PTGS2	
actinomycin D		biologic drug		-0.756	2.46E-12	CAV1, CCN1, CD55, CXCL1, CXCL8, CYP1A1, CYP24A1, DUSP1, ERRF1, ETS1, FAS, FOS, GADD45A, HBEGF, HK1, HMG2A, ID2, IL1R2, IRF1, IRS2, ITPR2, JUN, MAOA, MCL1, MUC2, PMAIP1, I	496 (18)
KDM1A		enzyme		-0.758	0.0000571	I12, CTSS, CXCL16, DAPP1, DKK1, EIF2AK2, FRRS1, ID2, IFI44, IFIT3, IFITM3, IGF2BP2, IL1RN, IQGAP2, IRF7, LATS2, LGALS3BP, MYO1B, ONECUT2, PARP14, PLXNB2, PTPRB, RARG, RHOU	268 (7)
desmopressin		biologic drug		-0.761	0.00623	ESAM, FOS, HSPA1A/HSPA1B, HSPH1, LIMA1, NDRG2, PPP1R1B, RAP1GAP, SEC61B, TJP2, VDCA1	
bisindolylmaleimide iv		chemical - kinase inhibitor		-0.762	0.0279	CXCL8, EGR1, FOS, MUC2	
SB-431542		chemical reagent		-0.767	0.000407	BGN, BMP4, CD44, CYP1A1, FOS, GADD45B, GATA2, GJB2, ID2, IDI1, IL1R2, RUNX2, SQLE, TGF2, TJP1, TNFRSF12A	558 (22)
BRD4		kinase		-0.768	0.0000808	ABLIM1, ALDH1B1, BCL3, BTN3A2, CCNA2, CDC25A, CDKN2B, CEBPA, CXCL2, CXCR4, ETV6, FOS, ID2, IRF1, MCL1, MYB, PIM1, SLC38A5, SORD	486 (19)
TWIST1		transcription regulator		-0.775	0.000205	ALCAM, ALDH1A1, CD44, CELSR1, CLU, CXCL8, ETS1, FAS, FGFR2, FOS, FOSL1, GLI1, GSN, NTSE, RUNX2, S100A4, SLC28A3, TGF2, TGF2R2, ZYX	469 (23)
RNF31		enzyme		-0.777	0.000238	AURKA, CXCL1, CXCL16, CXCL2, CXCL3, CXCL8, CXCR4, IL15RA, IL1R2, IL1RN, NR5A2, SCARB1	437 (13)
MYC		transcription regulator		-0.78	9.33E-16	:HIVEP2, HLA-B, HLA-E, HOXA5, HSPB1, HSPH1, ID2, IFI35, IFI44, IFI11, IFIT3, IQGAP2, IRF7, ITM2B, JAG2, JUN, KDM6B, KLF4, KLF6, KLF6, KRT7, LDHA, LGMN, LIMA1, LOC102724788/PRODH	570 (19)
FGF7		growth factor		-0.787	0.00143	APRT, AQP5, CD44, CEBPA, CEBPD, FGFR2, IRF1, LPCAT1, RUNX2, S100A10, SMAD3	488 (22)
chromium		chemical drug		-0.788	0.00404	AJUBA, ALG2, CXCL8, CYP1A1, ELF3, ENTPD5, PPIF, TNFAIP2	194 (7)
NR1H4		ligand-dependent nuclear receptor		-0.789	0.000103	ABCC2, AMBP, CASP9, CCL15, CEBPA, CYP2B6, CYP3A5, EDN1, FAS, FGF19, HNF4A, KLF4, LCN2, LDHA, NDRG2, NR0B2, NR5A2, PGM1, PPARG, PTGS2, SCARB1, TXNIP	525 (23)
SOCS3		phosphatase		-0.792	0.0385	ATF3, EGR1, FOS, IL1RN, IRF1, IRS2, JUN, MUC2, TFF3	
ESR2		ligand-dependent nuclear receptor		-0.793	3.05E-14	IL1, FGF19, FOS, GADD45B, GYG1, HMG2A, HPGD, IFI35, IFI44, IFI11, IFIT3, IRF7, KLF4, KRT20, LGALS3BP, LOXL4, MAOA, MDK, MSLN, MXD1, NDRG2, NEDD9, NYFA, PARP12, PARP14, PDK	618 (21)
S100A8		other		-0.798	0.000591	AKAP12, ALDH1A1, ATF3, BCL3, CXCL2, CXCL3, CXCL8, DDIT4, EFNA1, FAS, FOSL1, GJB2, GPRC5A, LOC102724788/PRODH, PHLDA1, PLK3, SEMA3B, SGK1, TXNIP	496 (20)
NR1H2		ligand-dependent nuclear receptor		-0.798	0.00143	ABCA2, CXCL16, CXCL2, ELOVL6, GLI1, HK1, HMGC2, IL1RN, IRLP8, PNPLA2, PTGS2, REN, SCARB1	374 (22)
vitamin D		chemical drug		-0.811	0.0291	CCN1, CYP1A1, CYP24A1, GPR158, REN, SGK1, VDR	
12-(3-adamantan-1-yl-ureido) dodecanoic acid		chemical reagent		-0.816	0.00427	BIRC3, CARD6, CASP4, CASP7, CASP9, FAS, MCL1, SPHK2, TRAF4	
selumetinib		chemical drug		-0.816	0.00246	ABCC1, FOS, FOSB, FOSL1, JUN, RUNX2	489 (24)
ZBTB20		transcription regulator		-0.816	0.0409	ACSS2, CYP2B6, CYP3A5, IGF2BP2, NEDD9, PDK4	
MEX3A	0.444	other		-0.816	0.00984	AURKA, CD44, KCNE3, NRP1, PDK4, PPARG	
NEUROG1		transcription regulator		-0.816	0.0393	ASS1, CEMIP, CXCL1, GASK1B, LRIG1, NEO1, S100A4	
HBB		transporter		-0.816	0.0218	CXCL2, CXCL3, CXCL8, GDF15, LIF, SCARB1	403 (16)
evodiamine		chemical - endogenous non-mammalian		-0.816	0.000672	BIRC3, CASP9, CXCL8, CYP1A1, MCL1, PTGS2	
ZBTB16		transcription regulator		-0.819	0.00124	ACER2, BCL6, CCNA2, CD44, CD55, DDC, DHRS3, EIF2AK2, F2R, F2RL1, GALNT6, HPGD, ID2, ME1, NFKBIZ, PIK3R1, PTGS2, RARG, REL, RUNX2, TSC22D1, TSC22D3	
MDM2		transcription regulator		-0.832	0.0248	ATF3, BBC3, CCNA2, CXCL8, ETS1, HIPK2, IGF2BP6, IL1RN, NR0B2	
ritonavir		chemical drug		-0.849	1.19E-09	:AM5, CEACAM6, CEP135, CEP70, CXCL8, CYP1A1, CYP2B6, CYP3A5, HMGC2, IDI1, KITLG, MAOB, ME1, MSMD1, MYB, PAD12, PPARG, SC5D, SLC39A10, SQLE, TMPPRSS4, TRIM31, TSC22F	474 (16)
TRIB3		kinase		-0.853	0.00000468	CDC25A, CEBPA, DDIT4, GDF15, PCK2, PMAIP1, PPARG, PSPH, RUNX2	498 (22)
ERBB3		kinase		-0.863	0.0000447	ADAM9, AMOTL2, BGN, CCN1, CCNG2, CLU, CXCR4, DUSP1, EGR1, HBEGF, HMG2A, IGF2, PTGS2, SERPINA3, SGK1, STMN1, TGM2	443 (19)
CALCA		other		-0.863	0.000212	CD44, CXCL8, CXCR4, CYP24A1, EDN1, ESAM, FOS, LIMA1, NDRG2, PPP1R1B, RAP1GAP, RUNX2, SEC61B, TJP2	452 (24)
GLI2	-1.025	transcription regulator		-0.871	0.0169	BMP4, CLU, CXCL2, CXCL3, GLI1, GLI2, JAG2, PI3, RUNX2, UGCG, VDR	
HLX		transcription regulator		-0.873	0.000928	CD44, CLDN1, CTSS, CXCL8, EGR1, GDF15, JUN	314 (7)
mirdametnib		chemical drug		-0.882	0.0239	CXCL8, DDIT4, ETV1, KLF4, MCL1	
Go6983		chemical - kinase inhibitor		-0.883	0.0000716	CLDN1, FOS, PPARG, PRKCA, PTGS2, SCARB1	449 (21)
fenofibrate		chemical drug		-0.884	0.000787	:ACSL1, CASP4, CD68, CDC25A, CLU, CPT1A, CXCL8, DGAT2, EDN1, FBXO32, GADD45A, GYG1, ID2, JAG2, JUN, PCK2, PDK4, PNPLA2, PTGS2, PTPN21, SC5D, SCARB1, TXNIP, UGT1A10 (i	462 (25)
MYOD1		transcription regulator		-0.892	0.0211	ASS1, BCL6, CYP2S1, DUSP1, EIF2AK2, FOSL1, FYN, GADD45A, HES6, HUIRP, HSPA4L, ID2, IGF2, KLF6, LIF, PFKM, SHCBP1, TEAD2, TJP1, TRIM21	
ARNTL		transcription regulator		-0.896	0.0484	ANGPT1, CCNG2, CEBPA, ELOVL6, HMGC2, NR1D1, TBC1D4	
SMAD7		transcription regulator		-0.898	0.00929	ACVR1, BGN, CCNA2, CDKN2B, CGREF1, FAS, FSTL3, GADD45A, HBEGF, HDAC9, ID2, LTBP3, SMAD3, TGF2, TGFBR2	433 (21)
lomastat		chemical drug		-0.9	0.0241	CXCL3, CXCL8, HBEGF, TJP1	
EPHB4		kinase		-0.905	0.0000512	BMP4, CXCR4, FGFR2, GATA2, IGF2, KITLG, PDLIM7, RASA1, TGF2, TGFBR2, WNT11	
ciprofloxacin		chemical drug		-0.905	0.0203	ACAA1, ADAM8, ALDH2, BMP4, CD68, DNAJC3, LGMN, MYO6, NRP1, PLXNB2, VDCA1	
VIP		other		-0.91	0.0414	CEBPD, CFTR, CLCF1, CXCL2, CXCL3, CXCL8, FOS, IRF1, PTGS2, TJP1	
mir-135		microRNA		-0.911	0.0188	EDN1, KLF4, MCL1, MTSS1, RUNX2	
Wnt		group		-0.927	0.024	CD44, CEBPA, GLI1, ID2, PPARG, RUNX2	
HEXIM1		transcription regulator		-0.927	0.0319	ANGPT1, ANXA1, BBC3, TGF2	
ERBB4		kinase		-0.927	0.000345	ADAM9, CASP4, DUSP1, EGR1, GADD45A, HBEGF, HMG2A, IGF2, JUN, PTGS2, SERPINA3, SERPINE2, TBXAS1	471 (20)
glucosamine		chemical - endogenous mammalian		-0.928	0.00309	ASS1, CEBPA, CXCL1, CXCL3, CXCL8, GPD1, PTGS2, REN, TXNIP	494 (24)
PRNP		other		-0.933	0.00143	ADAM8, CASP9, CD44, DKK1, EGR1, FOSL1, HSPA1A/HSPA1B, HSPB1, ID2, IGF2, PLPP3	469 (22)
NCOA1		transcription regulator		-0.941	0.0141	CASP7, CEBPA, CYP1A1, CYP2B6, EGR1, FGFR2, FOS, GJB2, GYG1, IL1RN, NFKBIZ, NR0B2, PARD6B, PPARG	
clofibrate		chemical drug		-0.942	0.0000927	ACAA1, CEACAM1, CPT1A, CXCL8, CYP1A1, DPP4, FAS, GADD45A, HMGC2, IL1RN, MYB, PEX11A, PTGS2, SULT2B1	340 (21)
Alpha catenin		group		-0.952	0.00000002	ADAM8, AXIN2, BCL3, BGN, BIRC3, CXCL2, DKK1, ENG, EREG, IGF2, IGF2BP2, IGF6, IRF1, NFKBIZ, PTGS2, SGK1, STEAP2, STEAP4, TGM2, TNFAIP2, TNFRSF12A, TSPAN8, ZYX	410 (16)
ERN1	0.515	kinase		-0.952	0.000000137	:EBPD, CXCL2, DGAT2, DNAJB9, DNAJC3, ETS1, FAS, ITGB6, JUN, MAP1LC3B, MCL1, NCOA3, PDIA5, PPARG, PROS1, SDF2L1, SEC24D, SEC61A1, SLC25A28, TINAGL1, TMED3, TXND5C, V	419 (18)
canrenoate potassium		chemical drug		-0.958	0.00818	CD68, EDN1, LGALS3, PTGS2	
NS-398		chemical reagent		-0.96	0.0113	ANGPT1, CXCL8, CXCR4, F2R, GATA6, MCL1, MUC2, PPARG, PSMB8, PTGS2, RUNX2	
miR-141-3p (and other miRNAs w/seed AACACUG)		mature microRNA		-0.963	0.0302	AKR1C1/AKR1C2, CDK6, GADD45A, GRB7, MSLN, PMAIP1, RNF128, TGF2	
MTTP		transporter		-0.97	0.00112	CPT1A, CXCL3, ERN1, HMGC2, JUN, PPARG, RUNX2	182 (7)
WWTR1		transcription regulator		-0.971	0.00000641	CCN1, CCNA2, CD44, CXCL1, CXCL2, CXCL3, CXCL8, EMP1, ID2, LAMA5, LATS2, RUNX2, UCA1	
TG		other		-0.975	0.0165	ANGPT1, CEBPA, CPT1A, IL1R2, PDK4	
CSSL1		growth factor		-0.976	0.0105	BCL6, CYP2B6, CYP3A5, FOS, HNF4A, IRF1, PIK3R1, SERPINH1	
Sch-23390		chemical drug		-0.984	0.000672	EGR1, FAS, FOS, FOSB, FOSL1, PLD2	419 (23)
HDAC1		transcription regulator		-0.986	0.0000314	:IN2, BBC3, BCL6, CCNA2, CD44, CDC25A, CEACAM1, CEACAM6, CEBPA, CXCL1, CXCL8, DUSP1, EGR1, FAS, FOS, GLI1, LCN2, PMAIP1, PPARG, PTGS2, RHOB, RUNX2, SGK1, STX1A, TGF2	473 (20)
pentobarbital		chemical drug		-0.987	0.00387	CYP2B6, FOS, JUN, JUND	478 (20)
PI3K (complex)		complex		-0.99	5.26E-12	:DDIT4, DKK1, DUSP1, ETS1, FBXO32, FOS, FOSL1, GATA2, GLI1, GLI2, HBEGF, HK1, HMGC2, IGF2, IGF2BP2, IL1RN, JUN, LCN2, MCAM, MCL1, MT2A, NOX1, PIM1, PPP1R1B, PTGS2, RGS2, R	488 (21)
PLAG1		transcription regulator		-0.997	0.0051	BTN3A2, CNKSR1, IGF2, QSOX1, S100A2, STX1A, TGM2, TSPAN4	
pregna-4,17-diene-3,16-dione		chemical - endogenous non-mammalian		-1	0.0241	CEBPA, MCL1, PPARG, PTGS2	
AH1		other		-1	0.0363	CCNG2, CMTM7, IL1RN, REPS2	
KDM6A		enzyme		-1	0.0126	ANKS4B, CSPG4, DKK1, HNF4A, TM4SF4, UPK3B	
GAS2L3		other		-1	0.00651	F2R, FAS, LIF, SAT1	
fontolizumab		biologic drug		-1	0.00818	CXCL1, FAS, IFI35, IL15RA	
TRG		other		-1	0.000593	CAV1, CAV2, CXCL1, NTSE	
SEL1L		other		-1	0.0363	COL17A1, DNAJC3, DOCK5, KANK1, NTN4, PRKCA, TGFBR2, UQCRF5, ZFH3	
ASXL1		transcription regulator		-1	0.0158	CLP1, FAM162A, GPCPD1, HOXA5, PELI2, PPARG	
MYT1		transcription regulator		-1	0.00818	ARHGDB, DAPP1, PTPRB, STEAP3	
NKX2-2-AS1		other		-1	0.041	AK4, FAM162A, FAM210A, PDK4	
LMNA		other		-1	0.0005	:4, CCNG2, CEBPA, EDN1, ERN1, FUT4, GATA6, GLIS3, IFI44, IFI11, IRF1, JUN, JUND, MAFF, MCAM, MMP15, MXD4, NPC1, PLD2, PPARG, RESF1, SEMA7A, SKAP2, SLC22A23, ST6GALNAC4,	459 (17)
EFNA1	-0.373	other		-1	0.00012	CLDN2, CRABP2, EPHA2, FOSL1, GATA6, HERC6, IRF7, ITGB6, KRT13, NEDD4L, NTSE, RASA1	255 (7)
Gcg		other		-1	0.00193	ALDH1B1, ASS1, ATP1B1, FOS, ME1, METTL7B, PEX11A, RARRES1, RNASE4	
EMD		other		-1	0.0123	EGR1, HOXA5, IRF1, PPL	
FABP1		transporter		-1	0.0279	FAAH, FGF19, PNPLA2, PPARG	
Z-DEVD-FMK		chemical - protease inhibitor		-1	0.00144		

Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
chelythrine		chemical drug		-1	0.0279	CXCL3,MCL1,NOX1,PIM1	
Immunoglobulin		complex		-1.001	2.96E-09	M210A,FAS,FGFR2,FLNB,FOS,FOSB,GALM,GLI1,HLA-E,HSPA6,IFIT3,IFNGR2,IL1R2,IL1RN,IRF1,IRF7,KLF4,LCN2,LGALS3,LGALS3BP,LOC102724788/PRODH,LTBP3,MAFF,MAP3I	477 (19)
metformin		chemical drug		-1.035	0.000977	ATF3,BCL3,CAV1,CXCL8,CYP2B6,CYP3A5,DDIT4,EGLN1,ERN1,FOS,GADD45B,GPD1,IFI44,IL1RN,INSIG1,NR0B2,PARP14,PFKM,PPP1R3B,PTGS2,RUNX2,SCARB1	411 (22)
PPARA		ligand-dependent nuclear receptor		-1.037	0.00000104	SE,CYP11A1,CYP2B6,EDN1,ELOVL6,FOS,GPD1,HLA-E,HMGC,HMGC52,HNF4A,IDI1,IFITM3,IGFBP2,IGFBP6,IL1RN,INSIG1,LGALS4,LIPG,LSS,MAT2A,MSMO1,NR1D1,PKD4,PEX1	433 (21)
apigenin		chemical - endogenous non-mammalian		-1.039	0.0217	CDK6,CXCL3,CXCL8,CYP1A1,DGAT2,DPP4,DV1L,FOS,PTGS2	
haloperidol		chemical drug		-1.052	0.00377	EGR1,FOS,FOSB,HMGC,HSPG2,PPP1R1B,PRKAR2A,PRKCA,RASA1,SC5D,SIGMAR1	394 (23)
HIC1		transcription regulator		-1.055	0.0291	CYP24A1,EPHA2,FHL2,LCN2,LIF,LRP8,MCAM	
IRF4		transcription regulator		-1.061	0.00216	B2M,BCL6,BIRC3,CD68,CDK6,CTSS,CXCL3,CXCR4,IL15RA,IL1RN,IRF1,IRF7,PLSCR1,PRKCA,PROCR,RHOB,RUNX2,TRIM21,ZFP36L1	467 (17)
UPF2		other		-1.066	0.000012	CLU,KANK1,NEO1,NRP1,PTGS2,PTPN21,RCAN1,TSPAN13,TSPAN8	
FLZ		chemical drug		-1.067	0.00207	DDIT4,FAS,PMAIP1,PTGS2	
harimine		chemical - endogenous non-mammalian		-1.067	0.00287	CYP1A1,FOS,PTGS2,RUNX2	
SLC16A2		transporter		-1.067	0.0368	CIRBP,KLF9,SEMA7A,SLC16A1,SLC16A3	
Mt1		other		-1.067	0.0241	ATF3,CEBPA,FOS,JUN	
Mt2		other		-1.067	0.0148	ATF3,CEBPA,FOS,JUN	
farglitazar		chemical drug		-1.067	0.00095	EDN1,REN,SGK1,SULT2B1	
calyculin A		chemical toxicant		-1.067	0.0363	EGR1,MCL1,PRKCA,TGM2	210 (7)
choline		chemical - endogenous mammalian		-1.067	0.0268	BBC3,DNMT3A,ERRF1,IGF2,PTGS2	
hydroxypropyl-beta-cyclodextrin		chemical drug		-1.067	0.0461	CD68,HMGC,NPC1,SCARB1	
TAF4		transcription regulator		-1.069	0.00232	BCL6,CLDN1,EHF,ETS1,GJB2,HBEFG,IDI,IL1RN,KLF4,MAFF,MAP4K4,MXD1	
paricalcitol		chemical drug		-1.072	0.0406	F2RL1,PTGS2,REN,TFPI,VDR	
TFAP2A		transcription regulator		-1.081	0.0000401	ALCAM,ANXA1,BIRC3,CCND1,CEBPA,CXCL1,CXCL2,EREG,F2R,IGF2,KLF4,MT2A,PAG1,PLAAT3,PPARG,RAB27B	449 (21)
sulforafan		chemical drug		-1.089	0.00203	ABCC2,AKR1B10,AKR1C1,AKR1C2,AKR7A3,ALDH1A1,CD44,CXCL8,DDC,ENTPD5,FAS,FOS,GATA6,GSTA4,HIPK2,PML,PTGS2	506 (22)
KDM2B	-0.33	enzyme		-1.091	0.0368	CDKN2B,CRAP2,FOS,GATA6,LAMA5	
KMT5B		enzyme		-1.091	0.000178	DUSP1,MT2A,SGK1,TSC22D3	
FASN		enzyme		-1.093	0.00636	AJUBA,AMOTL2,CAV1,CXCL8,DDIT4,DGAT2,ELOVL6,PNPLA2,PTGS2	412 (21)
CDK19		kinase		-1.095	1.29E-15	L1,CXCL2,CXCL8,DDIT4,EPHA2,FAS,GADD45A,HBEFG,HSPA4L,JAG2,JUN,LIF,LSS,MXD1,MXD4,PLK3,PPP1R15A,PROCR,RAP2B,SAT1,SEC61A1,TCN2,TRAF4,TSC22D1,TXNIP	
CYP27A1		enzyme		-1.103	0.0207	ABCC2,CYP2B6,CYP3A5,HMGC	
SS18-SSX2		fusion gene/product		-1.103	0.00144	AXIN2,CDC25A,DKK1,MCL1	
parthenolide		chemical drug		-1.118	0.00259	AXIN2,CXCL2,CXCL3,CXCL8,LIF,PKD4,PTGS2	425 (18)
eprenone		chemical drug		-1.119	0.0268	CD68,EDN1,LGALS3,PPARG,PTGS2	
miR-26a-5p (and other miRNAs w/seed UCAAGUA)		mature microRNA		-1.121	0.000503	CDK6,CHORDC1,CXCL3,EPHA2,HSPG2,PTGS2,TGFB2	
sorafenib		chemical drug		-1.123	0.0126	CDK6,CXCL8,ERN1,MCL1,PIM1,PPP1R15A	
CDX2		transcription regulator		-1.127	5.77E-08	AOC1,AXIN2,CAV1,CDHR5,CLDN1,CLDN2,CLU,CTSE,DDC,ETS1,FXYP3,GLI2,HEPH,HNF4A,HOXA3,HOXA5,JUN,KLF4,LAMC2,MTUS1,MUC2,PARD6B,SLC26A6,UGT1A10 (include	471 (24)
PP1		chemical - kinase inhibitor		-1.129	0.000134	ANGPT1,CXCL16,CXCL8,CXCR4,FOS,IL1RN,JUN,PTGS2,TJP1	
manidipine		chemical drug		-1.131	0.000178	CXCL8,FOS,HMGC,JUN	
BDKRB2		G-protein coupled receptor		-1.131	0.00507	CD44,EDN1,PTGS2,REN	
ZNF106		other		-1.134	0.00521	HSPB1,IFITM3,LGALS3,NCMAP,SERPINA3,TNFRSF12A,UGT8	511 (27)
lysophosphatidylinositol		chemical - endogenous mammalian		-1.134	0.00846	CFTR,CPT1A,CXCL3,CXCL8,INSIG1,LDHA,PFKM	
trichloroethylene		chemical toxicant		-1.134	0.0227	CDK6,EGR1,IDI2,PLD1,RHOB,SLC16A1,TXNIP	163 (7)
GPS2		transcription regulator		-1.134	0.0366	CDK6,CXCL8,DHRS3,HIVEP2,RHOB,SGK1,TBC1D2	
benzene		chemical toxicant		-1.134	0.0227	CDK6,EGR1,IDI2,PLD1,RHOB,SLC16A1,TXNIP	
SATB1		transcription regulator		-1.138	0.000559	CEACAM1,DNMT3A,ETS1,F5,FEZ2,FOSB,GADD45B,GDF15,IL1R2,IRF7,KITLG,PTGS2,SGK1,SIPA1L2,SMAD3,TRPS1,TSC22D3,TUBA4A,WARS1	
HNF1A		transcription regulator		-1.143	0.0000212	DC,DPP4,ELF3,FAM107B,FAS,FUT8,FXYP3,GOLT1A,HGD,HHLA2,HMGC,HNF4A,HNF4G,ITM2B,KDM2B,LINC01559,LRRC31,MT1X,MTMR11,NR0B2,NR1D1,NR5A2,RNASE4,RUNX	514 (17)
AGTR1		G-protein coupled receptor		-1.151	0.000731	DUSP1,EDN1,FOS,JUN,PTGS2,REN,SGK1,TXNIP	349 (22)
NR2F2		ligand-dependent nuclear receptor		-1.154	0.00984	ALDH2,ANGPT1,GATA6,HNF4A,NR5A2,NRP1	247 (10)
NPC2		transporter		-1.154	0.0125	AKR1C3,CREB5,MAP1LC3B,PPARG,PTGS2	
honokiol		chemical - endogenous non-mammalian		-1.154	0.0212	CDK6,FOS,MCL1,PPARG,PTGS2	
SOCS1		other		-1.157	0.00392	CD44,CXCL2,CXCL8,DUSP1,FAS,FOS,IFI44,IFIH1,IFIT3,IRF1,IRF7,IRS2,JUN,PTGS2,TGM2	345 (17)
NR4A1		ligand-dependent nuclear receptor		-1.157	0.00017	ATF3,ATP5MC3,AXIN2,CEBPA,CRAP2,DAPK1,EHF,GALM,GPD1,HOCAR1,KITLG,MAT2A,MMP7,NTSE,NUCB2,PCK2,PKD4,PFKM,PGM1,PPARG,SAT1,SMAD3,STARD10,SUCLA2,T	425 (22)
LRP6		transmembrane receptor		-1.165	0.00754	ALDH1A1,AXIN2,CAV1,CD68,DKK1,FOS,MMP7	437 (21)
dimethyl itaconate		chemical reagent		-1.172	0.000319	ATF3,ERN1,IFIT3,IFITM3,IRF1,LCN2,NFKBIZ	
ESRRA		transcription regulator		-1.172	0.000303	ACSL1,CEBPA,CKB,GRB7,GSDMB,HK1,HMGC,IDI1,KRT13,KRT20,LDHA,MAOB,NR0B2,NR1D1,NR1P1,PCK2,PKD4,PPARG,PPP1R1B,RUNX2,WNT11	419 (17)
ANXA1	0.312	enzyme		-1.176	0.00592	ANXA1,COL18A1,CXCL2,CXCL8,CXCR4,PTGS2,TSC22D3	369 (20)
KCNK9		ion channel		-1.195	0.00347	CTSE,GADD45B,LCN2,REN,SLC16A3,SNCG,TM4SF4	
FOSL1	0.522	transcription regulator		-1.197	0.000071	CCN1,CD44,CXCL8,EDN1,EGR1,FOS,FOSB,FOSL1,HPGD,JUN,MT2A,NRP1,RUNX2,SERPINE2	467 (20)
5-N-ethylcarboxamido adenosine		chemical reagent		-1.207	0.0000501	BAG3,BCL3,CDKN2B,CEBPD,CXCL8,DUSP16,EGR1,GADD45A,IFIT3,KLF6,NRP1,NT5E,PROCR,RGS2,TXNIP,UBC,VDR	465 (20)
DACH1		transcription regulator		-1.213	0.000134	BMP4,CDC25A,CXCL3,CXCL8,EGR1,FOS,JUN,KLF4,PTGS2	360 (12)
CDK5		kinase		-1.214	0.0212	CASP9,CXCL2,JUN,PMAIP1,PPP1R1B	
L-histidine		chemical - endogenous mammalian		-1.219	0.00207	ATF3,DDIT4,EGR1,PPP1R15A	417 (16)
IL13		cytokine		-1.256	3.59E-09	CXCL3,CXCL8,CXCR4,EGR1,FAM162A,FAS,FLOT1,FXYP3,GSN,HK1,HRH1,IFNGR2,IL1R2,IL1RN,JUN,KITLG,KLF6,KLK6,MAOA,MCL1,MSMO1,MT1X,MTSS1,MUC2,PAPSS1,PHLD	457 (19)
Esra		transcription regulator		-1.265	0.0115	ACAT1,ACO1,ATP5MC3,CPT1A,GALM,PCK2,PKD4,PGM1,PPP1R1B,PTGS2,REN	
FBXW7		enzyme		-1.267	0.0026	CEBPD,DGAT2,DNAJA1,HMGC,HSPB1,HSPH1,JUN,PPARG,RHOB,SOLE	434 (18)
miR-125b-5p (and other miRNAs w/seed CCCUGAG)		mature microRNA		-1.272	0.0000824	AJUBA,CASP7,CBX7,CCNA2,CD44,CDC25A,CDK6,CYP1A1,GPR160,IDI2,IL1RN,JUN,SH2B3,TSPAN8,VSIR	363 (13)
STAT6		transcription regulator		-1.274	7.37E-13	,GBP3,GNA14,HIPK2,HMGC,HMGC52,HRH1,IFI44,IFIH1,IFIT3,IFITM3,IL1RN,IMPDH1,IRF1,IRF7,IRS2,KDM6B,LGALS3BP,LIF,LMO7,MYB,NCOA3,NEDD9,OAS3,PKD4,PKIB,PLD1,F	525 (19)
mir-155		microRNA		-1.287	0.000894	BCL6,CD68,CEBPA,CLDN1,CXCL8,DNAJB1,DUSP5,EDN1,IFIT3,IRF7,MYB,PPARG,PTGS2	361 (20)
SPARC		other		-1.291	0.000339	AKR1C3,CEBPD,CLDN1,CYP1A1,DV1L,GPD1,LGX4,LRP8,NIPAL1,PAG1,SLC22A5,TMCS,TRIM25,WNK4,ZHX2	
L-triiodothyronine		chemical - endogenous mammalian		-1.299	6.07E-09	A,DNMT3A,DUSP1,DUSP5,DV1L,EDN1,EFNA1,EGR1,ENG,FAS,FOS,FUOM,GDF15,GLI2,GNA14,GPCPD1,IDI2,IGFBP6,KLF9,LCN2,LGALS3,LGALS4,ME1,MSMO1,MYOM3,NR1D1,N	445 (23)
oleic acid		chemical - endogenous mammalian		-1.302	0.0000368	ACSL1,ATF3,BBC3,CD68,CLU,CXCL8,DGAT2,DUSP1,EDN1,EGR1,FOS,GADD45A,GADD45B,GDF15,HMGC,LCN2,PKD4,PNPLA2,PTGS2,REN	446 (20)
SYK		kinase		-1.304	0.000125	AKAP12,BIRC3,CD44,CFTR,CXCL8,CXCR4,EDN1,FOSL1,GADD45A,GLI1,IRF1,PIM1,RASSF6,TSC22D1,TSC22D3,USP53	503 (21)
calphostin C		chemical - kinase inhibitor		-1.318	0.0000223	AXIN2,CDC25A,CLU,CXCL8,DKK1,DUSP1,ETS1,FOS,MAOB,MUC2,PPARG,PTGS2,SCARB1	457 (24)
PTGER4		G-protein coupled receptor		-1.32	3.65E-08	DC3,CCNG2,CD44,CDK6,CXCL8,CXCR4,EDN1,EGR1,GAB1,GLI3,HERC6,IFI35,IFIH1,IRF1,IRF7,MAFF,NOX1,PARP14,PTGS2,RNF213,RNF24,RUNX2,SLFN5,TBC1D4,TRIM21,ZFP	428 (21)
APOE		transporter		-1.321	3.43E-13	A1,CPT1A,CTSS,CXCL3,CYP3A5,ECM1,EDN1,EGR1,F2R,F2RL1,FOS,HMGC,HSPA1A,HSPA1B,HSPG2,IGFBP6,IRF1,JUN,KLF4,LCN2,LIMS2,LIPG,LRP8,MYO1B,NPNT,NQO2,PI	511 (22)
PPARGC1B		transcription regulator		-1.331	0.0243	CKB,FBXO32,GRB7,HMGC,LSS,PKD4,RUNX2,SOLE	
LDLR		transporter		-1.331	0.0000337	AURKA,AXIN2,BGN,CCNA2,CD55,CD68,CEBPA,DUSP1,E2F7,EGR1,ELOVL6,GALM,HMGC,HSPG2,IL1RN,IRF7,LCN2,PCK2,PKIB,PPARG,PPP1R15A,PSME2,RUNX2,SC5D,SCAR	475 (18)
pyrrolidine dithiocarbamate		chemical reagent		-1.333	0.0000281	ANXA1,ASS1,BIRC3,CFTR,CXCL1,CXCL2,CXCL3,CXCL8,CXCR4,IRF1,IRF7,MMP7,NOX1,PLD1,PPARG,PSMB8,PTGS2	411 (17)
4-phenylbutyric acid		chemical - endogenous mammalian		-1.335	0.0053	ATP2A3,CASP9,CXCL8,DNAJB9,ERN1,GSN,MXD1,PADI2,PEX11A,PTGS2,SERPINA1	497 (21)
valproic acid		chemical drug		-1.336	1.85E-09	,EDN1,ELOVL6,ERN1,ETV6,FAS,GADD45B,HMGC52,IDI2,IDI1,IGSF1,JUN,JUND,LIMA1,LRP8,MCL1,MRPS2,MSMO1,MYOF,NFYA,NR0B2,OSBPL5,P3H2,PKIB,PNPLA2,PPARG,PSM	593 (23)
EP400		other		-1.342	0.0158	CCNA2,CCNF,CDC25A,E2F7,INCEP,PPARG	
NFIL3		transcription regulator		-1.342	0.0125	FAS,GADD45A,GADD45B,IDI2,PTGS2	
STS		enzyme		-1.342	0.000622	CD68,CEBPD,EEF1A2,HSPA1A,HSPA1B,IGFBP2,PNPLA2,PPARG	
DUSP5	0.488	phosphatase		-1.342	0.00234	ALDH1A3,DUSP2,EGR1,IDI2,ZFP36	
JAK inhibitor 1		chemical - kinase inhibitor		-1.342	0.0107	CXCL1,CXCL2,CXCL3,PTGS2,SGK1	
FUS-DDIT3		fusion gene/product		-1.342	0.00655	CXCL8,IGFBP6,LCN2,NPAS2,STX1A,TSC22D3	
immethridine		chemical reagent		-1.342	0.0078	CD44,CTSS,CXCL3,LCN2,SERPINA3	
SP2509		chemical reagent		-1.344	0.000723	,CDK6,CRAP2,DHRS3,DNMT3A,EIF2AK2,ELOVL6,FLRT3,FRY1,GATA6,GLI2,HMGA2,IGSF9,INPP1,KLF4,MAP4K4,MICALL2,MYO1B,NPNT,PPP2R5B,SGK1,SMAD3,SOX12,SRI,S	517 (22)
HNF4A	-0.821	transcription regulator		-1.346	1.32E-11	5,GJB2,GPR160,GRHL3,GRIN2D,GSN,GSTA4,GYG1,HBEFG,HGD,HHLA2,HLA-B,HLA-C,HNF4A,HNF4G,HSPA4L,HSPH1,IFITM2,INCEP,IPPRID2,JUN,KDM8,KRT7,LCN2,LDHA,LG	489 (23)
triptolide		chemical drug		-1.355	3.29E-08	AKAP12,BBC3,CAV1,CDKN2B,CXCL1,CXCL8,DPP4,DUSP1,EFNA1,EMP1,ENG,F2RL1,FAS,HBEFG,HPGD,IGFBP2,JUN,KITLG,MCAM,MCL1,MMP7,PMAIP1,PTGS2,SOX4,TJP1	489 (23)
PTGER2		G-protein coupled receptor		-1.373	0.013	AURKA,CCNA2,CKAP2L,CXCL8,CXCR4,ECM1,EGR1,IL1R2,PIM1,PTGS2,TBL3	
TAB1		enzyme		-1.385	0.00015	BIRC3,CXCL8,IFIH1,IRF7,JUN,MCL1,PTGS2,RGS2	448 (23)
CBL		transcription regulator		-1.387	0.019	CDKN2B,CFTR,CXCL2,CXCL3,FGFR2,FOS,RUNX2	
PD 153035		chemical drug		-1.399	0.000393	CXCL8,FOS,KRT13,KRT20,MCL1,PTGS2	433 (20)
TMBIM6		other		-1.412	0.0123	DNAJB9,ERN1,MAP1LC3B,SEC61A1	
EFNA4		kinase		-1.414	0.000865	CRABP2,FOSL1,IRF1,IRF7,ITGB6,KRT13,KRT7,NT5E	
RHO		G-protein coupled receptor		-1.414	0.00309	B2M,CASP7,CD44,CEBPD,CTSS,FOS,IMPDH1,NT5E,SGK1	319 (7)
EFNA3		kinase		-1.414	0.00102	CRABP2,FOSL1,IRF1,IRF7,ITGB6,KRT13,KRT7,NT5E	
methylmercury		chemical toxicant		-1.414	0.015	CDK6,CYP1A1,EGR1,IDI2,PLD1,RHOB,SLC16A1,TXNIP	
epigallocatechin-gallate		chemical drug		-1.417	0.0000268	1,CASP9,CCN1,CEBPA,COL18A1,CXCL1,CXCL3,CXCL8,EDN1,EGR1,FAS,FGF19,FOS,FOSB,FOSL1,GADD45A,GADD45B,GBP3,GJB2,GLI1,IRF1,JUN,JUND,PRKCA,PTGS2,REL,SI	453 (22)
rosiglitazone		chemical drug		-1.429	2.99E-11	3,EDN1,EGLN1,ELOVL6,ETS1,FOS,FOSL1,GPD1,GYG1,HOCAR1,HMGC52,HPGD,IFIT3,IGF2,IGFBP2,IGFBP6,IL1RN,INSIG1,IRF1,IRF7,IRS2,KLF4,KRT20,LCN2,LDHA,MAT2A,NOX1,	378 (20)
HDAC4		transcription regulator		-1.45	0.00342	ATF3,FOS,FOSL1,GADD45A,HDAC9,HMGC,IFITM3,JUN,LDHA,PRKCA,PTGS2,RGS2,RUNX2,TNFRSF12A,TSPAN13	433 (19)
baicalein		chemical drug		-1.455	0.0196	CXCL8,CYP1A1,FOS,JUN,MCL1,PTGS2	
miR-24-3p (and other miRNAs w/seed GGCUCAG)		mature microRNA		-1.461	0.0212	BBC3,CCNA2,DUSP1,PMAIP1,SMAD3	
heme		chemical - endogenous mammalian		-1.463	0.00782	CD55,CLDN1,CXCL2,CXCL3,LCN2,LIF,SCARB1,TJP1	463 (18)

Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
miR-203a-3p (and other miRNAs w/seed UGAAAU)		mature microRNA		-1.471	0.0107	CDK6,F2RL1,KLF4,PRKCA,RUNX2	
tyrphostin AG 1478		chemical - kinase inhibitor		-1.493	0.00288	CAV1,CXCL8,CXCR4,EDN1,FOS,HBEGF,MCL1,PTGS2,RUNX2,S100A10	417 (19)
pitavastatin		chemical drug		-1.495	0.000672	HMGCR,IDI1,LSS,PTGS2,SCARB1,SQLE	248 (10)
STEAP3	-0.4	transporter		-1.508	0.0000728	ACER2,CD44,ERRFI1,GCNT2,NEDD9,PIK3R1,S100A10,TGF2,TGM2,TNFRSF12A,ZYX	
GLI1	-0.756	transcription regulator		-1.518	5.11E-08	4,CEP70,CLU,DKK1,FAS,FOXO1,GATA6,GLI1,GLI2,HXA5,IGF2,IGFBP6,IL1R2,INSIG1,JA2,ILK4,NDRG2,NPDC1,NOQ2,PGM2L1,PIM1,REG4,RHOB,RUNX2,SH2B3,TSC22D1	489 (19)
RPTOR		other		-1.521	0.00437	BCL3,CDK6,EGLN1,HMGCR,IDI1,IF144,JUN,LHA,LSS,MSMO1,PPP1R3B,RUNX2,SC5D,SQLE	485 (18)
Ro41-5253		chemical reagent		-1.528	0.000672	CRABP2,IRF1,PPARG,RARG,SMPD3,TGFB2	305 (11)
PLA2G10		enzyme		-1.536	0.0232	BMP4,DHRS3,FAS,KDM6B,KRT13,NABP1,PHLDA1,PPP1R10,PTGS2,TRAF4	
luteolin		chemical drug		-1.546	0.0208	CDK6,CYP11A1,FAS,FOS,HNF4A,JUN,PTGS2	
diphenyleneiodonium		chemical reagent		-1.55	0.00473	ATF3,CXCL2,CXCL3,CXCL8,DUSP2,EGR1,FOS,NOX1,PTGS2	433 (19)
tazemetostat		chemical drug		-1.553	0.000872	K6,CRABP2,DHRS3,DNMT3A,EIF2AK2,ELOVL6,FLRT3,FRYL,GATA6,GLI2,HMG2,IGSF9,INPPL1,KLF4,MAP4K4,MICALL2,MYO1B,NPNT,PPP2R5B,SGK1,SMAD3,SOX12,SRI,STEAP	
mir-30		microRNA		-1.566	0.00047	ARID5B,BBC3,GADD45A,KLF9,NEDD4L,RUNX2,PTGS2,STK39,UGT8	
15-deoxy-delta-12,14-PGJ 2		chemical - endogenous mammalian		-1.576	3.27E-08	CAV2,CEBPD,CXCL2,CXCL8,DNAJB1,EGR1,EHF,FOS,GADD45A,GDF15,GSN,HSPB1,IRF1,JUN,KLF4,MAP1LC3B,MCL1,MDX1,MYB,NOX1,PLAAT4,PPARG,PTGS2,REL,RUNX2,SC	427 (17)
miR-133a-3p (and other miRNAs w/seed UUGUCC)		mature microRNA		-1.586	0.0125	CXCL3,KRT7,MALAT1,MCL1,RUNX2	
SMARCA5		transcription regulator		-1.604	0.00468	ALDH1B1,ASS1,B2M,BCL6,CD44,CELSR1,EPHA2,FAS,IFITM2,IRF7,PHLDA1,PLAC8,PLXND1,UNC93B1	199 (7)
N-nitro-L-arginine methyl ester		chemical drug		-1.614	0.00143	ACO1,ATF3,BGN,CD68,CXCL2,CXCL3,CXCL8,FAS,HMGCR,INSIG1,PDK4,PTGS2,REN	407 (20)
LDB1		transcription regulator		-1.616	0.0000359	*1,ANXA1,AXIN2,BBC3,CASP4,CGAS,CLDN2,COL18A1,DP4,ENG,F2R,GSN,HXA5,IFIH1,IRS2,MDK,NT5E,PAG1,PATZ1,PLSCR1,SERPINE2,SLC16A1,SMAD3,TGFB2,TRIM25,TXI	
LMO2		transcription regulator		-1.616	0.0000384	*1,ANXA1,AXIN2,BBC3,CASP4,CGAS,CLDN2,COL18A1,DP4,ENG,F2R,GSN,HXA5,IFIH1,IRS2,MDK,NT5E,PAG1,PATZ1,PLSCR1,SERPINE2,SLC16A1,SMAD3,TGFB2,TRIM25,TXI	
EWSR1-FLI1		fusion gene/product		-1.623	0.0162	ARID5B,CAV1,CCN1,EDN1,HPGD,NFKBIZ,SRLF5,TGFB2,TRNP1	
metribolone		chemical reagent		-1.626	2.65E-15	*1,ERRFI1,ETV1,FHL2,FOS,GDF15,GTPBP2,HES6,HK1,HMGCR,HMGCS2,HSPH1,IDI1,IFITM2,IRS2,LDHA,LRIG1,MAOA,ME1,MMP7,MRPL34,NEDD4L,NOQ2,PROS1,PYGB,REG4,S	552 (21)
simvastatin		chemical drug		-1.626	0.0000191	*1,ANXA1,CCN1,CD55,COTL1,CXCL2,CXCL3,CXCL8,CYP2B6,EDN1,F2R,FOS,HK1,HMGCR,IRF1,KLF4,LCN2,MAP1LC3B,MPP6,NRIP1,PTGS2,RHOB,RHOU,SCARB1,SDC4,ST6GAL	304 (19)
ARHGDI3		other		-1.633	0.000153	ALCAM,ANXA1,EDN1,KANK1,PADI1,RGS2	
ACSS2		enzyme		-1.633	0.000518	ACAA1,DGAT2,HMGCR,LSS,PPARG,SCARB1	338 (13)
(-)-norephedrine	-0.621	chemical drug		-1.633	0.0000467	HMGCR,IDI1,LSS,MSMO1,NPC1,SQLE	195 (8)
dihydrotestosterone		chemical - endogenous mammalian		-1.635	1.92E-09	*;GPD1,GSN,HMGCR,HXA5,HPGD,HSPA1A/HSPA1B,HSPB1,IDI1,IGFBP2,IQGAP2,IRS2,JUN,KITLG,LAMA5,LDHA,MAFF,MCAM,ME1,MMP7,NEDD4L,PDE9A,PHF21A,PHLDA1,PM	530 (23)
MYCN		transcription regulator		-1.646	0.00403	2,ABCB10,ABCC1,ALDH1A1,AMOTL2,ATXN2,B2M,CAV1,CXNG2,CLU,COL18A1,DNMT3A,DUSP2,FGFR2,GATA6,LD2,LDHA,MAT2A,PMAIP1,POLR2L,S100A10,SLC16A1,SORD,TGM	454 (13)
MAP2K5		kinase		-1.646	0.00000935	ACSS2,CXCL8,CYP24A1,ELOVL6,FOS,HMGCR,IDI1,INSIG1,JUN,LSS,MSMO1,PTGS2,SQLE	379 (21)
BMP10		growth factor		-1.648	0.00019	ALDH1A3,ANGPT1,CD55,ECM1,ENG,FGFR2,FOS,GLI1,HPGD,IDI2,LCN2,PHLDA1,SERPINA3,SERPINE2	257 (7)
TSC2		other		-1.652	1.53E-08	*1,ANXA1,ATF3,AXIN2,BCL3,CASP9,CD68,EGLN1,EGR1,FOS,GSN,HMGCS2,HSPB1,IF144,IFITM3,IRS2,LGALS3,MAOB,MCL1,MUC2,PDK4,PGM2L1,PHLPP1,PKIB,PPP1R3B,PRKCA,	500 (23)
26s Proteasome		complex		-1.661	0.000478	BAG3,BCL3,BIRC3,CCNA2,CD68,CDC25A,CXCL3,CXCL8,EREG,FOSL1,HBEGF,IFI35,MAP1LC3B,PRKCA,PTGS2,TGM2,TRAF4,TXNIP	476 (21)
RPSA		translation regulator		-1.664	0.00295	CXCL3,DUSP1,DUSP2,GBP3,PTGS2,REL	505 (20)
N-[N-(3,5-difluorophenacetyl-L-Ala)]-S-phenylglycine t-butyl ester		chemical - protease inhibitor		-1.664	0.0443	CXCL1,CXCL2,CXCR4,REL,RND3,S100A4	
apicidin		chemical - endogenous non-mammalian		-1.664	0.000518	ATP2A3,CXCL8,FAS,GSN,ROR1,TGM2	
SIN3A		transcription regulator		-1.673	0.00309	BCL6,CCNG2,CYP11A1,FBXO3,GADD45B,KLF6,PTGS2,TGFB2,TXNIP	412 (14)
GAPDH		enzyme		-1.673	0.00189	CXCL1,DUSP1,HLA-C,IFITM2,OAS3,TXNIP,WARS1	
IL10RA		transmembrane receptor		-1.677	9.18E-10	*;CTSE,CYP2S1,DDIT4,DPEP1,ECM1,EDN1,EHF,ENTPD5,ETV1,FAS,GNE,HPGD,IL15RA,IL1RN,IRF7,IRF7,KCNE3,KITLG,LCN2,MAOB,MYB,NDRG2,NR5A2,P3H2,PLAAT3,PROCR,	273 (12)
docosahexaenoic acid		chemical drug		-1.681	0.000924	ACSS2,CD44,CPT1A,CXCL8,CXCR4,DNAJB9,ELOVL6,ERN1,FAS,FOS,HPGD,PIK3R1,PNLA2,PTGS2,SERPINH1,SORL1,TGFB2,TGFB2,UGT11A10 (includes others)	485 (22)
H-7		chemical - kinase inhibitor		-1.683	0.000731	CLCF1,CYP11A1,EGR1,FAS,FOS,PIM1,SMAD3,VDR	482 (20)
NKX2-1		transcription regulator		-1.698	0.00000467	*R2,AQP5,BMP4,CDKN2B,CBPA,CLU,DP4,ESAM,FAM3D,FXRD3,GLCO1,IGFBP6,KITLG,LCN2,MTUS1,MYB,PARDB6,QSOX1,RNASE4,ROR1,SEC14L2,TFF3,TGFB2,UGT8,WNT	
CD300LF		other		-1.709	0.000249	ACSS2,CPT1A,CXCL8,GPD1,HK1,IL1RN,PCK2	257 (7)
miR-34a-5p (and other miRNAs w/seed GGCAGUG)		mature microRNA		-1.727	0.000812	ATF3,AXIN2,CD55,CDC25A,CDK6,FAM221A,GSDMB,HID1,IFITM2,KLF4,LGALS3BP,MYB,PLAAT4,PPARG,TRPS1,TSPAN13	240 (7)
Sb202190		chemical - kinase inhibitor		-1.73	0.0137	CD55,CFTF,CXCL8,CYP11A1,DKK1,EGR1,FGFR2,FOS,PHLDA1,PTGS2,RHOB,SGK1,VDR	
rotenone		chemical toxicant		-1.746	0.0366	BIRC3,CXCL2,DNAJB9,FOS,PTGS2,SLC16A1,TXNIP	
MYB	0.316	transcription regulator		-1.749	0.0000075	ATP2B1,AURKA,AXIN2,BIRC3,CDKN2B,CXCL16,CXCL2,CXCR4,ESAM,FUT8,IGF2,JUN,KITLG,KLF4,LCN2,LIF,MAT2A,METTL7B,MTSS1,MYB,NEDD9,PTGS2,SDC4,ZC3H12A	419 (18)
glutathione		chemical - endogenous mammalian		-1.768	0.0484	ABCC1,ASS1,ATF3,CA9,PTGS2,ZBTB10,ZBTB4	
raloxifene		chemical drug		-1.774	8.36E-08	*;BMP4,CLK1,CLU,DDIT4,DUSP1,ENG,F2R,FLNB,GPRC5A,HSPA1A/HSPA1B,JUN,KLF6,KRT7,MDX4,MYO1B,NCOA3,PLK3,PTGS2,RAP1GAP,SLC22A5,SMAD3,SNCG,TGFB2,TGFE	476 (23)
SS18-SSX1		fusion gene/product		-1.783	0.00000242	AXIN2,BBC3,CDC25A,DKK1,PMAIP1,SHCBP1	313 (7)
iron		chemical - endogenous mammalian		-1.801	0.0174	CEBPA,GADD45A,GADD45B,LCN2,NFYA,PPP1R15A,SLC39A8	
trogliatazone		chemical drug		-1.802	3.85E-13	P1A1,CYP2B6,CYP3A5,DGAT2,DHRS3,EGR1,ENTPD5,ETS1,FOS,FOSL1,GADD45A,GDF15,GPD1,HIPK2,JUN,KLF4,KRT13,KRT20,LOC102724788/PRODH,MAOB,MCL1,ME1,MYB,I	491 (20)
staurosporine		chemical - kinase inhibitor		-1.818	0.0000954	BBC3,CFTF,CXCL8,CYP11A1,FAS,FOS,FOSL1,GATA2,IGF2,MCL1,NEDD9,PIM1,PTGS2,RCAN1,SERPINA3,SMAD3,VDR	514 (23)
wortmannin		chemical - kinase inhibitor		-1.821	0.00724	ATF3,CD44,CDKN2B,CEBPD,CXB,CXCL16,CXCL8,EGR1,F2R,FOS,GPD1,IRF1,IRS2,JUN,MCL1,MT2A,NT5E,PTGS2,SCARB1	497 (22)
HMOX1		enzyme		-1.824	0.00141	ANGPT1,CDK6,CXCL1,CXCL2,CXCL3,CXCL8,CYP11A1,ENG,FOS,IL1RN,MAP1LC3B,PROCR,PTGS2,TGFB2,ZFP36	454 (20)
BCL3	0.773	transcription regulator		-1.827	0.00092	CXCL2,CXCL3,CXCL8,DUSP5,EGR1,FOS,IDI2,IRF1,JUN,PDK4	431 (18)
FOXA2		transcription regulator		-1.831	0.00864	AGR2,CD55,CBPA,CPT1A,CXCR4,DDC,DDIT4,HES6,HMGCS2,HNF4A,HPGD,MTUS1,MUC2,NR5A2,PIM1,PPARG,PROS1,RARG,SERPINA1,SPINK1,TBXAS1	418 (16)
mir-15		microRNA		-1.838	0.0517	CDK6,HSPA1A/HSPA1B,LATS2,MCL1,MYB,PIM1,PTGS2	
lithium chloride		chemical drug		-1.841	0.000143	ASS1,AXIN2,BCL3,BMP4,CD44,DKK1,FOS,GDF15,HMGCR,IDI1,KRT20,LSS,MT2A,MYB,PLD1,PPARG,PTGS2	436 (22)
Sn50 peptide		chemical toxicant		-1.845	0.00384	BIRC3,CXCL2,CXCL8,FAS,IFNGR2,LIPG,MMP7,PPARG,PTGS2	413 (18)
mir-26		microRNA		-1.854	0.000193	CDK6,CHORDC1,CXCL3,HPGD,MCL1,PTGS2,STK39	198 (7)
KLF2		transcription regulator		-1.857	1.99E-08	CL3,BMP4,CAV1,CD44,CD55,CDKN2B,CBPA,CXCL2,CXCL8,CXCR4,ECM1,EDN1,EFNA1,F2RL1,FUT4,GADD45A,IGF2,IL1RN,IRF7,IRF7,KCNE3,KITLG,LGALS9,MT2A,PLPP3,PPARG,PROS1,PTGS2,RUNX	410 (16)
CST5		other		-1.863	0.0000168	*1/AKR1C2,ARHGAP29,CAV1,CD44,CEMIP,CEP170,CHD2,DNAJB4,DOCK5,EPN3,FER,GPRC5A,IGSF9,IQGAP2,ITPRID2,JMJD1C,NPAS2,NRP1,NT5E,PMAIP1,PPL,PYGB,RUNX2,SK	
SREBF1		transcription regulator		-1.887	1.38E-08	*.LOVL6,FAS,FBXO32,HMGCR,HNF4A,HSPA1A/HSPA1B,IDI1,IL1R2,INSIG1,IRS2,LGALS3,LSS,MDK,MSMO1,NPC1,NR0B2,PCK2,PMPCA,PPARG,PTGS2,SC5D,SCARB1,SERPINA1,;	301 (16)
G protein alpha		group		-1.89	0.0943	ANKS4B,CHPF,FOS,GNAZ,LYSMD4,QPCT,SPCS3,TMED3	
NLRX1		other		-1.89	0.0106	BCL10,BIRC3,CARD10,IRF1,MAP3K14,PIK3R1,REL	
ATP7B		transporter		-1.89	0.003	ELOVL6,HMGCR,IDI1,LSS,MSMO1,SHCBP1,SQLE	
PPP3R1		phosphatase		-1.89	0.034	AQP5,BAG3,BCL3,CLIC5,GBP3,H1-0,PDE9A	
TCF4		transcription regulator		-1.892	0.00000175	*;G,CDKN2B,CSRNP1,CTSE,FAS,GBP3,GNE,GRB7,H1-0,IGF2,MCL1,NEDD9,PARP8,PLAC8,PML,PP1F,PRDX4,RUNX2,SDF2L1,SEC11C,SEC24D,SERINC5,SP140L,TAPBPL,TAI*	273 (7)
SFTPA1		transporter		-1.912	0.000000216	AGR3,AKR1C1/AKR1C2,CCN1,CXCL2,CXCL3,ECM1,EGR1,ERN1,FOS,FOSB,GABRP,HBEGF,HSPA6,LRIG1,PDK4,PHLDA1,PLAAT4	445 (19)
ZNF217		transcription regulator		-1.912	0.00115	AGR2,CDKN2B,CREB5,GPRC5A,MYO1B,RCAN1,SEC14L2,SEMA3A,SH3RF2,STRA6,ZHX2	
THZ2		chemical - kinase inhibitor		-1.912	0.000111	FHL2,GLI2,HRH1,LIF,MCL1,RUNX2,SMAD3	
mir-29		microRNA		-1.93	0.00411	CDK6,CLDN1,DKK1,DNMT3A,KLF4,MCL1,PIK3R1,RUNX2,SCARB1,TRAF4,ZFP36L1	371 (11)
Go 6976		chemical - kinase inhibitor		-1.932	0.00427	CD55,CXCL2,CXCL3,CXCL8,ETS1,FOS,PLD1,PRKCA,PTGS2	452 (23)
resolvin D1		chemical - endogenous mammalian		-1.933	0.00134	BCL6,CXCL2,CXCL3,CXCL8,CXCR4,JUN,PTGS2	424 (19)
UCN-01		chemical drug		-1.934	0.00656	CDC25A,CXCL8,MCL1,RHOB,XPA	470 (21)
amino acids		chemical - endogenous mammalian		-1.936	0.0363	FOS,FOSB,IGF2,JUN	
SUMO2		enzyme		-1.937	0.000865	CAV1,CAV2,CEACAM1,CXCL16,NR0B2,PIK3R1,RNASE4,TSC22D3	
PAX7		transcription regulator		-1.938	0.000814	ASS1,CXCR4,F2RL1,FAM107B,IDI2,MSLN,NPNT,PPARG,RNF128,SEMA3E,TOB1	367 (7)
ingolimid		chemical drug		-1.941	0.566	CXCL2,FOSB,FOSL1,RUNX2	
fludarabine		chemical drug		-1.949	0.0571	CXCL2,FAS,IRF1,MCL1	
RBM5		other		-1.953	0.00000116	ADAM9,ANXA1,ATP5MC3,BIRC3,IFITM3,INSIG1,MCL1,MYO1B,NCOA3,PIM1,SERPINH1,TSPAN6	
BDNF		growth factor		-1.959	0.0000429	*R4,DUSP1,EGR1,ELOVL6,FLNB,FOS,FOSB,GNAI1,GPC4,HMGCR,HSPA4L,JUN,LCN2,MACROD1,MALAT1,PLTXNB2,PPP1R1B,PTPN9,S100A10,SCARB1,SEMA3E,SERPINH1,SH3I	469 (21)
dichlororibofuranosylbenzimidazole		chemical toxicant		-1.961	0.0123	CXCL8,CYP11A1,CYP24A1,CYP3A5	
PRDM16		transcription regulator		-1.963	0.098	GBP3,IFI44,IRF7,OAS3	
SERCA		group		-1.964	0.0000795	EGR1,FOSL1,JUN,ZFP36	
fisetin		chemical toxicant		-1.964	0.149	BIRC3,FOS,MCL1,PTGS2	420 (15)
taurine		chemical - endogenous mammalian		-1.964	0.122	ABCC2,CEBPA,CPT1A,PTGS2	
SIRT1		transcription regulator		-1.967	0.00000285	GADD45A,GBP3,GLI1,GLI2,HJURP,HMGCR,HXA5,IFI44,IFIT3,IFITM3,IRF7,KDM2B,KIF13B,LGALS3,LGALS3BP,MAOA,MAT2A,MCL1,MGAT1,NEDD4L,NPNT,NR1D1,PARP12,PARI	428 (21)
MIR101		group		-1.969	0.00651	DUSP1,MCL1,PTGS2,STMN1	
naringenin		chemical - endogenous non-mammalian		-1.969	0.0368	CPT1A,CXCL1,CXCL8,CYP11A1,PTGS2	
PD184352		chemical drug		-1.969	0.0241	CXCL3,EGR1,FOS,MCL1	
HDAC5		transcription regulator		-1.97	0.0079	ACSL1,AURKA,CPT1A,DAPK1,HMGCR,HMGCS2,JUN,KLF6,PPARG,RUNX2	504 (22)
TNIP1		other		-1.972	0.14	CXCL2,CXCL3,HLA-B,LCN2	
EZR		other		-1.973	0.0268	ATF3,DDIT4,FAS,IGFBP2,PTGS2	
TRAF3		enzyme		-1.977	0.165	BIRC3,CXCL2,CXCL3,FAS,MAP3K14,MCL1,PPFBP2	
LY294002		chemical - kinase inhibitor		-1.979	2.63E-15	*CL3,CXCL8,DUSP1,EGR1,EREG,ETS1,F2R,FAS,FER,FEZ2,FOS,FOSB,FOSL1,GDF15,GPD1,GST4,HBEGF,HMGCR,IDI1,IGF2,IGFBP2,IL1R2,IL1RN,IRF1,IRS2,JUN,LAMC2,LCN2,	510 (20)
ARRB2		other		-1.98	0.00863	CXCL2,CXCL3,EGR1,GRK5,NFKBIZ,PTGS2	399 (17)
tosylphenylalanyl chloromethyl ketone		chemical - protease inhibitor		-1.981	0.0319	BIRC3,CXCL2,CXCL8,PTGS2	
SGPL1		enzyme		-1.982	0.0363	ABCC1,PPARG,PTGS2,SEC61A1	
DNMT1		enzyme		-1.982	0.472	CYP24A1,IGF2,LRP8,PPARG,PTGS2	
IL37		cytokine		-1.982	0.0279	CXCL2,CXCL3,CXCL8,IL1RN	
SL 327		chemical - protease inhibitor		-1.982	0.0461	BBC3,FOS,FOSB,NEDD4L	
fucoidin		chemical reagent		-1.982	0.0571	CLDN1,CXCL8,IRF7,MCL1	
mir-34		microRNA		-1.984</			

Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
N-acetyl-L-cysteine		chemical drug		-1.985	0.000163	3,BIRC3,CASP4,CASP9,CAV1,CCN1,CFTR,CXCL3,CXCL8,CXCR4,DUSP1,EDN1,EGR1,FAS,FBXO32,FOS,HBEFG,JUN,MAP1LC3B,NFKB1Z,PTGS2,RHOB,RUNX2,SLC16A1,TGFB2	468 (20)
R-WIN 55,212		chemical reagent		-1.986	0.0571	CASP7,CASP9,CDK6,CXCL8	
levothyroxine		chemical - endogenous mammalian		-1.987	0.306	BBC3,FOS,GDF15,IGFBP6,PCSK6	
NR1D1	0.662	ligand-dependent nuclear receptor		-1.987	0.122	EGR1,FOS,ME1,NR1D1	
STAT5B		transcription regulator		-1.993	0.0000474	RD13B,BCL6,BIRC3,CASP4,CASP9,CDK6,CYP2B6,CYP3A5,DAPK1,DDC,DGAT2,FAS,FOS,GADD45A,GADD45B,GPD1,IRF1,MCL1,ME1,MTMR11,NIPAL1,NT5E,PCSK5,PDK4,PIM1,I	484 (20)
anakinra		biologic drug	Inhibited	-2	0.0165	ABCC2,CXCL1,EDN1,PIM1,PTGS2	
CBX7	0.635	other	Inhibited	-2	0.0123	CLDN1,CTSS,CXCL8,GDF15	
ZBED2		other	Inhibited	-2	0.000593	GATA6,IRF7,OAS3,PIM1	153 (7)
SPDEF	-1.01	transcription regulator	Inhibited	-2	0.249	BIRC3,CXCL8,PRKCA,SMAD3,STMN1	
PPP1R15B		phosphatase	Inhibited	-2	0.00144	CHAC1,PPARG,PPP1R15A,SES2	
LRPAP1		other	Inhibited	-2	0.0319	CXCL8,PTGS2,SERPINA3,SORL1	
PPP2R5C		other	Inhibited	-2	0.00818	BCL3,BIRC3,CXCL8,REL	354 (10)
S100A6		transporter	Inhibited	-2	0.0514	ATF3,AURKA,CXCL2,CXCL8	
JAG2	-0.547	growth factor	Inhibited	-2	0.122	BCL6,CXCL1,CXCL3,IL1RN	
PAEP		other	Inhibited	-2	0.0123	CXCL1,CXCL16,EDN1,HBEFG	
NBEAL2		other	Inhibited	-2	0.00818	CXCL16,CXCL2,CXCL3,GATA2	396 (7)
ADAMTS12		peptidase	Inhibited	-2	0.0363	ALDH1A3,LCN2,MID1,TNFAIP2	
tranilast		chemical drug	Inhibited	-2	0.0176	CXCL1,CXCL8,NRP1,TXNIP	
glutamy-L-selenocysteine		chemical - endogenous mammalian	Inhibited	-2	0.00818	CLU,EGR1,JUN,PSME1	
AG490		chemical - endogenous mammalian	Inhibited	-2.004	0.0000213	ACAT1,AKR1C3,BIRC3,CD68,CFTR,CXCL2,CXCL8,EDN1,FOS,HPGD,IGF2,IRF1,MCL1,PIM1,PTGS2,S100A10	484 (23)
miR-30c-5p (and other miRNAs w/seed GUAAACA)		mature microRNA	Inhibited	-2.005	0.0000251	ACVR1,BCL6,IRS2,JUN,KRT7,LOXL4,MAP4K4,MAT2A,NT5E,PGM1,PPARG,RAB27B,RUNX2,SH2B3,SLC12A4,STX1A,TGFB2,TMED3,TNFAIP2,TRPS1	
INSR		kinase	Inhibited	-2.01	4.57E-10	CXCR4,DGAT2,DUSP1,EDN1,EGR1,EREG,FOS,GADD45A,GATA6,GRB7,HBEFG,HMGR,HPGD,IDI1,IFITM2,IGF2,INSIG1,KLF9,LAT2,LSS,MAOA,MAOB,MSMO1,MUC2,PDK4,PHL	489 (26)
miR-199a-5p (and other miRNAs w/seed CCAGUGU)		mature microRNA	Inhibited	-2.032	0.0000655	APOL1,BCAM,BGN,CELSR1,ETS1,GPRC5A,KLF4,LAMC2,LCN2,MMP7,NEDD9,PTGS2,TGFB2	
Nr1h		group	Inhibited	-2.06	0.0000872	ALDH1A1,ATP1B1,BCL3,CAV1,CXCL1,CXCL8,EDN1,ELOVL6,F2R,GLI1,IFIH1,LAT2,NFKB1Z,NPC1,NR5A2,PML,PTGS2,REN,SBNO2,SCARB1,SP110,SYT7	535 (22)
THRB		ligand-dependent nuclear receptor	Inhibited	-2.111	0.0000856	3,CDK6,CEBPA,CFTR,CPT1A,CXCL2,CXCL3,CXCR4,DDC,DKK1,ENG,FOS,FOSL1,GSN,IGFBP2,JUN,KLF9,MACC1,ME1,MMP7,NR5A2,PDK4,PPARG,PTGS2,RUNX2,STRA6,UOCR	459 (22)
MEOX2		transcription regulator	Inhibited	-2.121	0.000514	ANGPT1,CXCL1,CXCL2,CXCL3,CXCL8,EDN1,EFNA1,HBEFG	309 (7)
EPCAM		other	Inhibited	-2.121	0.0000313	ATF3,EGR1,FHL2,FOS,FOSL1,HMG2A,JUN,RUNX2	505 (21)
miR-182-5p (and other miRNAs w/seed UUGGCAA)		mature microRNA	Inhibited	-2.137	0.000254	CDK6,DDX60L,HERC6,MALAT1,MTSS1,NMI,RARG,SAMD9,SERPINE2,SLFN5,SP110	
Ro31-8220		chemical - kinase inhibitor	Inhibited	-2.174	0.00139	CD55,CLDN1,CXCL8,DUSP1,EGR1,FSTL3,PLD1,PTGS2	
miR-27a-3p (and other miRNAs w/seed UCACAGU)		mature microRNA	Inhibited	-2.183	0.0532	BBC3,PMAIP1,PPARG,SMAD3,ZBTB10	440 (20)
RCAN1	0.7	other	Inhibited	-2.183	0.00135	CCNA2,CCNF,CXCL8,FOS,PTGS2,RCAN1	
STK40		kinase	Inhibited	-2.186	0.0323	CEBPA,CXCL1,CXCL8,FUT4,JUN,PPARG,PTGS2,WNT11	469 (22)
ethylene glycol tetraacetic acid		chemical reagent	Inhibited	-2.194	0.0368	BIRC3,CXCL8,EGR1,FOS,RCAN1	
NRF1		transcription regulator	Inhibited	-2.2	0.122	ATP1B1,CLDN1,CXCL8,IL1RN,TJP1,VDAC1	
FBXO32	0.306	enzyme	Inhibited	-2.2	0.0534	ALDH1A3,AXIN2,CXCL2,CXCL3,DNAJB9,DNAJC3,GADD45A,PTGS2	
HSPB1	0.966	other	Inhibited	-2.2	0.00919	BBC3,CCNA2,CXCL2,CXCL3,CXCL8	462 (21)
PS-1145		chemical - kinase inhibitor	Inhibited	-2.2	0.00183	CXCL1,CXCL8,IRF1,PTGS2,SERPINA3	405 (16)
Bay 11-7082		chemical - kinase inhibitor	Inhibited	-2.201	0.00176	CD44,CXCL1,CXCL2,CXCL3,CXCL8,IL15RA,MCL1,MMP7,PIM1,PTGS2,S100A4	407 (16)
mifepristone		chemical drug	Inhibited	-2.206	0.00000838	1,CEBPD,CFTR,CLU,COL18A1,CYP3A5,DDIT4,DUSP1,EGR1,EHF,FAS,FOS,HBEFG,HPGD,IGF2,IRS2,JUN,KLF4,LAMA5,LAMC2,MYB,NCOA3,NQO2,PADI2,PTGS2,RAP1GAP,RGS2	545 (21)
MAF		transcription regulator	Inhibited	-2.213	0.116	ACSS2,HMGR,IDI1,LSS,NT5E,SQLE	
GADD45A	0.716	other	Inhibited	-2.213	0.00367	CXCL2,CXCL3,FOSB,JUN,MMP7	488 (18)
USP18		peptidase	Inhibited	-2.219	0.0165	BBC3,IFIH1,IFITM3,IRF1,IRF7	
DLK1		other	Inhibited	-2.232	0.00367	GLI1,IRF1,IRF7,PPARG,REL	433 (13)
ACKR2		G-protein coupled receptor	Inhibited	-2.236	0.0579	EIF2AK2,IFI44,IFIT3,IRF7,OAS3	
SIRT2		transcription regulator	Inhibited	-2.236	0.0078	HMGR,IDI1,LSS,SC5D,SQLE	
DBI		other	Inhibited	-2.236	0.0000979	ACSS2,ELOVL6,HMGR,LSS,PPARG,SQLE	94 (6)
PNPT1		enzyme	Inhibited	-2.236	0.000131	CXCL8,EIF2AK2,IFI44,IFIH1,IFIT3,IRF7,LGALS3BP,PARP12,PARP14,RNF213	391 (12)
SU6656		chemical toxicant	Inhibited	-2.236	0.0268	ATF3,EGR1,PHLDA1,PTGS2,ZFP36L1	
PRDM1		transcription regulator	Inhibited	-2.271	5.49E-08	CDK6,CLDN1,CRISPLD2,CXCL2,CXCL3,CXCR4,DDIT4,DUSP16,ECM1,F5,FOS,FOSL1,IG2,IRF7,MCL1,ME1,MT2A,MTMR11,PCSK6,PLAAT4,PLAC8,PMAIP1,PSMB10,PSMB8,SERP	471 (19)
FOXO1		transcription regulator	Inhibited	-2.277	0.00189	ANXA1,AURKA,AXIN2,CAV1,CCNA2,CCNF,CD25A,FOS,FUT4,IL1RN,JUN,LDHA,MMP7,STMN1,TGFB2,TJP1	462 (19)
U0126		chemical - kinase inhibitor	Inhibited	-2.278	4.03E-21	EIF2AK2,ELOVL6,EMP1,EPHA2,EREG,ERRF1,ETS1,ETV1,FGFR2,FOS,FOSB,FOSL1,GADD45B,GDF15,GLI1,GSN,GSTA4,HBEFG,HMGR,HPGD,IDI1,IL1R2,IRF1,JDP2,JUN,JUND	488 (19)
mir-8		microRNA	Inhibited	-2.284	6.68E-08	3,CCNG2,CDC25A,CDK6,CLDN1,CLDN12,DNAJC3,ERRF1,ETS1,FGFR2,GRB7,GSE1,HOXA5,ITGB6,KITLG,KLF4,LATS2,MSLN,MYO10,PIP5K1A,PMAIP1,RNF128,SERPINE2,TGFB2	376 (7)
PSMB11		peptidase	Inhibited	-2.326	0.00283	CAV1,CLDN2,CREB5,CTSS,CXCL3,GADD45A,GADD45B,HSPA1A,HSPA1B,LGALS3,NTN4,PTGS2,RHOB,TGFB2,TNFRSF12A	
TFRC		transporter	Inhibited	-2.335	0.000026	ATF3,BBC3,CCNA2,CHAC1,DDIT4,FOS,GADD45A,IG2,JUN,LDHA,ME1,PPARG,PPP1R15A,TGFB2,TNFRSF12A	311 (7)
elaidic acid		chemical - endogenous mammalian	Inhibited	-2.35	0.0000443	ACSL1,ALDH1A1,CEBPA,DGAT2,DHRS3,ELOVL6,GNE,HMGR,IDI1,LCN2,LPP,LSS,SC5D,SQLE,TFPI	
miR-155-5p (miRNAs w/seed UAAUGCU)		mature microRNA	Inhibited	-2.361	0.00126	BRPF3,CCN1,CLDN1,CXCL1,CXCL2,CXCL3,CXCL8,DNAJB1,ETS1,MYB,NT5E,PIK3R1,PLXND1,PMAIP1,PPL,PTGS2,RAB27B,SLC30A1	383 (18)
DUSP1	0.918	phosphatase	Inhibited	-2.362	0.00000306	APOL6,CXCL1,CXCL2,CXCL3,CXCL8,DKK1,DUSP1,FOSL1,GDF15,GJB2,IFIT3,IL1RN,IRF1,JUN,MXD1,NRP1,PEX11A,PIK3R1,PTGS2,TGFB2,ZFP36	437 (18)
ETV6-RUNX1		fusion gene/product	Inhibited	-2.372	0.0000166	C42EP2,CXCC5,DDIT4,ENG,ID2,IFI35,IFIH1,IFIT3,IL15RA,IRF1,IRF7,JUN,KLF6,LAT2,NEDD4,NM1,PAG1,PIM1,PLXNB2,PMAIP1,PML,PPP1R15A,S100A4,SH2B3,STMN1,SWAP70,	155 (5)
BAPTA-AM		chemical reagent	Inhibited	-2.376	0.000644	AQP5,ATF3,CXCL8,CYP1A1,CYP3A5,EGR1,FOS,JUN,PTGS2	410 (19)
XBP1		transcription regulator	Inhibited	-2.392	0.000533	CL2,CXCL8,DNAJB9,DNAJC3,ETS1,FAS,GOLPH3L,KLF4,MAP1LC3B,NCOA3,NUCB2,PDI45,SDF2L1,SEC11C,SEC24D,SEC61A1,SEC61B,SEC61G,SERPINA1,SPCS3,SRPRB,SSR1	390 (16)
ZMPSTE24		peptidase	Inhibited	-2.418	0.0218	ATF3,CXCL2,CXCL3,DDIT4,GADD45A,GADD45B	
SUMO3		other	Inhibited	-2.425	0.00984	CAV1,CAV2,CEACAM1,CXCL16,PML,RNASE4	
lapatinib		chemical drug	Inhibited	-2.425	0.000393	EREG,FOS,FOSB,FOSL1,HBEFG,JUN	516 (23)
isoquercitrin		chemical drug	Inhibited	-2.433	0.0000467	HMGR,HMGC2,INSIG1,MSMO1,SC5D,SQLE	72 (4)
SAFB2		other	Inhibited	-2.449	0.000859	B2M,BBC3,FOS,HLA-C,HLA-E,JUN	
ELL2		transcription regulator	Inhibited	-2.449	0.0638	DNAJB9,DNAJC3,FUT8,REXO2,SEC24D,SEC61A1	
MNT		transcription regulator	Inhibited	-2.449	0.000214	BCL6,CCNG2,FBXO32,GADD45B,KLF6,TXNIP	
CISH		other	Inhibited	-2.449	0.154	CXCL3,DUSP2,EDN1,PPP1R15A,PTGS2,SORL1	
miR-16-5p (and other miRNAs w/seed AGCAGCA)		mature microRNA	Inhibited	-2.454	0.0000967	CD25A,CDK6,CHORDC1,CLDN12,DMTF1,DNAJB4,GOLPH3L,HERC6,HSPA1A,HSPA1B,JUN,KITLG,MCL1,MYB,PPIF,PTGS2,RAB30,SERPINE2,SKAP2,SLC16A3,SLC38A5,SRPRB,T	
flgrastim		biologic drug	Inhibited	-2.458	2.64E-12	2,F5,GADD45A,GATA6,GBP3,HIPK2,HPGD,IFI44,IFIT3,IL1R2,JUN,KLF6,KLF9,LDHA,LGALS3,MAFF,MYB,NHS,OAS3,PARP14,PATZ1,PDLIM1,PMAIP1,PRKAR2A,PRRG4,PSMB10,P	
PD98059		chemical - kinase inhibitor	Inhibited	-2.469	3.46E-23	1,ENG,EREG,ERRF1,ETS1,F2R,FAM13A,FAS,FOS,FOSB,FOSL1,GADD45A,HBEFG,HMG2A,HPGD,IGF2,IL1RN,INSIG1,JUN,JUND,LAMA5,LDHA,LIPG,MAT2A,MCL1,MMP7,MUC2,I	508 (17)
AIRE		transcription regulator	Inhibited	-2.53	0.000628	AKR1B10,AMBP,BMP4,EIF2AK2,HERC6,IFI44,IGF2,KLK6,MGAT1,NMI,PARP14,TFP3	
MACROH2A1		other	Inhibited	-2.53	0.00215	ALDH1A3,CDKN2B,EDN1,EGR1,ETS1,F2R,F2RL1,IGF2,FSTL3,GADD45A,IRF7,PPARG,TJP2	305 (13)
MAPK1		kinase	Inhibited	-2.563	5.07E-19	iB,GFOD1,GRB7,HLA-B,HLA-C,HLA-E,IFI35,IFI44,IFIH1,IFIT3,IFITM3,IGFBP6,IL1RN,IRF7,IRS2,ITPR2,JUN,JUND,LGALS3,LGALS3BP,LIF,MAOB,MCL1,NMI,NRP1,NT5E,OAS3,PARP	430 (24)
mir-210		microRNA	Inhibited	-2.566	0.184	EPB41L1,HOXA3,KLF6,SERTAD2,SMCHD1,STMN1,TP53I11	
ZFP36	0.298	transcription regulator	Inhibited	-2.595	0.0000389	BIRC3,CTSS,CXCL2,CXCL3,FOS,FOSL1,IRF1,JUN,LATS2,LCN2,MXD1,PIM1,PTGS2,UOCRFS1,ZFP36	422 (16)
IKZF1		transcription regulator	Inhibited	-2.601	0.0000184	CAV1,CAV2,CD68,CDK6,CXCL2,DEP1,DKK1,DTX3L,DUSP5,EMP1,IFIT3,KITLG,KLF4,LGMN,MYO10,NFKB1Z,PROS1,RNF19A,RNF213,S100A16,SERPINH1,SIPA1L2,SMAD3,TBC1	407 (8)
2-amino-5-phosphonovaleic acid		chemical - other	Inhibited	-2.607	0.00189	BBC3,CAMKK1,CCDC28A,DUSP1,EGR1,FOS,FOSB,GADD45A,GADD45B,HDAC9,JUN,OTULIN,PHLDA1,PLK3,PTGS2,RGS2	438 (20)
infliximab		biologic drug	Inhibited	-2.63	0.0422	CXCL1,CXCL8,DDIT4,EDN1,MT1X,MYO10B,PTGS2	
SH3TC2		other	Inhibited	-2.646	0.000402	ACSL1,EGR1,HMGR,IDI1,LSS,SC5D,SQLE	
SP600125		chemical - kinase inhibitor	Inhibited	-2.66	3.06E-08	3PG4,CXCL1,CXCL16,CXCL2,CXCL3,CXCL8,CYP1A1,DDIT4,DKK1,DUSP1,EGR1,FAS,FLRT3,FOS,FOSB,GADD45A,HNF4A,JUN,LAMA5,MCL1,NEDD9,NOX1,NR0B2,PARP8,PCK2,F	453 (19)
PTPRR		phosphatase	Inhibited	-2.668	0.0218	DHRS3,DNMT3A,ETS1,FOS,FOSL1,IFITM2,JUN,PLXNB2,PROCR,ROR1	
ARID1A		transcription regulator	Inhibited	-2.713	0.0000039	ANXA1,AXIN2,BMP4,CEACAM1,CEACAM6,CXCL1,CXCL2,CXCL8,EREG,F2R,IRS2,UCA1	484 (20)
PKD1		ion channel	Inhibited	-2.758	0.0000237	ALDH1A1,AMOTL2,ATP1B1,CCN1,CLCF1,CXCL16,CXCL2,DPEP1,FOSB,GLI2,HBEFG,HDAC9,HGD,MID1,NEDD9,NIPAL1,PML,PRAP1,OPCT,RASSF6,RUNX2,SMURF1,TBC1D4,ZI	301 (7)
PPARG	0.347	ligand-dependent nuclear receptor	Inhibited	-2.762	1.03E-11	1,GATA2,GDF15,GPD1,HCAR1,HIVEP2,HMGR,HMGC2,IGFBP6,INSIG1,IRS2,JUN,KLF4,KLF6,KRT20,LOC102724788/PRODH,ME1,MUC13,NOX1,NR1D1,PCK2,PDK4,PEX	505 (26)
herbimycin		chemical - kinase inhibitor	Inhibited	-2.763	0.00213	ATP2A3,CDK6,CXCL8,CXCR4,DUSP1,F2R,FOS,PTGS2	475 (22)
SAFB		other	Inhibited	-2.813	0.0051	B2M,BBC3,CXCL8,FOS,HLA-C,HLA-E,JUN,NEDD9	512 (19)
H89		chemical - kinase inhibitor	Inhibited	-2.882	0.00541	ANXA1,AQP5,BMP4,CD55,CLCF1,CXCL8,DUSP1,EGR1,EREG,FOS,ITPR2,PLD1,PTGS2,REN,SIGMAR1,SMAD3	466 (22)
COL18A1	-0.478	other	Inhibited	-2.882	0.000026	CCNBDP1,DDIT4,EDN1,EFNA1,EGLN1,ETS1,F2R,F2RL1,FOS,JUN,LDHA,MCL1,NRP1,PTGS2,VDAC1	483 (23)
bisindolylmaleimide I		chemical - kinase inhibitor	Inhibited	-2.919	0.0000206	BIRC3,CD44,CD55,CLCF1,CLDN1,CLU,CXCL8,EGR1,FOS,GDF15,JUND,MAT2A,MMP7,PLD1,PRKCA,PTGS2,RCAN1,TJP1,TJP2	461 (20)
mir-181		microRNA	Inhibited	-2.95	0.00473	ATP2B1,CXCL8,GATA6,KLF6,MCL1,PTGS2,RUNX2,SH2B3,TGM2	363 (12)
MAX		transcription regulator	Inhibited	-2.985	0.00132	BCL6,CCNG2,CD25A,CDKN2B,DUSP2,EDN1,FBXO32,GADD45A,GADD45B,ID2,KLF6,TXNIP	225 (3)
thalidomide		chemical drug	Inhibited	-2.985	0.0000133	ANGPT1,BIRC3,CAV1,CXCL8,DKK1,FOS,GADD45B,GDF15,NRP1,PIM1	483 (21)
SP110		transcription regulator	Inhibited	-2.985	0.0000144	ATF3,BCL3,BMP4,CCN1,CDKN2B,CLU,ETS1,F2R,FER,IFIH1,IFIT3,IFITM3,MAOA,MCL1,OAS3,PLSCR1,PPARG,PRKCA,SERPINA1,SOX4,TIA1,TXNIP	
GMNN	0.533	transcription regulator	Inhibited	-3	0.0202	ACVR1,ANGPT1,DUSP1,DUSP5,EPHA2,GBP3,NRP1,TEAD2,TGFB2	
SOX1		transcription regulator	Inhibited	-3	0.00917	ACVR1,ANGPT1,DUSP1,DUSP5,EPHA2,GBP3,NRP1,TEAD2,TGFB2	
SOX3		transcription regulator	Inhibited	-3	0.0162	ACVR1,ANGPT1,DUSP1,DUSP5,EPHA2,GBP3,NRP1,TEAD2,TGFB2	
SOX2		transcription regulator	Inhibited	-3.039	8.37E-13	S,FUT4,FYN,GAB1,GAB2,GADD45B,GATA2,GATA6,GBP3,GLI2,GRHL3,GSN,ID2,IER5L,INPP1,ITPR2,JUN,KANK1,KITLG,KLF4,KLF6,KRT7,LIMA1,LIMS2,NAAA,NR5A2,NRP1,OVOI	462 (13)
Irgm1		other	Inhibited	-3.178	4.02E-08	APOBEC3B,B2M,CCNA2,CGAS,CXCL16,FAS,GSDMD,HERC6,ID2,IFI35,IFI44,IFIH1,IFIT3,IFITM3,IRF1,IRF7,OAS3,TRIM21,TRIM25,TRIM56	293 (14)
SB203580		chemical - kinase inhibitor	Inhibited	-3.183	3.28E-08	CXCL3,CXCL8,CYP1A1,DKK1,DNAJC3,DUSP1,EFNA1,EGR1,EHF,EIF2AK2,EREG,FAS,FOS,FOSB,GADD45A,GSTA4,IFI35,IFIT3,IL1RN,IRF1,IRF7,JUN,JUND,MAT2A,MUC2,MXD1,P	508 (20)
rotlerin							



Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
SREBF2		transcription regulator	Inhibited	-3.376	0.00000216	ACSL1,ACSS2,BMP4,CXCL1,CXCL8,ELOVL6,HESE6,HMGR,IDI1,INSIG1,IRS2,LSS,MSMO1,PPARG,SC5D,SOLE,TFF3	491 (21)
Hdac		group	Inhibited	-3.414	4.46E-08	L6,CCNG2,CRABP2,CXCL8,CXCR4,CYP24A1,EDN1,EGR1,FBXO32,FOS,FOSL1,GADD45B,GLI2,HPGD,JUN,KLF6,KLF9,MT1E,MXD1,NPNT,NRP1,ONECUT2,SMPD3,STX1A,TGFBF	458 (19)
NKX2-3		transcription regulator	Inhibited	-3.499	6.72E-13	EDN1,EIF2AK2,F2RL1,GASK1B,GDF15,HLA-B,HLA-C,KLF4,LGMN,MMP7,PARP10,PARP12,PARP14,PLD1,PLSCR1,PMAIP1,PSMB8,PTGS2,RNF213,SAMD9,SEMA3A,SERPINE2,SF	
SCAP		other	Inhibited	-3.541	0.00000653	ACSL1,ACSS2,ATF3,CYP2B6,ELOVL6,HESE6,HMGR,HMGCS2,IDI1,INSIG1,LGALS3,LSS,MSMO1,PTGS2,SC5D,SOLE,TFF3	340 (11)
TRIM24		transcription regulator	Inhibited	-3.628	0.0000946	CYP24A1,FLRT3,GBP3,HERC6,IFI35,IFI44,IFIH1,IFIT3,IFNGR2,IRF1,IRF7,LGALS3,LGALS3BP,NMI,PARP12,PLAC8,PSMB10,PSMB8	314 (14)
mibolerone		chemical drug	Inhibited	-3.638	0.000157	ACSL1,ALCAM,AMD1,AQP5,CEACAM1,CLU,DHRS3,DNAJA4,HLA-E,INCENP,IRF7,JUN,LSS,MAT2A,SLC22A5,SOLE,STMN1,TMED3	
RC3H1		enzyme	Inhibited	-3.769	1.11E-09	APOBEC3B,CD44,CLDN1,CXCL2,EDN1,FOSL1,HSPB1,IFI44,IFIT3,IFITM3,IRF1,MT2A,NRP1,OAS3,PLSCR1,SHFL,TRIM21,TRIM25,TRIM56	460 (12)
IL1RN	0.525	cytokine	Inhibited	-4.188	5.89E-12	I,CD44,CHAC1,CTSS,CXCL1,CXCL3,CXCL8,CYP3A5,ERAP2,GSDMD,HDAC9,HERC6,IFI44,IFIH1,IFIT3,IRF1,IRF7,KLF6,LGALS9,LIF,NR0B2,OAS3,PMAIP1,PML,PTGS2,RARRES1,S	471 (17)
phosphatidylinositol		chemical - endogenous mammalian			0.0428	ACAT1,CXCL8	
sphingosylphosphocholine		chemical - endogenous mammalian			0.00789	FOS,JUN,TGM2	469 (18)
1,2-dioctanoyl-sn-glycerol		chemical reagent			0.0217	JUN,VDR	
octanoic acid		chemical - endogenous mammalian			0.0285	CEBPA,DGAT2,PPARG	
16,16-dimethylprostaglandin E2		chemical - endogenous mammalian			0.00789	CD44,FOS,NOX1	300 (12)
(+)-fluprostenol		chemical drug			0.0217	NOX1,PPARG	
epoprostenol		chemical - endogenous mammalian			0.0408	EGR1,FOS,PTGS2	
12(S)-hydroxyeicosatetraenoic acid		chemical - endogenous non-mammalian			0.00546	PAG1,PPARG,PTGS2	445 (18)
ATP-gamma-S		chemical reagent			0.000384	BTG1,CD55,CXCL2,CXCL8,CXCR4,EREG,IL15RA,IL1R2,NRP1,PTGS2,WARS1	524 (21)
zidovudine		chemical drug			0.0241	BCL10,BCL3,CPT1A,CXCL8	
acyclovir		chemical drug			0.049	DUSP2	
propylthiouracil		chemical drug			0.0169	AKR1C3,CXCL2,GSN,IGF2,JUN,LOC102724788/PRODH,NRP1,NSMF,PHLDA1,QPCT,SPINK1	
3-aminoisobutanoate		chemical - endogenous mammalian			0.049	CPT1A	
L-cysteine		chemical - endogenous mammalian			0.00789	CXCL8,FOS,PCK2	424 (18)
L-methionine		chemical - endogenous mammalian			0.0208	CLU,CXCL2,GADD45B,MAT2A,PCK2,RHOB,SPHK2	
sorbitol		chemical - endogenous mammalian			0.00387	CCN1,ERRF1,SGK1,SORD	171 (7)
glycerol		chemical - endogenous mammalian			0.0408	GLI1,PPARG,SCARB1	
pelargonidin		chemical - endogenous non-mammalian			0.049	CYP1A1	
amphotericin B		chemical drug			0.0343	CXCL8,IL1RN,LCN2	
ginsenoside Rb1		chemical - endogenous non-mammalian			0.0285	CXCL8,FOS,HBEGF	
saikosaponin A		chemical reagent			0.000343	BMP4,CDKN2B,FOS,JUN	422 (13)
epothilone B		chemical drug			0.0408	FAS,MCL1,TBC1D1	
troandomycin		chemical drug			0.049	CYP3A5	
3,7,12-trihydroxycoprostanol		chemical - endogenous mammalian			0.049	CYP3A5	
6beta-hydroxyestradiol-17beta		chemical - endogenous non-mammalian			0.049	CYP2B6	
estrone		chemical - endogenous mammalian			0.0343	CYP2B6,IRS2,PIK3R1	
taurothiocholate-3-sulfate		chemical - endogenous mammalian			0.049	ABCC2	
glycochenodeoxycholate		chemical - endogenous mammalian			0.0285	BIRC3,HPGD,NR0B2	
Srebp		group			0.0123	ACSL1,ACSS2,FOS,NPC1	
taurochenodeoxycholate		chemical - endogenous mammalian			0.00697	HPGD,NR0B2	
cholesterol sulfate		chemical - endogenous mammalian			0.00789	FOSL1,JUN,NR1D1	241 (11)
CP-55940		chemical reagent			0.0368	CXCL8,GADD45A,GRK5,JUN,UBC	
fluoride		chemical - endogenous mammalian			0.00651	FAS,FOS,GADD45A,RUNX2	234 (13)
dopamine D1 receptor		group			0.0428	FOS,FOSB	
TEAD		group			0.0109	CAV2,CCN1,CD44	
Histone H2b		group			0.0428	IRF1,PPP1R3B	
asialo GM1 ganglioside		chemical - endogenous mammalian			0.0217	CXCL8,MUC2	
thromboxane A2		chemical - endogenous mammalian			0.049	PTGS2	
2'-adenylic acid		chemical - endogenous mammalian			0.049	TXNIP	
dibutyryl cGMP		chemical reagent			0.0217	AQP5,PTGS2	
Rp-8-CPT-cAMPS		chemical - kinase inhibitor			0.049	SCARB1	
ADP		chemical - endogenous mammalian			0.0343	CXCL8,FOS,REN	
desoxycorticosterone		chemical - endogenous mammalian			0.0478	CXCL2,FOS,PTGS2	
monooleylphosphatidic acid		chemical - endogenous mammalian			0.00697	EREG,PLPP3	
pCPT-cAMP		chemical - kinase inhibitor			0.0478	EGR1,FOS,JUN	
clobetasol propionate		chemical drug			0.0185	ABCC1,CYP3A5,FAS	
beclomethasone dipropionate		chemical drug			0.049	CYP3A5	
bevacizumab		biologic drug			0.0478	ANGPT1,CXCR4,NRP1	
afatinib B1		chemical - endogenous non-mammalian			0.0109	CYP1A1,CYP3A5,IRS2	
GON4L		transcription regulator			0.0285	CCNA2,CCNF,MYB	
ADRA1		group			0.0217	EGR1,FOS	
dienogest		chemical drug			0.0217	CXCL8,PTGS2	
pivaloyloxymethyl butyrate		chemical drug			0.049	ATP2A3	
(6)-gingerol		chemical - endogenous non-mammalian			0.0428	CDK6,PTGS2	
cyanuric acid		chemical reagent			0.049	CXCL8	
eicosa-11Z, 14Z-dienoic acid		chemical - endogenous mammalian			0.049	PNPLA2	
styrene		chemical toxicant			0.0217	EGR1,HSPA1L	
peptide YY 3-36		biologic drug			0.049	FOS	
ATXN8OS		other			0.0217	ANGPT1,TGFBF2	
MEG3		other			0.0285	GDF15,JUN,PHLPP1	
decabromobiphenyl ether		chemical toxicant			0.0135	CYP2B6,CYP3A5	
trans-cinnamaldehyde		chemical drug			0.0241	CXCL8,EGR1,FAS,PTGS2	
pyrvinium		chemical drug			0.0316	AXIN2,ID2	
2-amino-5-azotoluene		chemical toxicant			0.00546	ABCC2,CYP2B6,CYP3A5	
hydroxamic acid		chemical - other			0.049	CXCR4	
JINK1/2		group			0.041	AXIN2,FAS,PTGS2,RHOB	
Sos		group			1.62E-08	I,CRABP2,ELOVL6,FOS,IRS2,KLF6,KRT13,LGALS3BP,LGALS4,LRP8,LTBP3,MAOA,MAP4K4,MXD1,NR1P1,PHLDA1,PKN1,PLD1,PTGS2,RAP1GAP,SEMA3B,SEMA3E,SMURF1,STM	515 (23)
Pdgfr		group			0.0232	EGR1,EREG,HBEGF	
LTB4R/LTB4R2		group			0.049	CXCL8	
Goq		group			0.049	PTGS2	
NDPK		group			0.049	CXCL8	
Rsk		group			0.0135	CXCL2,CXCL8	
Foxo		group			0.00106	ABCC2,CDKN2B,FBXO32,GADD45A,PMAIP1	388 (7)
CaMKII		complex			0.0207	BIRC3,CD44,FOS,IRF1	
Actin		group			0.0285	ABCC1,CD44,LPP	
C4BP		complex			0.00546	HMGR,IDI1,MSMO1	
RNA polymerase II		complex			0.0000425	CXCL8,CXCR4,CYP1A1,CYP24A1,DKK1,DUSP1,FOS,FOSL1,GADD45A,GADD45B,GDF15,HNF4A,HSPA1A/HSPA1B,IL1RN,JUN,KITLG,NCOA3,NR5A2,PPARG,PRR15L,PTGS2,RND	461 (13)
tyrosine kinase		group			0.0135	CD44,CYP1A1	
beta-glucuronidase		group			0.049	PTGS2	
nicotinic acetylcholine receptor		complex			0.0428	FOS,JUN	
15-LOX		group			0.00697	MAOA,PPARG	
MKK3/6		group			0.049	CXCL8	
Histone h3		group			0.00000515	PA,CSPG4,CXCL8,CYP3A5,DKK1,DUSP16,DUSP2,EFNA1,EGR1,FGFR2,FOS,GATA2,GATA6,GLI1,HNF4A,HOXA5,ID2,IFITM3,IGFBP2,IRF7,JUN,MEIS2,MTUS1,PMAIP1,PPARG,PR	502 (21)
Fgf		group			0.0212	FOS,JUN,LPCAT1,PTGS2,RUNX2	
Gli		group			0.0123	GLI1,JAG2,RUNX2,S100A4	
MSK1/2		group			0.0024	DUSP1,FOS	
adenosine deaminase		group			0.049	CXCL3	344 (7)
Erm		group			0.0217	CAV1,CD44	
ETS		group			0.0207	EGR1,ENG,FOS,HPGD	
growth factor receptor		group			0.049	FOS	
N-cor		group			0.00143	ACSL1,AXIN2,CDK6,CTSS,CXCL2,DHRS3,ELOVL6,HBEGF,HIVEP2,PTGS2,RHOB,SGK1,TBC1D2	451 (13)
Ctnna		group			0.0217	AXIN2,CXCR4	
desmethoxyangonin		chemical - endogenous non-mammalian			0.049	CYP3A5	
dihydrokawain		chemical - endogenous non-mammalian			0.049	CYP3A5	

Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
Stat1 dimer		complex			0.00354	EIF2AK2,IRF1,PIM1	153 (7)
Stat1-Stat2		complex			0.0109	EIF2AK2,IRF1,IRF7	
Smad2/3-Smad4		complex			0.0478	CDKN2B,HMGA2,IRF7	
Integrin		complex			0.0478	FOS,JUN,TGFB2	
Bcl9-Cbp/p300-Cttnb1-Lef/Tcf		complex			0.00789	AXIN2,CD44,MMP7	
rifamycin SV		chemical drug			0.049	BCL6	
2,2',4,4',5,5'-hexabromodiphenyl ether		chemical reagent			0.049	CYP1A1	
endrin		chemical toxicant			0.0024	CEBPA,PPARG	197 (7)
5,7-dimethoxyflavone		chemical - endogenous mammalian			0.049	CYP1A1	
DE 71		chemical reagent			0.049	CYP1A1	
3',5'-methoxyflavone		chemical reagent			0.049	PTGS2	
perfluorooctanoic acid		chemical reagent			0.0408	CXCL8,DNMT3A,HMGR	
stevioside		chemical - endogenous non-mammalian			0.0135	PPARG,PTGS2	
miocamycin		chemical drug			0.049	MUC2	
aurapten		chemical - endogenous non-mammalian			0.00109	CPT1A,CXCL8,PTGS2	170 (7)
Hottip		other			0.0217	SMAD3,TGFB2	
JUN/JUNB/JUND		group			0.041	CCN1,FOS,FOSL1,JUN	
Rxr		group			0.000139	ABC110,ABCC2,CPT1A,CTSS,CYP24A1,CYP2B6,CYP3A5,GADD45A,HBEGF,INSIG1,KDM6B,NR0B2,NR5A2,PKD4,PPARG,PTGS2	456 (23)
RAR-RXR		complex			0.0217	IRF1,TGM2	
tylophorine		chemical drug			0.0135	JUN,PTGS2	
MLN8054		chemical drug			0.00697	BBC3,PMAIP1	
perhexiline		chemical drug			0.0232	DEPP1,LSS,SERPINA3	
chlorcyclizine		chemical drug			0.0185	DEPP1,LSS,SERPINA3	
rh-endostatin		chemical drug			0.00354	FAS,JUN,MAP1LC3B	
Cytochrome bc1		complex			0.049	MAOA	
CDKN2B-AS1		other			0.0285	CDKN2B,CXCL8,PTGS2	
zinc oxide		chemical drug			0.0316	MT1E,MT1X	
vanillyl-N-nonylamide		chemical drug			0.0021	ATF3,CCNG2,GADD45A	
sucralose		chemical reagent			0.0135	CEBPA,PPARG	
loxoprofen		chemical drug			0.049	MUC2	
tacedinaline		chemical drug			0.0021	ELF3,FOS,IGF2	
obatoxax		chemical drug			0.0021	ATF3,MCL1,PMAIP1	
PRC2		complex			0.024	CEACAM1,CEACAM6,CXCL1,CXCL8,GATA6,MMP7	
G-Actin		group			0.049	JUN	
thyroid hormone receptor		group			0.0363	CPT1A,FOS,KLF9,NR5A2	
3-iodothyronamine		chemical - endogenous mammalian			0.049	IRS2	
25-hydroxyvitamin D		chemical drug			0.0024	CYP24A1,VDR	
bendamustine		chemical drug			0.00789	AURKA,MCL1,PMAIP1	367 (7)
PKR dimer		complex			0.049	ATF3	
MAP2K4/7		group			0.049	PTGS2	
Retinoic acid-RAR-RXR		complex			0.00546	CRABP2,DUSP1,TGFB2	
bovine testicular hyaluronidase		biologic drug			0.049	CD44	
dihydromethysticin		chemical - endogenous non-mammalian			0.049	CYP3A5	
NF279		chemical reagent			0.049	CXCL8	
muraglitazar		chemical drug			0.00697	EDN1,REN	302 (7)
ZM 323881		chemical - kinase inhibitor			0.049	RCAN1	
ALKBH5		enzyme			0.0232	CAV1,CLU,DNAJA1,FYN,IGF2,JAG2,PRDX4,RGS2,SERPINA5	
LRRRC26		ion channel			0.0316	CXCL1,CXCL8	
GSK 189254		chemical drug			0.049	FOS	
MBNL3		other			0.0024	ABLIM1,CD44	
INTS11		other			0.00697	EGR1,FOSB	
trypsin		group			0.0232	CXCL8,FOS,PTGS2	
(-)-OSU 6162		chemical drug			0.049	FOS	
ASB9		transcription regulator			0.049	CKB	
RNF187		enzyme			0.0217	HBEGF,JUN	
IGF2BP2		translation regulator			0.0135	ELOVL6,LIMS2	
CYP2R1		enzyme			0.049	VDR	
FIJD		enzyme			0.000452	DNAJB1,HSPA1A/HSPA1B,HSPB1	
Pad2		other			0.049	PTGS2	
SLC22A2		transporter			0.0217	CPT1A,SLC22A5	
LPIN1		phosphatase			0.0144	CEBPA,CPT1A,HMGR,PPARG,PTGS2	
patulin		chemical toxicant			0.0428	ATF3,CYP1A1	
LGALS12		other			0.0217	CEBPA,PPARG	
RNF217-AS1		other			0.049	INTU	
pridopidine		chemical drug			0.049	FOS	
LINC01139		other			0.0109	EGR1,LDHA,SLC16A3	
PDCD10		other			0.0428	KLF4,PROCR	
SSC5D		transmembrane receptor			0.049	CXCL8	
TMC8		other			0.049	CIB1	
SLC27A4		transporter			0.0135	CEBPA,PPARG	
RHOJ		enzyme			0.00183	AKAP12,ANXA1,CAV1,GSN,RND3	
IL1RL2		transmembrane receptor			0.0408	CXCL1,CXCL2,CXCL8	
TFAP2D		transcription regulator			0.049	MT2A	
BSCL2		other			0.0393	ACSL1,AKR1C3,CEBPA,GPD1,PNPLA2,PPARG,PTGS2	
NPC1	0.332	transporter			0.000345	CAV1,CAV2,CD68,EGR1,HMGR,IDI1,KLF4,LGALS3,LIPG,LSS,MMP15,NPC1,PTGS2	413 (17)
MARCHF3		other			0.0217	CXCL1,CXCL8	
FBXO11		enzyme			0.049	BCL6	
FBXO25		enzyme			0.0024	EGR1,FOS	127 (5)
ZNF652		other			0.0428	TGFB2,TGFB2	
APOL1	0.986	transporter			0.0144	CXCL2,IFNGR2,MUC13	
TRIM29		transcription regulator			0.0428	CD44,PMAIP1	
CD3-TCR	-0.497	complex			0.049	TOB1	
SRF-ELK1		complex			0.049	FOS	
Gpcr		group			0.0217	FOS,JUN	
KREMEN1		other			0.049	AXIN2	
BCAS2		other			0.0217	BBC3,PMAIP1	
H2BW2		other			0.049	DNMT3A	
PCOLCE2		other			0.049	SCARB1	
SLC15A4		transporter			0.049	IRF7	
ATOH7		other			0.0217	FGF19,SOX4	
ZC3H14		other			0.0478	IL15RA,NMI,TSC22D1	
SLC51B		transporter			0.049	NROB2	
ADTRP		enzyme			0.049	TFPI	
RSP03		kinase			0.00789	AXIN2,GLI1,PTGS2	236 (7)
STEAP1	0.932	transporter			0.0024	CEBPA,PPARG	
PPIP5K1		phosphatase			0.049	RUNX2	
RNA5EH2A		enzyme			0.0000303	IFI35,IFI44,IFIH1,IFIT3,IFITM3,IFNGR2,IRF1,IRF7,NMI,PTGS2,TRIM21	
PRDM5		transcription regulator			0.00108	APOBEC3B,CEMP,GADD45B,IDO2,MYB,NCOA7,OVOL1,PML,RUNX2,S100A2,STK32C,TINAGL1	
PRG3		other			0.049	CXCL8	
PRKAG3		other			0.000519	ACVR1,AMD1,ATP1B1,CCNDP1,CD55,EGR1,HIVEP2,KDM2B,KLF4,MAT2A,NEO1,NRIP1,RHOU,RNF128,SNCG,SORD,TSPAN8,UGT1A10 (includes others),ZFP36	
HSPBP1		other			0.0135	HSPA1A/HSPA1B,HSPA1L	
FNDC3B		other			0.049	RUNX2	

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Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
RND2		enzyme		0.049	0.049	RHOB	
FCN1		other		0.049	0.049	CXCL8	
PPP2R2D		other		0.049	0.049	PPARG	
HCAR1	0.404	G-protein coupled receptor		0.0185	0.0185	EDN1,SLC16A1,SLC16A3	
POLR3G		enzyme		0.0232	0.0232	AURKA,KLF6,S100A4	
procyanidin B2		chemical - endogenous non-mammalian		0.049	0.049	PTGS2	
BUD23		enzyme		0.0217	0.0217	CXCL8,TSC22D3	
TMEM184A		other		0.049	0.049	DUSP1	
B3GNT6		enzyme		0.049	0.049	MUC2	
UBN1		transcription regulator		0.049	0.049	CCNA2	
LMAN1		other		0.049	0.049	F5	
IKBIP		other		0.0135	0.0135	CXCL2,NFKBIZ	
USP9Y		peptidase		0.049	0.049	MUC2	
C1QL4		other		0.0024	0.0024	CEBPA,PPARG	
IQCB1		other		0.049	0.049	BBC3	
CLDN9		other		0.049	0.049	TJP1	
ZMIZ2		transcription regulator		0.00109	0.00109	AXIN2,CD44,JUN	
Histone h4		group		0.00103	0.00103	AKAP12,CDC25A,CXCL3,CXCL8,CYP24A1,DKK1,DUSP16,FOS,IRF1,KIF13B,NEDD4L,OAS3,PMAIP1,PPARG,PTGS2,RUNX2,TGFBR2	478 (20)
CUZD1		other		0.0217	0.0217	EREG,ID2	
TRIM17		enzyme		0.049	0.049	MCL1	
ZNF580		transcription regulator		0.049	0.049	CXCL8	
CCDC22		other		0.049	0.049	BIRC3	
MBOAT7	0.307	enzyme		0.0185	0.0185	ACSS2,ELOVL6,HMGCR	
SELENOS		other		0.0343	0.0343	CAV1,CEBPA,PPARG	
CIRBP	0.347	translation regulator		0.0135	0.0135	CXCL2,CXCL3	
IFNA17		cytokine		0.0285	0.0285	EIF2AK2,IFIH1,PLAAT4	
potassium channel		group		0.00697	0.00697	FOS,JUN	
sGC		complex		0.0217	0.0217	EGR1,FOS	
TCF/LEF		group		0.0343	0.0343	JUN,PTGS2,RUNX2	
GPR39		G-protein coupled receptor		0.0316	0.0316	CLU,PNPLA2	
NAA30		enzyme		0.00697	0.00697	FAS,PMAIP1	
GALNT4		enzyme		0.0428	0.0428	SMAD3,TJP1	
EIF3M		other		0.0316	0.0316	CDC25A,MT2A	
ARID2		transcription regulator		0.0217	0.0217	BMP4,FGFR2	
METTL8		enzyme		0.0024	0.0024	CEBPA,PPARG	
MDGA2		other		0.0232	0.0232	CASP9,FAS,SESN2	
CACNA1C		ion channel		0.00546	0.00546	CAV1,PTGS2,S100A10	163 (7)
PIWIL4		other		0.0316	0.0316	FGFR2,TGFBR2	
MLL11		other		0.049	0.049	CD44	
RGMB		other		0.0021	0.0021	CXCL2,CXCL3,LCN2	
BATF2		other		0.0024	0.0024	CCN1,JUN	296 (7)
BCO1		enzyme		0.00287	0.00287	ARRDC3,NR1D1,PPARG,SCARB1	
MAPKBP1		other		0.049	0.049	CXCL8	
ZG16B		other		0.049	0.049	CXCR4	
KCTD10		ion channel		0.049	0.049	RHOB	
Dcpp1 (includes others)		other		0.049	0.049	OTUD7B	
NSD1		transcription regulator		0.0343	0.0343	BMP4,KLF6,ZFP36L1	
harman		chemical - endogenous non-mammalian		0.049	0.049	CYP1A1	
USP47		peptidase		0.049	0.049	CDC25A	
CPB1		peptidase		0.049	0.049	CASP4	
FGF14		growth factor		0.049	0.049	FOS	
CERK		kinase		0.0368	0.0368	CLCF1,CXCL1,CXCL2,CXCL8,CXCR4	
QRFP		other		0.00354	0.00354	ACSL1,CEBPA,PPARG	
CDC73		other		0.0078	0.0078	GATA2,HMGCS2,IGF2,IRF1,LGALS3	290 (7)
CAMSAP2		other		0.049	0.049	TJP1	
DSC2		other		0.049	0.049	CD44	
TRPM3		ion channel		0.049	0.049	EGR1	
FAM3B		cytokine		0.0241	0.0241	CASP4,CAV1,LCN2,LDHA	
KLHL21		other		0.00697	0.00697	DUSP1,NFKBIZ	
MLXIP		transcription regulator		0.0024	0.0024	ARRDC4,TXNIP	
STEAP2	0.777	enzyme		0.0024	0.0024	CEBPA,PPARG	
LRRC4		other		0.049	0.049	STMN1	
CCDC8		other		0.049	0.049	BBC3	
NSD2		enzyme		0.000426	0.000426	BACE2,CDC25A,CXCR4,FOS,GADD45A,IRF7,JUN,PRKCA	249 (7)
FANK1		transcription regulator		0.049	0.049	JUN	
SLC4A7		transporter		0.049	0.049	SLC16A1	
CLEC12A		other		0.0316	0.0316	IFIT3,IRF7	
SBDS		other		0.000345	0.000345	AKR1C1/AKR1C2,AKR1C3,CHAC1,DNAJB1,EGR1,FBXO32,FOS,GADD45B,HSPA6,MAFF,MAOA,MT2A,PPP1R15A	398 (14)
TCIM		other		0.00354	0.00354	CXCL1,CXCL8,PTGS2	441 (11)
LTPB4	-0.661	growth factor		0.00546	0.00546	BMP4,ID2,TGFBR2	
Gata6os		other		0.049	0.049	GATA6	
Hedgehog		group		0.0106	0.0106	CCNA2,FOXL1,GATA6,HOXA5,IGF2,KLF4,VIL1	
Sapk		group		0.000452	0.000452	FBXO32,FOS,GADD45A	254 (10)
GPX6		enzyme		0.049	0.049	PPP1R1B	
MBNL2		other		0.049	0.049	ABLIM1	
GPR68		G-protein coupled receptor		0.0217	0.0217	DUSP1,PTGS2	
nickel sulfide		chemical reagent		0.049	0.049	PTGS2	
rimantadine		chemical drug		0.049	0.049	CXCL8	
Eif2		complex		0.0135	0.0135	EIF2AK2,PTGS2	
sphingomyelinase		group		0.0428	0.0428	JUN,PTGS2	
P-TEFb		complex		0.0135	0.0135	BBC3,CXCL8	
black raspberry extract		chemical drug		0.00943	0.00943	ADAMTS6,AKR1B10,AMBIP,CD44,CLDN1,DUSP5,KRT20,MCL1,PIP5K1A,PLK3,SCEL,SLC30A1	
FAS-AS1		other		0.049	0.049	FAS	
Myosin2		complex		0.049	0.049	PPARG	
Pro-inflammatory Cytokine		group		0.00699	0.00699	ABCC2,ASS1,CD55,CLU,LCN2,LGALS9,LIPG,PI3,SDC4	
proanthocyanidin derivative		chemical - other		0.0135	0.0135	CYP1A1,JUN	
Tpl2 kinase inhibitor		chemical - kinase inhibitor		0.049	0.049	PTGS2	
IL7R		transmembrane receptor		0.00344	0.00344	C1orf116,CXCL8,DAPK1,DPP4,FHL2,MCL1,MMRN2,PCSK6,PIM1,SKAP1,TJP3	
TAF9		transcription regulator		0.0217	0.0217	CXCL8,IRF1	
cis-vaccenic acid		chemical - endogenous mammalian		0.049	0.049	PNPLA2	
iguratimod		chemical drug		0.0428	0.0428	CXCL2,CXCL3	
IDH2		enzyme		0.00387	0.00387	CEBPA,EGR1,PPARG,TGFBR2	248 (7)
hispidulin		chemical drug		0.049	0.049	EGR1	
urotensin II		biologic drug		0.0428	0.0428	CXCL8,SMAD3	
NNZ 2566		biologic drug		0.049	0.049	ATF3	
neurotrophin		chemical drug		0.049	0.049	SEMA3A	
vasopressins		biologic drug		0.049	0.049	FOS	
firtecan pegol		chemical drug		0.0135	0.0135	CA9,CXCR4	
pycnogenols		chemical drug		0.00697	0.00697	CXCL8,PTGS2	
HCV 796		chemical drug		0.049	0.049	MAP1LC3B	
mediator		complex		0.049	0.049	FOS	
7S NGF		complex		0.0217	0.0217	CLU,FOS	

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Ppp2c		group			0.0232	CDKN2B,DUSP1,PIM1	
p85 (pi3r)		group			0.0478	MCL1,PPARG,PTGS2	
Mucin		group			0.0217	CXCL8,PTGS2	
Pik3r		group			0.0316	BBC3,CXCL8	
Rho gdi		group			0.049	RHOB	
LAMTOR5		other			0.0232	CXCL8,LDHA,S100A4	
BCOR		transcription regulator			0.0207	ARID5B,ETV6,GLI1,GLI2	
PMF1/PMF1-BGLAP		transcription regulator			0.049	SAT1	
ASCL2		transcription regulator			0.0428	CXCR4,EGR1	
FLII		other			0.0135	CLDN1,CXCL8	
MEIS2	0.552	transcription regulator			0.0316	CDKN2B,ETV1	
PF-4523655		biologic drug			0.049	DDIT4	
PDGFD		growth factor			0.0428	CXCR4,PTGS2	
cucurbitacin E		chemical - endogenous non-mammalian			0.049	PTGS2	
bitertanol		chemical drug			0.0135	CYP1A1,CYP3A5	
ARHGEF17		other			0.049	FOS	
interferon beta-1a		biologic drug			0.0011	ATP5MC3,CXCR4,DNAJA1,DNAJB1,GADD45B,IFI35,IL1RN,IRF1,IRF7,NMI,PSMB8,PSME1,SERPINA1,TBXAS1,UOCRFS1	219 (8)
idelalisib		chemical drug			0.0428	MCL1,UGCG	
IER3		other			0.0428	BIRC3,MCL1	
RAB11FIP3		other			0.0135	FOS,JUN	
ANTXR1		transmembrane receptor			0.049	HSPA1A/HSPA1B	
pidilizumab		biologic drug			0.049	CXCR4	
Atf		group			0.0217	JUN,PTGS2	
DIO1		enzyme			0.0135	SLC16A1,SLC16A3	
NCOR2		transcription regulator			0.0017	AXIN2,BIRC3,CEBPA,CTSS,CXCL8,FOS,HBEGF,JUN,PTGS2	506 (25)
MEDI-547		biologic drug			0.049	EPHA2	
PF-4691502		chemical drug			0.0135	BBC3,PMAIP1	
GSK0660		chemical reagent			0.0428	FBXO32,PKD4	
NELFB		other			0.0185	ATF3,GADD45A,GADD45B	
cercosporin		chemical - endogenous non-mammalian			0.0109	AXIN2,CDC25A,DKK1	
IGF2R		transmembrane receptor			0.0109	IGF2,NEDD9,NPC1	
APOA4		transporter			0.0285	DGAT2,FOS,SCARB1	
TMC6		transporter			0.049	CIB1	
GTF2H2		transcription regulator			0.049	KLIF9	
SYTL4		transporter			0.049	STX1A	
FAK4		kinase			0.0185	NOX1,PPARG,TJP1	
NOD1		other			0.0123	CARD6,CXCL2,CXCL8,DUSP1	
RAP1GAP	-0.574	other			0.0428	CDK6,FOS	
GPLD1		enzyme			0.049	LGALS3BP	
MBNL1		other			0.0185	ABLIM1,SOX4,TGFB2	
GNA14	-0.765	enzyme			0.000000306	AKAP12,ATF3,BMP4,CSPG4,CXCL3,CXCL8,DUSP5,GADD45A,HBEGF,IL1RN,KLF6,LIF,PHLDA1,PTGS2,SGK1,ZFP36L1	309 (14)
REV1		enzyme			0.00354	BBC3,PMAIP1,SES2	367 (7)
ITGA5		transmembrane receptor			0.0317	CD44,FOS,IGF2,IGFBP2,JUN,TGFB2	
CD244		transmembrane receptor			0.0109	CXCL8,EGR1,FOS	
EDN2		growth factor			0.049	PTGS2	
TLX1		transcription regulator			0.0461	GATA2,MCL1,MYB,NMI	
YWHAQ		other			0.00507	CASP7,CASP9,ETV1,MMP7	
CTF1		cytokine			0.00863	CEBPD,FOS,IRF1,PNPLA2,PPARG,SERPINA3	506 (19)
OPRK1		G-protein coupled receptor			0.0021	FOS,NRP1,PLXND1	297 (7)
AHRR		transcription regulator			0.049	CYP1A1	
FAF1		other			0.00109	AXIN2,DKK1,RUNX2	289 (7)
KIFAP3		other			0.049	FOS	
TFDP1		transcription regulator			0.0299	CASP7,CASP9,FGFR2,MYB,STMN1	
RAB27A		enzyme			0.049	CD44	
AGR2	-0.77	other			0.0428	EGR1,FOS	
LGALS8		other			0.0109	CXCL1,CXCL3,CXCL8	
ZBTB33		transcription regulator			0.000557	BBC3,BCL6,FAS,MMP7,S100A4	
PPY		other			0.049	FOS	
PROK2		other			0.0316	CDC25A,FOS	
IDH1		enzyme			0.013	EGR1,GLI1,PPARG,PPP1R15A,RUNX2,SERPINH1,TGFB2	
POU2F1		transcription regulator			0.00262	ACSL1,BBC3,BCL6,CD55,CXCL8,CYP1A1,CYP2B6,DDIT4,FRRS1,GADD45A,JUND,PDE9A,REL,SES2	412 (12)
RXRβ		ligand-dependent nuclear receptor			0.00288	ACSL1,ALDH1A1,CTSS,CYP24A1,ECM1,FLRT3,HBEGF,IGFBP6,LCN2,S100A4	353 (13)
LINC01370		other			0.049	GLIS3	
LINC01503		other			0.049	FOSL1	
entolimod		biologic drug			0.0316	CXCL2,CXCL3	
WBP11		phosphatase			0.049	TUBGCP6	
GPHA2		other			0.049	FOS	
SYMPK		other			0.0024	CLDN2,TJP1	
dodecylbenzenesulfonic acid		chemical reagent			0.049	Pi3	
cyproconazole		chemical drug			0.0024	CYP2B6,GADD45B	
recombinant interferon alpha		biologic drug			0.049	RNF213	
SNX9		transporter			0.049	ADAM9	
OSMR		transmembrane receptor			0.00345	BCL3,BIRC3,CASP4,CXCL2,FOS,PIM1,SBNO2,SERPINA1,ZFP36	394 (18)
KSR2		kinase			0.049	CXCL8	
CIC		transcription regulator			0.0185	ETV1,FOSL1,MAFF	
NMB		other			0.0024	FOS,JUN	444 (22)
MPZ		other			0.00000241	DNAJC3,HMGCR,ID2,JUN,PPP1R15A,SDF2L1,SOX4,SQLE	
NFYB		transcription regulator			0.0139	AMD1,APOBEC3B,CAV1,CDC25A,CHPT1,DPP4,FAS,FGFR2,FRYL,GADD45A,GPR160,KDM8,PAQR5,PITPNM3,RHOB,RUNX2,S100A4,SCARB1,SLC25A28,SLC39A8,TGFB2,TJP1	
CDK5R1		kinase			0.0123	CXCL8,FOS,PMAIP1,PPP1R1B	
LY96		transmembrane receptor			0.0408	CXCL2,CXCL3,CXCL8	
LBP		transporter			0.0478	CXCL3,CXCL8,IL1RN	
DAB2IP		other			0.0109	CD44,CLU,EGR1	
GNE		kinase			0.0428	CHAC1,JDP2	
PIAS2	-0.386	transcription regulator			0.0185	CDKN2B,FOS,IRF1	
DAB2		other			0.0428	FOS,HMGCR	
PHF19		other			0.0135	FGF19,HOXA5	
LOC102724788/PRODH	-1.858	enzyme			0.0217	LOC102724788/PRODH,PTGS2	
CHRM3		G-protein coupled receptor			0.0144	CCN1,EGR1,FOS	
SMC3		other			0.0343	CCNG2,IRS2,SOX4	
PNN		other			0.0343	GDF15,JUN,MMP7	
MDM4		transcription regulator			0.0478	BBC3,HIPK2,LGALS3	
Lysosomal Protease		group			0.049	MAP1LC3B	
miR-338-5p (miRNAs w/seed ACAUAU)		mature microRNA			0.049	SPINK1	
mir-338		microRNA			0.0217	RUNX2,SPINK1	
miR-516a-5p (miRNAs w/seed UCUCGAG)		mature microRNA			0.049	KLK10	
mir-506		microRNA			0.0428	CXCL8,SPDEF	
mir-488		microRNA			0.0217	ADAM9,CXCL8	
miR-27b-5p (miRNAs w/seed GAGCUUA)		mature microRNA			0.049	ATP2B1	
mir-196		microRNA			0.0343	ANXA1,FOS,HMGA2	
miR-293-3p (miRNAs w/seed GUGCCGC)		mature microRNA			0.049	DKK1	
miR-467a-5p (and other miRNAs w/seed AAGUGCC)		mature microRNA			0.049	DKK1	
miR-129-5p (and other miRNAs w/seed UUUUUGC)		mature microRNA			0.0343	DNMT3A,ETV6,SOX4	

Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
mir-129		microRNA			0.049	CXCL8	
mir-345		microRNA			0.049	ABCC1	
mir-193a-3p (and other miRNAs w/seed ACUGGCC)		mature microRNA			0.0144	ETS1,MCL1,RPS6KB2	
mir-489		microRNA			0.0217	ADAM9,MMP7	
miR-135a-5p (and other miRNAs w/seed AUGGCUU)		mature microRNA			0.0285	PPARG,RUNX2,TRPS1	
miR-125a-3p (miRNAs w/seed CAGGUGA)		mature microRNA			0.049	FYN	
miR-605-5p (miRNAs w/seed AAUCC)		mature microRNA			0.049	SEC24D	
miR-142-5p (and other miRNAs w/seed AUAAAGU)		mature microRNA			0.049	TGFBR2	
miR-23a-5p (and other miRNAs w/seed GGGUCC)		mature microRNA			0.049	LOC102724788/PRODH	
miR-186-5p (miRNAs w/seed AAAGAAU)		mature microRNA			0.0144	AURKA,HMGA2,TGFBR2	
miR-328-3p (and other miRNAs w/seed UGGCCCU)		mature microRNA			0.0135	CD44,CEBPA	
mir-199		microRNA			0.0408	DNMT3A,EDN1,EGLN1	
miR-690 (miRNAs w/seed AAGGCUA)		mature microRNA			0.049	CEBPA	
Mir690		microRNA			0.049	CEBPA	
miR-130a-3p (and other miRNAs w/seed AGUGCAA)		mature microRNA			0.0343	CXCL2,CXCL3,HOXA5	
mir-205		microRNA			0.0478	AXIN2,INPPL1,RUNX2	
miR-197-3p (and other miRNAs w/seed UCACCAC)		mature microRNA			0.0428	ACVR1,TGFBR2	
mir-663		microRNA			0.0024	CXCR4,HSPG2	
mir-1301		microRNA			0.049	KLF6	
mir-887		microRNA			0.049	PLD2	
MED15	0.292	transcription regulator			0.00789	BBC3,LIMA1,S100A2	
MIR3619		microRNA			0.049	PLD2	
KREMEN2		other			0.049	AXIN2	
PPP1R13B		phosphatase			0.0217	BBC3,LATS2	
TRIM28		transcription regulator			0.0452	CASP7,CXCR4,ETS1,MYEOV,PMAIP1,RCAN1,S100A4	
RGS19		enzyme			0.00546	AXIN2,BMP4,DKK1	
MLK		group			0.049	MMP7	
NUCB2	-0.489	other			0.0316	FOS,PTGS2	
RIPK4		kinase			0.0217	GRHL3,OVOL1	
HOXB9		transcription regulator			0.0101	CXCL8,EREG,REN,TGFB2	
WSB1		other			0.0217	CA9,HIPK2	
ABHD5		enzyme			0.0316	PKD4,PNPLA2	
ANXA4		other			0.049	CXCL8	
Is3		other			0.0217	EGR1,IRS2	
HBP1		transcription regulator			0.0232	H1-0,PIM1,PTGS2	
TIAL1		transcription regulator			0.0217	MAP1LC3B,TIA1	
NPVF		other			0.049	FOS	
KRT14		other			0.00984	CXCL1,CXCL8,GJB2,CLK10,CLK6,MMP7	299 (7)
RCE1		peptidase			0.0488	B2M,GPC4,HBEGF,RCN1,TGFB2	
HDAC3		transcription regulator			0.0192	BIRC3,CD55,CXCL2,CXCL8,ELOVL6,FOS,LGALS9,ME1,PHLPP1,PTGS2	
miR-211-3p (miRNAs w/seed CAGGGAC)		mature microRNA			0.049	CDK6	
MTA2		transcription regulator			0.0363	GATA2,ID2,JUN,SQLE	
IL1R2	-0.516	transmembrane receptor			0.0144	CXCL2,CXCL3,CXCL8	
F10		peptidase			0.0285	CCN1,CXCL8,EGR1	
ATN1		transcription regulator			0.0145	ATP1B1,ATP1B3,BCL6,CCNDBP1,ETV1,GRK5,GSN,HBEGF,MCAM,PSME1,SOX4,STMN1,TUBA4A	
DRD1		G-protein coupled receptor			0.00207	EGR1,FOS,FOSB,S100A10	441 (20)
TLE1		transcription regulator			0.0000174	ATF3,DUSP1,EGR1,FOS,MCL1,MEIS2	313 (7)
Scd2		enzyme			0.049	PPARG	
BORCS8-MEF2B		transcription regulator			0.049	JUN	
HCRT		other			0.0109	EGR1,FOS,KITLG	
GJA5		transporter			0.049	REN	
RBX1		enzyme			0.0428	MCL1,RHOB	
UTS2		other			0.0217	FOS,HPGD	
eprenetapopt		chemical drug			0.0368	BBC3,CARD10,GADD45B,MCL1,PMAIP1	
pituitary adenylate cyclase-activating polypeptide		biologic drug			0.00102	ACER2,AKR1B10,AXIN2,EGR1,ERRF1,FOSL1,FRRS1,MACROD1	
SLC30A9		transporter			0.049		
CAMK2		group			0.049	CYP1A1	
IL4I1		enzyme			0.00789	BIRC3	
DLC1		other			0.00354	CXCL1,CXCL8,TOB1	211 (7)
UGT2B4		enzyme			0.049	CDK6,CDKN2B,S100A10	
Nisch		other			0.0316	NROB2	
SIGLEC7		transmembrane receptor			0.049	FAS,FOS	
SIGLEC9		other			0.049	PTGS2	
ZNF613		transcription regulator			0.049	PTGS2	
COL4A2		other			0.049	ID2	
LY6D		other			0.049	FAS	
COX4I1		enzyme			0.0285	TSTA3	
FOXC1		transcription regulator			0.0279	PDK4,TGFB2,TSPAN8	
GNB2		enzyme			0.00863	CXCR4,MMP7,RUNX2,TSC22D1	
ELK4		transcription regulator			0.00287	CXCL3,DUSP1,FOSB,IL1R2,JAG2,TSC22D3	
PPM1B		phosphatase			0.0428	EGR1,FOS,FOSL1,NCOA7	250 (12)
BCAR1		enzyme			0.0232	CEBPD,HBEGF	
XIAP		enzyme			0.0363	CDKN2B,EGR1,MMP7	
ITGA1		other			0.0279	CDK6,CXCL1,CXCL8,PTGS2	
SUPT16H		transcription regulator			0.0363	CAV1,MMP7,PPARG,PTGS2	
DDB2		other			0.0185	DUSP5,EGR1,HSPA1A/HSPA1B,ID2	
GCLC		enzyme			0.000452	BBC3,EIF2AK2,SEMA3A	
SSPN		other			0.0316	FOS,JUN,SLC39A8	231 (7)
RNGTT		phosphatase			0.049	CEACAM5,PTGS2	
MAPKAP1		other			0.0408	SCARB1	
RAD51AP1		other			0.0316	CXCR4,DAPK1,SLFN5	
FABP2		transporter			0.0232	CD44,KLF4	
INSIG2		other			0.0343	CPT1A,HMGCR,PPARG	
GPI		enzyme			0.0478	ELOVL6,HMGCR,INSIG1	
LIMA1	0.456	other			0.0144	CAV1,CXCL8,STEAP4	
PIAS4		transcription regulator			0.0343	ID2,MMP7,VDR	
PIKfyve		kinase			0.0144	CXCL2,IRF1,PKD4	
SLC22A1		transporter			0.0428	ALDH1A1,ATF3,MAP1LC3B	
RPS6KA4		kinase			0.0185	CPT1A,SLC22A5	
WNK4	-0.875	kinase			0.0217	DUSP1,FOS,JUN	
ADRA1B		G-protein coupled receptor			0.029	CFTR,WNK4	
ADRA1A		G-protein coupled receptor			0.00316	CEBPD,DUSP1,EGR1,FOS,JUN,LIF	461 (23)
KCNE3	1.117	ion channel			0.000104	AKR1C3,CDHR5,CSRNP1,EPN3,FOSB,HMGCS2,HSPA1A/HSPA1B,KCNK5,KLF4,PHLDA1,PLK3,PTGS2	
ADRA1D		G-protein coupled receptor			0.029	CEBPD,DUSP1,EGR1,FOS,JUN,LIF	
ONECUT1		transcription regulator			0.00156	AMBPD,CDC25A,CEBPA,CEBPD,CLDN2,CXCL1,CXCL3,EHF,FAS,GSTA4,HMGCR,HNF4A,HSPA1A/HSPA1B,HSPH1,KDM8,LAMC2,MYOF,NROB2,PMAIP1,RARG,RBM48,SERPINA1,S	141 (5)
TNPO2		transporter			0.049	CXCL8	
PFFKB2		kinase			0.049	PDK4	
Zfp54		other			0.049	PPARG	
GATAD2B		transcription regulator			0.0024	CXCL8,PTGS2	
MEOX1		transcription regulator			0.0109	BMP4,GLI1,GLI2	
TIA1	0.395	other			0.0185	CCNA2,MAP1LC3B,PTGS2	
TYMP		growth factor			0.049	CXCL8	

Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
PTPRE		phosphatase			0.0285	CXCL2,CXCL3,TSC22D1	
TPSD1		peptidase			0.0428	CXCL8,PTGS2	
SLC1A2		transporter			0.049	FOS	
RAC2		enzyme			0.00358	ANXA1,FHL2,FOS,LDHA,MACF1,RUNX2,TSC22D1,ZYX	
IAPP		other			0.00234	BACE2,FOS,HMGCR,IDI1,MSMO1	303 (7)
KIDINS220		transcription regulator			0.0217	EGR1,FOS	
GPHB5		other			0.049	FOS	
anatabine		chemical - endogenous non-mammalian			0.0135	IL1R2,PTGS2	
SCN7A		ion channel			0.049	FOS	
RNF7		enzyme			0.049	JUN	
AURKAIP1		enzyme			0.049	AURKA	
RDX		other			0.049	ABCC2	
IGFBP4		other			0.0316	IGFBP6,MCAM	
CKS1B		kinase			0.0428	CCNA2,CXCL8	
TERC		other			0.00134	AURKA,CLU,EGR1,H1-0,HMGCR,NR1D1,TUBB2A	
CD3E		transmembrane receptor			0.015	BCL10,CBLB,FAS,FOS,JUN,MYB,PIK3R1,PTGS2	
PROK1		growth factor			0.000178	CXCL8,MCL1,PTGS2,RCAN1	447 (24)
FOLR1		transporter			0.00729	ACVR1,ARHGDI1,BIRC3,CAV1,MDK,MPP6,PPARG,S100A4,SHCBP1,SORD,ST3GAL4	
PPP2R2A		phosphatase			0.0217	SAT1,SERPINE2	
NAPB		transporter			0.049	CYP1A1	
FANCC		other			0.000438	ATP1B1,AXIN2,DKK1,FHL2,GDF15,MMP7,MYOF,PTGS2,RND3,SKAP2,TBC1D9	400 (12)
PIP5K1C		kinase			0.0428	ERRF1,PIP5K1A	
N4BP1		other			0.0109	HLA-B,JUN,MAP3K14	
ANKS1A		other			0.049	FOS	
bis(4-hydroxyphenyl)sulfone		chemical reagent			0.0316	CEBPA,PPARG	
5-methoxytryptophan		chemical - endogenous mammalian			0.049	PTGS2	
venetoclax		chemical drug			0.049	MCL1	
20-hydroxyprostaglandin E2		chemical - endogenous mammalian			0.049	PPARG	
MYCT1		other			0.0217	EGLN1,MXD4	
BCL6B		transcription regulator			0.0109	CASP7,CASP9,S100A4	
CCL22		cytokine			0.0217	CXCL2,CXCL3	
HNRNP2B1		other			0.000102	ARSL,CEMIP,CLDN1,GDF15,GSN,HIPK2,IGFBP2,ITPRID2,MEIS2,MUC13,PGM2L1,PITPNC1,PKIB,ROR1,SEMA3B,SERPINA1,SRI,TGFB2,TRIM31,USH1C,VIL1	
AP2A1		transporter			0.0135	CEBPA,MT2A	
NKX3-1		transcription regulator			0.00115	CASP7,ETS1,FOS,PIK3R1,PIM1,SDC4,SOX4,STEAP1,VIL1	252 (11)
LPAR2		G-protein coupled receptor			0.0428	CXCL8,PTGS2	
DLST		enzyme			0.00697	JUN,PIK3R1	
SND1		enzyme			0.0000554	EMP1,EREG,ETV1,PTGS2,QPCT,SLCO4A1,SMURF1,SOX4	
IGBP1		phosphatase			0.0109	CLDN1,IRF1,TJP1	
CD160		transmembrane receptor			0.00789	FOS,JUN,MCL1	236 (7)
LUC7L3		other			0.049	PTGS2	
TOR2A		other			0.00697	ACAT1,FOS	
CNOT7		transcription regulator			7.93E-10	B2M,CEACAM6,CLDN1,HERC6,IFI35,LGALS3BP,OAS3,PARP12,PLSCR1,PSMB8,SP110,TAP2,TFF3	200 (7)
CARD14		other			0.0316	BCL10,CXCL2	
IFNGR2	0.403	transmembrane receptor			0.00697	GBP3,IRF1	290 (10)
GFRA2		transmembrane receptor			0.00697	EGR1,FOSB	165 (7)
HSPB8		kinase			0.0185	BMP4,CXCL8,MAP1LC3B	
TRIM33		transcription regulator			0.0316	GATA2,TGFB2	
NMU		other			0.0319	FOSB,IL1R2,MYB,ZFP36L1	
CITED1		transcription regulator			0.0217	CYP24A1,IGF2	
OXTR		G-protein coupled receptor			0.0428	FOS,RUNX2	
GPD1	-1.167	enzyme			0.0167	ADGRF1,BCL6,CGREF1,CYP2B6,ELOVL6,GADD45A,GPCPD1,RARRES1,SERPINA3,SERPINE2	
Cyp2c70		enzyme			0.0232	CYP3A5,HMGCR,HNF4A	
NFKB1B		transcription regulator			0.00454	CARD6,CASP7,CASP9,CXCL1,CXCL2,CXCL8,DAPK1,EGR1	396 (15)
CFH		other			0.0316	CXCL2,PPARG	
WBP1		other			0.049	MCL1	
ZNF350		transcription regulator			0.00697	GADD45A,HMGA2	341 (7)
Zfp55		other			0.049	PPARG	
BMX		kinase			0.0285	CXCL8,FOS,HSPA1A/HSPA1B	
ANGPTL3		growth factor			0.0109	ACSS2,ELOVL6,HSPG2	
COMMD1		transporter			0.0319	BIRC3,DDIT4,EGLN1,LDHA	
KPNB1		transporter			0.00697	BBC3,PMAIP1	
MAP3K10		kinase			0.00354	CXCL8,GLI1,GLI2	
SLC27A1		transporter			0.00697	CEBPA,PPARG	
HOXB7		transcription regulator			0.00095	ANGPT1,CXCL1,CXCL8,REN	229 (11)
GNB1		enzyme			0.00259	CXCL3,DUSP1,F2R,FOSB,IL1R2,JAG2,TSC22D3	277 (9)
IL4R		transmembrane receptor			0.0478	ACSL1,ADAM8,FAS,FXD3,PPARG,RUNX2	
TFF1		other			0.049	PTGS2	
TMSB10/TMSB4X		other			0.00109	CXCL8,FAS,MMP7	
RAD9A		enzyme			0.0428	CDC25A,KLF12	
RGD1560225		other			0.000452	EDN1,ITPR2,PTGS2	
IGF2BP3		translation regulator			0.00697	CD44,IGF2	202 (7)
STK38		kinase			0.0316	CXCL2,CXCL3	
DMTF1	0.372	transcription regulator			0.0428	BBC3,DMTF1	
MLL3		transcription regulator			0.0428	EDN1,SGK1	
F2RL3		G-protein coupled receptor			0.0316	EGR1,FOS	
GPS1		other			0.0316	AXIN2,FOS	
MECOM		transcription regulator			0.0165	CEBPA,GATA2,ITPR2,MAP3K14,PML	
FABP5		transporter			0.0478	CXCL8,IFIT3,PPARG	
IL18RAP		transmembrane receptor			0.0428	CXCL8,PTGS2	
IL2RB		transmembrane receptor			0.0408	ETS1,FOS,JUN	
BBC3	0.317	other			0.0217	BBC3,STMN1	
Pla2g2a		other			0.049	PTGS2	
PLA2G2A		enzyme			0.00354	CD44,CXCL8,PTGS2	468 (20)
SHOX2		transcription regulator			0.0316	FGFR2,RUNX2	
SIN3B		transcription regulator			0.0000423	BCL6,CCNG2,FBXO32,GADD45B,KLF6,LDHA,TXNIP	338 (7)
SRY		transcription regulator			0.0232	BBC3,FOSL1,MAOA	
TNKS		enzyme			0.0428	AXIN2,MCL1	
VIPR1		G-protein coupled receptor			0.0408	CXCL2,CXCL3,IRF1	
WAC		other			0.0316	PKD4,PPARG	
MED13L		other			0.0428	KITLG,LIF	
EPGN		growth factor			0.049	FOS	
C5AR2		G-protein coupled receptor			0.0101	CXCL2,CXCL3,CXCL8,EIF2AK2	
IFT20		other			0.0135	GLI1,GLI2	
PLAGL2		transcription regulator			0.0135	IGF2,LDHA	
SP2		transcription regulator			0.00507	CEACAM1,FOS,MAT2A,SERPINH1	
TAX1BP3		transcription regulator			0.049	FOS	
ADCYAP1R1		G-protein coupled receptor			0.0428	DUSP5,FOS	
LMNB1		other			0.00454	B2M,GPC4,HBEGF,HMGCR,MSMO1,RCN1,SQLE,TGFB2	
NOXA1		other			0.049	NOX1	
CCR4		G-protein coupled receptor			0.0428	CXCL3,FOS	
PDPN		other			0.049	CD44	
CRABP1		transporter			0.049	CRABP2	

Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
FOXH1		transcription regulator			0.0135	ALDH1A1,ALDH1A3	
MZF1		transcription regulator			0.0232	MYB,PADI1,PRKCA	
glucocalyxin A		chemical - endogenous non-mammalian			0.0316	LCN2,PTGS2	
HOXB6		transcription regulator			0.049	REN	
YWHA8		other			0.0428	BCAM,DUSP1	
PPP3CA		phosphatase			0.0188	CPT1A,MAOB,PLD1,PLPP3,PTGS2,RCAN1,RUNX2,S100A4,SDC4	
PEA15		transporter			0.0109	JUN,PLD1,PLD2	
UTS2R		G-protein coupled receptor			0.00789	ACAT1,PPARG,SCARB1	
RNF17		other			0.0316	EGLN1,SERPINA3	
PON1		phosphatase			0.0232	CD68,PPARG,SCARB1	
THEM4		enzyme			0.049	PTGS2	
HIVEP3		transcription regulator			0.0428	ALG2,S100A4	
DSPP		other			0.0316	BGN,RUNX2	
TAPBP	0.646	transporter			0.00546	HLA-B,HLA-E,TAP2	
PELI2	1.015	enzyme			0.0217	CXCL2,CXCL8	
SDC1		enzyme			0.0232	CXCL2,CXCL3,TGM2	
Tnxa-ps1		other			0.049	DUSP1	
TFAP2B		transcription regulator			0.0478	EDN1,IGF2,MT2A	
ENTPD1		enzyme			0.0144	CXCL2,CXCL3,CXCL8	
RBP1		transporter			0.0232	ALDH1A1,PPARG,STRA6	
BAG3	0.487	other			0.0185	CDKN2B,MAP1LC3B,MCL1	
IRAK2		kinase			0.0408	CXCL2,CXCL8,MAT2A	
CD99		other			0.00789	CAV1,FOSB,JUND	
ARHGDI8	1.094	enzyme			0.049	PTGS2	394 (7)
PTGER1		G-protein coupled receptor			0.0232	CXCL8,FOS,PTGS2	
MAML1		transcription regulator			0.0408	CXCL8,EGR1,RND3	
BCL10	0.695	transcription regulator			0.0408	CD44,CXCL2,CXCL8	
PEX5L		ion channel			0.0232	HMGCR,IDI1,LSS	
CNR2		G-protein coupled receptor			0.0363	CXCL8,EGR1,GRK5,PTGS2	
PBX1		transcription regulator			0.0239	AMD1,CDKN2B,ETV1,HOXA3,REN	
M6PR		transporter			0.049	NPC1	
CX771		chemical reagent			0.00546	CD44,CXCR4,TJP1	
TAF6		transcription regulator			0.0461	ATF3,GADD45A,IRF1,JUN	
ROR2		kinase			0.000394	AURKA,AXIN2,CDC25A,CDKN2B,CEBPA,GALM,MAP1LC3B,MYB,PPARG,SLC17A9,TEAD2,TRAF4	
RARRES1	2.587	other			0.049	GRK5	
XPA	-0.522	other			0.0316	FOS,PTGS2	
16:0 ceramide-1-phosphate		chemical - endogenous mammalian			0.049	CXCL8	
RAB7A		enzyme			0.0316	EGR1,FOS	
ST14		peptidase			0.0285	CLDN2,CXCL2,CXCL8	
cytarabine/idarubicin		chemical drug			0.049	CEBPA	
RAB5B		enzyme			0.049	FOS	
PAK1		kinase			0.0268	FBXO32,FOSL1,PFKM,SCARB1,TFPI	
ITIH4		other			0.049	VDR	
CRY1		enzyme			0.0109	CEBPA,FOS,SGK1	
TOPBP1		other			0.0343	BBC3,CDKN2B,GADD45A	
HDC		enzyme			0.0478	CYP24A1,FOS,PTGS2	
CLEC11A		growth factor			0.019	ANXA1,FHL2,FOS,LDHA,RUNX2,TSC22D1,ZYX	
GNPAT	0.499	enzyme			0.0135	UGCG,UGT8	
CD164		other			0.049	CXCR4	
cytarabine/filgrastim/fludarabine phosphate		biologic drug			0.049	FOS	
ETS1-AS1		other			0.049	ETS1	
TCL1A		transcription regulator			0.000386	CD68,CTSE,CTSS,CXCL3,DNMT3A,FOS,GDF15,IL1R2,LCN2,MCL1,SEMA7A,STEAP4,TNFAIP2	447 (17)
HSF2		transcription regulator			0.0333	CLU,HSPA1A/HSPA1B,HSPB1,HSPH1,JUN	
ERC1		other			0.00697	CXCL8,PTGS2	317 (9)
CCDC80		other			0.00546	AXIN2,CEBPA,PPARG	361 (12)
ERO1A		enzyme			0.0135	CXCL2,CXCL3	
NFKBIE		transcription regulator			0.0109	CXCL3,CXCL8,LIF	
tofogliflozin		chemical drug			0.0217	CPT1A,DGAT2	
PRC1		other			0.049	PTGS2	
GREM1		other			0.0232	AXIN2,RUNX2,WNT11	
TF3	-4.091	other			0.0241	CD55,CLDN1,FOS,TJP1	
Gm35986		other			0.0316	HMGCR,IDI1	
farnesyl transferase		complex			0.00546	HBEGF,KLF6,MMP7	299 (7)
FLT3		kinase			0.0218	CDC25A,IFIT3,IRF7,MCL1,NOX1,PIM1	
ESRRB		transcription regulator			0.041	MCL1,NR0B2,PCSK6,PDIA5	
PLAA		other			0.0217	CLU,PTGS2	
DYSF		other			0.0000268	ANXA1,B2M,CD55,CD68,CTSS,DNAJB1,ERRF1,HSPA1A/HSPA1B,HSPB1,LGALS3,PROS1,S100A4,SERPINA3,TCEAL9	
tetramethylpyrazine		chemical - endogenous non-mammalian			0.049	CXCR4	
MST1R		kinase			0.0123	CXCL3,DVL1,FOS,JUN	
ADCY3		enzyme			0.049	NRP1	
SERPIND1		other			0.0316	EGR1,F2R	
IFNLR1		transmembrane receptor			0.0000623	ATF3,CXCL2,CXCL3,IFI44,IFIH1,IFIT3,IRF7,LIF,PTGS2,TNFAIP2	313 (13)
glyceraldehyde-BSA		chemical reagent			0.0428	CEBPA,PPARG	
methylglyoxal-BSA		chemical reagent			0.0428	CEBPA,PPARG	
HESX1		transcription regulator			0.00354	AXIN2,GATA2,MYB	
KIT		transmembrane receptor			0.0015	CD44,CDKN2B,CXCL3,CXCR4,ETV1,IFIT3,IL15RA,IRF1,KITLG,LGALS3,LIF,MCL1,RAB27B,TJP1	522 (20)
GTx-560		chemical reagent			0.049	PROS1	
EXOSC10		kinase			0.049	FOS	
EHMT2		transcription regulator			0.0174	BCAS3,MAP1LC3B,NCOA3,PKIB,PMAP1,PPL,PTGS2	
WNT10B		other			0.0144	CEBPA,PPARG,RUNX2	
CDKL2		kinase			0.049	CD44	
GNAQ		enzyme			8.05E-09	AK4,ATF3,BMP4,CD44,CSPG4,CXCL3,CXCL8,DUSP5,EDN1,EGR1,F2RL1,FOS,GADD45A,IL1RN,INSIG1,NDRG2,PHLDA1,PLSCR1,PTGS2,RHOB,SGK1,SLCO4A1,TGFB2,ZFP36L1	481 (19)
RING1		transcription regulator			0.00697	FOS,JUN	278 (6)
EEF1A1		translation regulator			0.00697	CCNA2,S100A4	
CD300C		transmembrane receptor			0.0316	CXCL2,CXCL8	
CAV2	-0.516	other			0.049	CAV1	
SLC25A13		transporter			0.0179	ADGRF1,BCL6,CGREF1,CYP2B6,ELOVL6,GADD45A,GPCPD1,RARRES1,SERPINA3,SERPINE2	
SRRM1		other			0.049	CD44	
CHRM2		G-protein coupled receptor			0.049	EGR1	
ACP1		phosphatase			0.0135	EPHA2,FOS	
NEK2		kinase			0.0135	FAS,GADD45A	
Mt3		other			0.0135	CEBPD,MT2A	
BEX2		other			0.0185	BBC3,ITGB6,SWAP70	
H4C3		other			0.0428	FOSB,TGFB2	
CDC42		enzyme			0.0188	ATF3,FOS,JUN,SCARB1,TGM2	
Cyp2a12/Cyp2a22		enzyme			0.0135	CYP3A5,HNF4A	
Flt1		kinase			0.049	ATF3	
GNMT		enzyme			0.00354	CYP1A1,NPC1,SCARB1	301 (7)
HSPA1A/HSPA1B	0.551	enzyme			0.0232	CXCL2,CXCL8,FOS	
Ifna4		other			0.0316	IRF7,TRIM38	
Irs4		other			0.0024	EGR1,IRS2	405 (17)
PPP1R15A	0.574	other			0.00295	CA9,CEBPA,GADD45A,MAP1LC3B,MCL1	

Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
Cxcl3		cytokine			0.00109	CEBPA,CEBPD,PPARG	
TCF7		transcription regulator			0.00754	AXIN2,BCL6,CEBPA,CEBPD,FOS,HNF4A,PPARG	242 (9)
PAXIP1		other			0.0316	CSPG4,DKK1	
Paxip1		other			0.0021	ANXA1,CEACAM1,REL	
TWSG1		other			0.0217	BCL6,ID2	
OBP2B		transporter			0.0316	CPT1A,PPARG	
HMG2		transcription regulator			0.0078	CXCL1,CXCL2,CXCL8,PHLDA1,RUNX2	375 (9)
NKRF		transcription regulator			0.0428	CXCL8,PTGS2	
H1-4		other			0.0217	GLI1,GLI2	
H1f4		other			0.00109	AXIN2,GLI1,GLI2	
RFX5		transcription regulator			0.0343	B2M,GCNT2,HLA-B	
S100A7		other			0.0144	CA9,CXCL1,CXCL8	
PPP2R5B	0.609	phosphatase			0.0217	SAT1,SERPINE2	
GCLM		enzyme			0.0217	FOS,JUN	498 (22)
GNRH2		other			0.00789	FOS,FOSB,JUN	
MPTOE028		chemical drug			0.049	MCL1	
HDAC8		transcription regulator			0.0109	BBC3,HOXA5,STX1A	
PEX14		transcription regulator			0.049	PTGS2	
DEK		transcription regulator			0.00789	BIRC3,CXCL8,MCL1	309 (7)
ID4		transcription regulator			0.00387	BBC3,CDKN2B,CEBPA,PPARG	248 (7)
ZYX	0.622	other			0.0316	FOS,HIPK2	
GNA15		enzyme			0.00000123	AKAP12,BMP4,CASP4,CAV2,CEBPD,CXCL2,CXCL3,CXCL8,FHL2,FOSL1,GADD45A,HLA-E,IL1RN,LGALS3,MAT2A,NOX1,PDLM1,PTGS2,RGS2,SERPINA3,ZFP36L1	413 (16)
spliceostatin A		chemical reagent			0.049	MCL1	
oligomycin A		chemical - endogenous non-mammalian			0.049	TXNIP	
Rp-cAMP triethylamine		chemical reagent			0.049	CXCL3	
CML advanced glycation end products		chemical reagent			0.049	EGR1	
SR11256		chemical reagent			0.049	EDN1	
cAMP-dependent protein kinase inhibitor		chemical drug			0.049	CYP3A5	
HADHB		enzyme			0.049	REN	
SOD1		enzyme			0.00563	ACO1,ASS1,B2M,BAG3,BMP4,CASP4,CKB,CLU,FAS,FGF19,FOS,GUK1,HSPB1,JUN,MAOB,MCL1,PSMB8,PTGS2,PTPN21,RUNX2,SNCG,STMN1,TGFBR2	483 (21)
3,4-(methylenedioxy)cinnamic acid		chemical reagent			0.049	MCL1	
CC-122		chemical drug			0.0217	IFIT3,IRF7	
polyinosine-polycytidylic acid/polyethylenimine formulation		chemical reagent			0.0217	IFIH1,PMAIP1	
COG112 peptide		chemical reagent			0.0316	CXCL2,CXCL3	
STF 083010		chemical reagent			0.049	NCOA3	
Immunoglobulin Lambda Light Chain		group			0.0428	ERN1,PMAIP1	
RB4		chemical reagent			0.049	MCL1	
ciliobrevin A		chemical reagent			0.0024	GLI1,GLI2	
RB3		chemical reagent			0.049	MCL1	
HNRNPAB		enzyme			0.0185	PTGS2,S100A4,TJP1	
J11-CI		chemical reagent			0.0144	CXCL2,CXCL3,PTGS2	
KMUP-1		chemical reagent			0.0144	HMGCR,PPARG,SCARB1	
CH-223191		chemical reagent			0.0408	CYP1A1,NT5E,PTGS2	
MLS000389544		chemical reagent			0.0024	PCK2,PK4	
NCGC00184710		chemical reagent			0.049	PK4	
finerenone		chemical drug			0.0217	LCN2,LGALS3	
arsenic trichloride		chemical reagent			0.049	GADD45A	
SYK023		chemical reagent			0.0135	CDC25A,CDKN2B	
meayamycin B		chemical reagent			0.049	MCL1	
1-(2-hydroxy-5-methylphenyl)-3-phenyl-1,3-propanedione		chemical reagent			0.0135	CEBPD,PPARG	
24-methylenecycloartanyl ferulate		chemical reagent			0.049	PPARG	
BCL201		chemical drug			0.049	MCL1	
KRT7-AS		other			0.049	KRT7	
acriflavine		chemical toxicant			0.0144	CA9,NT5E,PTPRB	
beractant		chemical drug			0.049	CXCL8	
sulfamethoxazole/trimethoprim		chemical drug			0.0217	CXCL8,IRF7	
asbestos		chemical toxicant			0.00789	CXCL8,FOSL1,JUN	
hydroxyl radical		chemical toxicant			0.0024	CAV1,KLF4	
AP20187		chemical reagent			0.0428	EGR1,FOS	
furosemide		chemical drug			0.0217	PTGS2,REN	
enzastaurin		chemical drug			0.0316	CXCL8,TJP1	
halofuginone		chemical drug			0.0000041	AKAP12,AOC1,BGN,CD44,CD55,CKB,CLIP2,CTSS,EGR1,EMP1,F2R,GY1,HK1,IFITM2,LGALS3BP,PCSK6,PLPP3,SLC39A8,ST3GAL2,STEAP3,TGFBR2,TGM2	
NBI 27914		chemical drug			0.049	FOS	
nicorandil		chemical drug			0.0428	ATF3,JUN	
diltiazem		chemical drug			0.0109	EDN1,FOS,JUN	
benzoquinone		chemical - endogenous mammalian			0.0428	APOL1,IRF1	
probenecid		chemical drug			0.049	ABCC1	
thenoyltrifluoroacetone		chemical reagent			0.0428	BIRC3,CXCL8	
carboxyamido-triazole		chemical drug			0.0135	BAG3,FOS	
LY379196		chemical - kinase inhibitor			0.0217	CD55,EGR1	
cantharidin		chemical drug			0.0232	BAG3,MCL1,SERPINH1	
SB202474		chemical - kinase inhibitor			0.049	CYP1A1	
EGTA acetoxymethyl ester		chemical reagent			0.0316	CXCL8,PTGS2	
2-aminoethoxydiphenylborane		chemical reagent			0.0144	CYP1A1,ITPR2,PTGS2	
S-methylisothiopseudouronium		chemical reagent			0.049	PTGS2	
phenylacetate		chemical - endogenous mammalian			0.0135	CAV1,CAV2	
itraconazole		chemical drug			0.00546	AGR2,CYP1A1,GLI1	
ifosfamide		chemical drug			0.0316	CYP2B6,SLC22A5	
N-(3-oxododecanoyl)-homoserine lactone		chemical reagent			0.0285	CXCL2,CXCL8,PTGS2	
dichlorodiphenyl dichloroethylene		chemical toxicant			0.00697	CYP2B6,CYP3A5	
trabectedin		chemical drug			0.00295	CCNG2,GADD45A,H1-10,LGMN,PPARG,SAT1	441 (12)
guanfacine		chemical drug			0.049	FOS	
phenylpropanoic acid		chemical - endogenous mammalian			0.049	ATP2A3	
amantadine		chemical drug			0.00697	DDC,FOS	
capsazepine		chemical toxicant			0.00789	CXCL8,FOS,PTGS2	
AR-A014418		chemical reagent			0.0428	CD44,GDF15	430 (21)
raltitrexed		chemical drug			0.00789	FAS,FXD3,SAT1	
atipamezole		chemical drug			0.0135	EGR1,FOS	
antimony potassium tartrate		chemical toxicant			0.049	ABCC2	
coomassie brilliant blue		chemical drug			0.0285	LIF,PTGS2,TJP1	
XCT790		chemical reagent			0.0316	MAOB,PK4	
pyridoxine		chemical - endogenous mammalian			0.0343	DKK1,JUN,PTGS2	
bisphenol A diglycidyl ether		chemical reagent			0.0185	EGLN1,TGFBR2,VDR	
alpha-ketoisocaproic acid		chemical - endogenous mammalian			0.0316	ATP2B1,ITPR2	
clioquinol		chemical drug			0.0144	FOS,JUN,KDM6B	
nimesulide		chemical drug			0.0478	CYP1A1,EREG,PTGS2	
cimetidine		chemical drug			0.0217	FAS,GDF15	
SR 144528		chemical reagent			0.0185	CXCL8,EGR1,IL1RN	
bupivacaine		chemical drug			0.0109	CASP9,FOSL1,JUND	
4-coumaric acid		chemical - endogenous mammalian			0.0428	CCNA2,PTGS2	
ferric nitrilotriacetate		chemical toxicant			0.0316	KLF4,PTGS2	
2,5-dihydroxymethylcinnamate		chemical - kinase inhibitor			0.049	EDN1	



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Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
LY311727		chemical reagent			0.049	PTGS2	
BN 50730		chemical reagent			0.049	PTGS2	
saccharin		chemical reagent			0.00697	CEBPA,PPARG	344 (7)
sterigmatocystin		chemical toxicant			0.049	CYP1A1	
hoechst 33342		chemical reagent			0.0135	EPC1,FOS	
emricasan		chemical drug			0.0316	CXCL2,CXCL3	
tecacet		chemical reagent			0.049	EDN1	
BW-755C		chemical drug			0.049	JUND	
ondansetron		chemical drug			0.049	FOS	
phenidone		chemical drug			0.049	REN	
cyclothiazide		chemical drug			0.049	EGR1	
flurothyl		chemical drug			0.049	FOS	
carbonyl cyanide p-(trifluoromethoxy)phenylhydrazone		chemical reagent			0.0285	CHAC1,PCK2,PSPH	
pustulan		chemical reagent			0.049	CXCL8	
trichloroacetic acid		chemical drug			0.049	MCL1	
L 733060		chemical reagent			0.049	FOS	
lansoprazole		chemical drug			0.0135	CXCL8,PTGS2	
1-(1-glycerododeca-1,3,5,7,9-pentaene		chemical toxicant			0.049	PTGS2	
volinaserin		chemical drug			0.00354	EGR1,FOS,REN	231 (7)
phenyl-N-tert-butylnitrene		chemical reagent			0.0478	CXCL8,HSPA1A/HSPA1B,PTGS2	
warfarin		chemical drug			0.0428	PROCR,PROS1	
n-nitrosomethylbenzylamine		chemical toxicant			0.0172	ADAMTS6,AKR1B10,AMBP,CD44,CLDN1,DUSP5,KRT20,MCL1,PIP5K1A,PLK3,PTGS2,SCEL,SLC30A1	
L-threo-safingol		chemical drug			0.049	CXCL8	
CHS-828		chemical drug			0.00546	ALDH1A1,CD44,LRIG1	
selfotel		chemical drug			0.049	FOS	
liarozole		chemical drug			0.0135	PI3,VDR	
alpha-methylhydrocinnamic acid		chemical - endogenous mammalian			0.0135	MCL1,MYB	
tetrabenzazine		chemical drug			0.049	PPP1R1B	
manumycin A		chemical reagent			0.0144	CXCL8,PLD1,PTGS2	
ibotenic acid		chemical toxicant			0.0135	FOS,JUN	
methylselenic acid		chemical reagent			8.19E-09	'4,CASP9,CCNA2,CD44,CDC14B,CDC25A,CLU,DNAJB9,DNAJC3,ELF3,GADD45A,GATA2,GDF15,H1-0,ID2,IRF1,JUN,KLF4,KRT20,MCL1,MXD1,NEDD4L,NMI,PATZ1,PRKCA,RHOB,F	566 (22)
butylated hydroxytoluene		chemical toxicant			0.00109	FOS,JUN,PTGS2	326 (13)
(R)-5-(2-azetidylmethoxy)-2-chloropyridine		chemical drug			0.049	FOS	
6-cyano-7-nitroquinoxaline-2,3-dione		chemical reagent			0.0021	EGR1,FOS,JUN	186 (7)
ethacrynic acid		chemical drug			0.0217	AKR1C1/AKR1C2,MCL1	
RW J 67657		chemical - kinase inhibitor			0.0428	CXCL8,PTGS2	
rofecoxib		chemical drug			0.0478	PTGS2,REN,TBC1D9	
dibenzoylmethane		chemical toxicant			0.0316	CYP1A1,PTGS2	
zimeclidine		chemical drug			0.0428	DEPP1,SERPINA3	
D609		chemical reagent			0.0478	CXCL8,JUN,PTGS2	
bergamottin		chemical - endogenous non-mammalian			0.0428	CYP1A1,CYP2B6	
clomipramine		chemical drug			0.0109	DEPP1,LSS,SERPINA3	
barbiturate		chemical drug			0.0135	CYP2B6,CYP3A5	
BTG3-AS1		other			0.049	ATF3	
clofarabine		chemical drug			0.049	CDC25A	
histone deacetylase		complex			0.0446	CCN1,CXCR4,CYP24A1,ID2,NDRG2	
Hif		complex			0.0408	CKB,CXCL8,LDHA	
D-sphingosine		chemical - endogenous mammalian			0.0185	CLDN1,CXCL2,PTGS2	
phytosphingosine		chemical - endogenous mammalian			0.049	CLDN1	
apomine		chemical drug			0.00697	HMGCR,NR0B2	
PK11007		chemical reagent			0.0316	BBC3,PMAIP1	
aspergillus beta-glucan		chemical - endogenous non-mammalian			0.049	CXCL8	
pneumocystis beta-glucan		chemical - endogenous non-mammalian			0.049	CXCL8	
cortistatin A		chemical reagent			0.0109	CEBPA,ETV6,IRF1	
sevelamer		chemical drug			0.0316	FGF19,NR0B2	
diazepam		chemical drug			0.0428	CXCL8,FOS	
flunitrazepam		chemical drug			0.049	CXCL8	
oxazepam		chemical drug			0.0024	GADD45B,TSC22D1	
thiabendazole		chemical drug			0.049	CYP1A1	
methylnitrosourea		chemical toxicant			0.00134	ATP1B3,AURKA,CLU,CXCL3,EGR1,JUN,PSME1	467 (18)
arachidonyl-2-chloroethylamide		chemical reagent			0.049	EGR1	
glyburide		chemical drug			0.0478	FOS,PPARG,SCARB1	
naphthalene-1-2-dione		chemical toxicant			0.049	CYP1A1	
trans-7,8-dihydroxy-7,8-dihydrobenzo(a)pyrene		chemical toxicant			0.049	CYP1A1	
anthracene		chemical toxicant			0.049	CXCL8	
tolrestat		chemical drug			0.049	CXCL8	
MUC2		other			0.049	CXCL8	
dieldrin		chemical toxicant			0.0316	CYP2B6,CYP3A5	
DDT		chemical toxicant			0.0428	CYP2B6,CYP3A5	
naftifine		chemical drug			0.049	SOLE	
2-amino-3-methylimidazo(4,5-f)quinoline		chemical toxicant			0.049	CYP1A1	
benzo(a)pyrene-7,8-dione		chemical toxicant			0.0024	AKR1C1/AKR1C2,CYP1A1	
Ro 31-7549		chemical - kinase inhibitor			0.049	PTGS2	
ketorolac		chemical drug			0.00789	CXCL8,PTGS2,REN	411 (20)
ethyl linoleate		chemical - endogenous mammalian			0.0135	PTGS2,SC5D	
Ki16425		chemical reagent			0.0428	PLPP3,PTGS2	
ONO-8711		chemical drug			0.049	FOS	
nitrendipine		chemical drug			0.000452	CYP2B6,CYP3A5,HMGCR	
acetic acid		chemical - endogenous mammalian			0.0109	EGR1,FOS,JUN	
isobutyric acid		chemical - endogenous non-mammalian			0.049	ATP2A3	
catechol		chemical - endogenous mammalian			0.0316	FOS,JUN	
mesalamine		chemical drug			0.0109	HPGD,PPARG,PTGS2	
eugenol		chemical - endogenous non-mammalian			0.0428	CXCL8,PTGS2	
theaflavin monogallate B		chemical - endogenous non-mammalian			0.049	PTGS2	
propyl gallate		chemical toxicant			0.0316	CXCL8,PTGS2	
epicatechin gallate		chemical drug			0.0241	CXCL8,GDF15,PTGS2,TP53111	
taprostene		chemical reagent			0.00697	DUSP1,TSC22D3	
AP-1 decoy		chemical reagent			0.049	DUSP1	
lavendustin A		chemical - kinase inhibitor			0.0024	CYP1A1,EDN1	
vanadyl sulfate		chemical reagent			0.0217	IL1R2,IL1RN	
potassium iodide		chemical drug			0.049	CXCL8	
MitoBioCK-6		chemical drug			0.00697	PCK2,PSPH	
mercuric chloride		chemical toxicant			0.0299	GADD45A,HBEGF,HSPA1A/HSPA1B,HSPB1,JUN	
spermine nitric oxide complex		chemical toxicant			0.0232	ACO1,CXCL8,S100A10	
chlorophyll a		chemical - endogenous non-mammalian			0.0135	FAS,PPARG	
zinc protoporphyrin IX		chemical - endogenous mammalian			0.0343	ANGPT1,FGFR2,PTGS2	
senexin B		chemical drug			0.000117	CXCL1,CXCL2,CXCL8	117 (5)
RUNX1-RUNX1T1		fusion gene/product			0.000892	CEBPA,CYP2S1,GRK5,ID2,IFITM3,KCNE3,KLHL24,MT2A,MTSS1,RND3,SH2B3,SORL1,SOX4	315 (11)
NUP98-KDM5A		fusion gene/product			0.0343	CDK6,MCL1,MYB	
FUS-ERG		fusion gene/product			0.049	PIM1	
EWSR1-ERG		fusion gene/product			0.049	PIM1	
NUP98-NSD1		fusion gene/product			0.0343	CDK6,MCL1,MYB	

Supplementary Table 4. Upstream regulator analysis based gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) after ATRA+PDT compared to PDT

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
PML-RARA		fusion gene/product			0.0299	EGR1,FOS,JUN,PSMB10,PSMB8	
retroinverso ERG inhibitory peptide 2		chemical reagent			0.0428	ARHGDI8,CXCR4	
retroinverso ERG inhibitory peptide 1		chemical reagent			0.0428	ARHGDI8,CXCR4	
miR-124 inhibitor		chemical reagent			0.049	MCL1	
anti-miR-32 inhibitor		chemical reagent			0.049	KLf4	
WZB117		chemical reagent			0.0135	CXCL3,PI3	
cathelicidin-WA		chemical - endogenous mammalian			0.00109	MUC2,TFF3,TJP1	
dexamethasone/INS/isobutylmethylxanthine		chemical reagent			0.049	CCNA2	
BIM5078		chemical reagent			0.049	SULT2B1	
pubchem compound 25247557		chemical reagent			0.0135	PK4,PEX11A	
REC2923		chemical reagent			0.00697	LDHA,SLC16A1	
tazarotene		chemical drug			0.0217	PLAAT4,RARRES1	
retinaldehyde		chemical - endogenous mammalian			0.0428	CD44,PTGS2	
thioridazine		chemical drug			0.0123	DEPP1,LSS,MCL1,SERPINA3	
CB-PIC		chemical reagent			0.0217	ABCB10,CASP9	
ethylenediaminetetraacetic acid		chemical drug			0.0232	CXCL8,EGR1,MCAM	
spermidine		chemical - endogenous mammalian			0.00651	AMD1,FOS,IGFBP2,SAT1	
spermine		chemical - endogenous mammalian			0.0285	IGFBP2,RUNX2,SAT1	
meclizine		chemical drug			0.0285	ABCC2,CYP2B6,CYP3A5	
CTOP		chemical reagent			0.049	FOS	
apamin		chemical toxicant			0.0316	FOS,JUN	
BMS200261		chemical reagent			0.049	CD55	
JMF3086		chemical reagent			0.00789	CXCL2,CXCL3,PTGS2	451 (16)
astressin 2B		biologic drug			0.0232	CXCL2,FOS,HPGD	
Z-IETD-FMK		chemical - protease inhibitor			0.0316	CXCL8,PLD1	
N-t-Boc-Phe-D-Leu-Phe-D-Leu-Phe		chemical reagent			0.049	PTGS2	
N-carbobenzyloxy-leucine-leucine-norvalinal		chemical - protease inhibitor			0.0343	CXCL8,MCL1,RARG	
BQ-788		biologic drug			0.0109	CXCL2,EDN1,MCAM	
myristoylated Protein Kinase C peptide inhibitor		chemical - kinase inhibitor			0.0135	CD55,PPARG	
NCB-0846		chemical - kinase inhibitor			0.049	JUN	
Ac-DEVD-CHO		chemical reagent			0.049	FOS	
aclarubicin		chemical drug			0.0217	MCL1,PTGS2	
idarubicin		chemical drug			0.0123	BBC3,GADD45A,MCL1,SESN2	
ibutamoren		chemical drug			0.049	FOS	
trandolapril		chemical drug			0.049	REN	
bisindolylmaleimide II		chemical - kinase inhibitor			0.0135	JUN,PPARG	
linalool		chemical - endogenous non-mammalian			0.0176	ACSL1,HMGCR,PCK2,SQLE	
geranylgeraniol		chemical - endogenous mammalian			0.0428	HMGCR,MCL1	
ETC-642		chemical reagent			0.049	HMGCR	
18-alpha-glycyrrhetic acid		chemical - endogenous non-mammalian			0.0316	PPARG,TJP1	
hyperforin		chemical drug			0.0343	ABCC2,CYP24A1,CYP2B6	329 (7)
myricetin		chemical - endogenous non-mammalian			0.00651	CYP1A1,EGLN1,PTGS2,SLC16A1	
kaempferol		chemical toxicant			0.0319	CYP1A1,JUN,PTGS2,RUNX2	
cytosine		chemical drug			0.049	FOSB	
naltindole		chemical drug			0.0285	IGF2,IGFBP2,UBC	
atropine		chemical drug			0.0428	FOS,PTGS2	
SN-38		chemical drug			0.00655	BIRC3,CASP9,CLU,FAS,GDF15,MCL1	395 (11)
yohimbine		chemical drug			0.0135	EGR1,FOS	
NHB2005		chemical reagent			0.0316	CASP9,ERN1	
tetrahydropalmatine		chemical - endogenous non-mammalian			0.0024	CXCL8,PTGS2	
noscipine		chemical drug			0.0285	BIRC3,MCL1,PTGS2	
omacetaxine mepesuccinate		chemical drug			0.0217	CASP9,MCL1	
arecoline		chemical drug			0.0207	F2R,MAOA,S100A4,TJP1	
2-methoxy-5-(2',3',4'-trimethoxyphenyl)-2,4,6-cycloheptatrien-1-one		chemical reagent			0.049	JUN	
harmaline		chemical drug			0.049	CYP1A1	
D-lysergic acid diethylamide		chemical drug			0.0024	DDC,SGK1	
LY 354740		chemical drug			0.049	FOS	
droxidopa		chemical drug			0.049	FOS	
S(-)-carbidopa		chemical drug			0.049	FOS	
tyrphostin AG 1296		chemical - kinase inhibitor			0.0144	CEACAM6,JUN,PTGS2	
phosphatidic acid		chemical - endogenous mammalian			0.0428	IGF2,PTGS2	
isovaleric acid		chemical - endogenous mammalian			0.049	ATP2A3	
oleoylethanolamide		chemical - endogenous mammalian			0.00789	CPT1A,FOS,FOSB	449 (25)
tridecanoic acid		chemical - endogenous mammalian			0.0109	DUSP5,KLF4,MXD1	
10-hydroxydecanoic acid		chemical - endogenous non-mammalian			0.049	IRF1	
n-6 docosapentaenoic acid		chemical - other			0.049	PTGS2	
fumagillin		chemical - endogenous non-mammalian			0.049	CAV1	
long-chain alcohol		chemical - endogenous non-mammalian			0.049	PTGS2	
12-hydroxyeicosatetraenoic acid		chemical - endogenous mammalian			0.0428	NOX1,PTGS2	
3'-adenylic acid		chemical - endogenous mammalian			0.049	TXNIP	
stavudine		chemical drug			0.00697	CPT1A,PPARG	
gambogic acid		chemical - endogenous non-mammalian			0.0232	BIRC3,EGLN1,PTGS2	
poractant alfa		chemical drug			0.049	CXCL8	
tosyllysine chloromethyl ketone		chemical - protease inhibitor			0.00546	CYP1A1,IRF1,PTGS2	374 (14)
OSU8-1		chemical - protease inhibitor			0.049	HBEGF	
5-hydroxytryptophan		chemical - endogenous mammalian			0.0217	FOS,PTGS2	
sarcosine		chemical - endogenous mammalian			0.049	FOS	
2-amino-3-phosphonopropionic acid		chemical - endogenous mammalian			0.00697	EGR1,FOS	300 (7)
quisqualic acid		chemical - endogenous non-mammalian			0.0316	EGR1,FOS	
pectin		chemical drug			0.0144	CD68,LGALS3,SMAD3	
allose		chemical - endogenous mammalian			0.049	TXNIP	
galactose		chemical - endogenous mammalian			0.0343	GPD1,VDAC1,VDR	
mannose		chemical - endogenous mammalian			0.0408	FOS,GPD1,MCL1	
3-deoxyglucosone		chemical - endogenous mammalian			0.049	HBEGF	
growth factor		group			0.00387	CLU,DUSP1,FOS,PTGS2	473 (18)
lactulose		chemical - endogenous mammalian			0.049	CXCL8	
allopregnanolone		chemical - endogenous mammalian			0.0144	FOS,LGALS3,PTGS2	
estramustine		chemical drug			0.049	CYP1A1	
steroid hormone		chemical - endogenous mammalian			0.0461	ACSL1,ACSS2,HMGCR,SCARB1	
oxysterol		chemical - other			0.0135	CREBRF,CXCR4	
epiallopregnanolone		chemical - endogenous mammalian			0.0478	CAV1,CXCL8,HMGCR	
kb-NB 142-70		chemical - endogenous mammalian			0.00697	LGALS3,PTGS2	
vinpocetine		chemical - kinase inhibitor			0.00109	DNAJB9,DNAJC3,ERN1	
pyocyanin		chemical drug			0.0428	CXCL3,CXCL8	
Fe3+		chemical reagent			0.0135	CXCL8,NOX1	
Cd2+		chemical - endogenous mammalian			0.049	HMGCR	
Cr6+		chemical toxicant			0.0285	CXCL3,FOS,PTGS2	
V2+		chemical reagent			0.0217	MT2A,SLC30A1	
D-alpha-hydroxyglutarate		chemical toxicant			0.049	CXCL8	
CIL56		chemical - endogenous mammalian			0.0135	GLI1,RUNX2	
RO5256390		chemical reagent			0.0135	ALDH1A1,CDK6	
		chemical reagent			0.049	IRS2	

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Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target Molecules in Dataset	Mechanistic Network
PC-SPES TCF		chemical drug group			0.000073 4.33E-10	ANXA1,B2M,CCNA2,CLU,DNAJB1,HLA-B,HLA-C,IMPDH1,IRF1,PPP1R15A,QSOX1,SCARB1,TIA1,TUBA4A,TUBB2A .LDH1A1,ARL4A,BMP4,CD44,CEACAM1,CYP24A1,DPEP1,ECM1,EGR1,FOS,LGALS3,MMP7,PCSK6,PTGS2,QPCT,RCN1,SERPINA1,SERPINA3,SERPINA5,TSC22D1,TSPAN8,UGCG	448 (18)