

Table SI. BLID enhances chemosensitivity of breast cancer cells.

Treatment	DTX, IC ₅₀ (nM)		DXR, IC ₅₀ (ng/ml)	
	SKBr3 cells	MDA-MB-231 cells	SKBr3 cells	MDA-MB-231 cells
UT	7.00	0.90	50.00	50.00
Liposomes only (scL)	6.50	1.00	43.00	40.00
scL vector	6.00	0.85	42.00	40.00
scLBLID	0.06	0.02	00.39	12.00
Fold-sensitization (IC ₅₀ UT/IC ₅₀ BLID)	117	36	128	4.20

A total of 4×10^3 SKBr3 and MDA-MB-231 breast cancer cells were plated per well in 96-well plates. After 24 h, the cells were transfected with scLBLID nanocomplex, scL vector or liposomes only, or left UT [vector or BLID plasmid DNA/well, 0.02 μ g (SKBr3 cells) or 0.06 μ g (MDA-MB-231 cells)]. At 2 days after transfection, DTX or DXR was added at increasing concentrations (in triplicate) for 48 h. An XTT assay was performed at 48 h post-incubation of cells with the drug, and the IC₅₀ value, which is the drug concentration yielding a 50% loss of cell viability, was calculated. scL, immunoliposomal nanocomplex of anti-transferrin receptor single chain (TfRscFv) antibody fragment and cationic liposome; UT, untransfected; DTX, docetaxel; DXR, doxorubicin; BLID, BH-3 like motif containing inducer of cell death.

Table SII. Comparison of chemosensitization effects of scLBLID and scLP53 in MDA-MB-231 cells.

Treatment	DTX, IC ₅₀ (nM)		DXR, IC ₅₀ (ng/ml)	
	scLBLID	scLP53	scLBLID	scLP53
UT	0.95	0.95	35.00	35.00
scL nanoparticle	0.02	0.03	4.20	15.00
Fold-sensitization (IC ₅₀ UT/IC ₅₀ scL nanoparticle)	47.50	29.70	8.30	2.30

A total of 4×10^3 MDA-MB-231 breast cancer cells were plated per well in 96-well plates. After 24 h, the cells were transfected with 0.06 μ g plasmid DNA/well of the scLBLID or scLP53 nanocomplex or left UT. At 2 days after transfection, DTX or DXR was added at increasing concentrations (in triplicate) for 48 h. An XTT assay was performed at 48 h post-incubation of cells with the drug, and the IC₅₀ value, which is the drug concentration yielding a 50% loss of cell viability, was calculated. scL, immunoliposomal nanocomplex of anti-transferrin receptor single chain (TfRscFv) antibody fragment and cationic liposome; UT, untransfected; DTX, docetaxel; DXR, doxorubicin; BLID, BH-3 like motif containing inducer of cell death.

Table SIII. RNA array analysis-based identification of top-ranked genes modulated in BLID shRNA- vs. scrambled control shRNA-transduced MCF-7 cells.

A, Upregulated genes		
Gene symbol (gene name; RefSeq accession number)	Fold increase/decrease (BLID shRNA vs. scrambled shRNA in MCF-7 cells)	P-value
AKR1C2 (aldo-keto reductase family 1, member C2; NM_001135241)	+26.8375	5.70x10 ⁻¹¹
RSAD2 (radical S-adenosyl methionine domain containing 2; NM_080657)	+26.7917	3.94x10 ⁻¹⁰
AKR1C1 (aldo-keto reductase family 1, member C1; NM_001353)	+22.0086	2.66x10 ⁻¹⁰
IFIT2 (interferon-induced protein with tetratricopeptide repeats 2; NM_001547)	+17.0637	1.70x10 ⁻⁹
IFIT3 (interferon-induced protein with tetratricopeptide repeats 3; NM_001031683)	+16.6726	2.05x10 ⁻⁹
CMPK2 [cytidine monophosphate (UMP-CMP) kinase 2; NM_001256477]	+14.5695	4.39x10 ⁻⁹
IFNL2 (interferon, λ 2; NM_172138)	+12.7334	1.15x10 ⁻¹⁵
AKR1C3 (aldo-keto reductase family 1; NM_001253908)	+12.5724	1.86x10 ⁻⁷
IFNB1 (interferon, β 1; NM_002176)	+10.0024	1.08x10 ⁻¹¹
IFI44L (interferon-induced protein 44-like; NM_001375646)	+9.6451	4.67x10 ⁻⁶
B, Downregulated genes		
Gene symbol (gene name; RefSeq accession number)	Fold increase/decrease (BLID shRNA vs. scrambled shRNA in MCF-7 cells)	P-value
TIMP3 (TIMP metalloproteinase inhibitor 3; NM_000362)	-7.5953	3.95x10 ⁻⁸
HPGD [hydroxyprostaglandin dehydrogenase 15-(NAD); NM_000860]	-5.3265	1.15x10 ⁻⁷
ANTXR1 (anthrax toxin receptor 1; NM_018153)	-4.6439	7.12x10 ⁻⁷
SH3BGRL (SH3 domain binding glutamic acid-rich protein like; NM_003022)	-4.1507	7.83x10 ⁻¹⁰
KCNMA1 (potassium large conductance calcium-activated channel, subfamily M, α member 1; NM_001014797)	-3.9221	2.30x10 ⁻⁷
AFAP1L2 (actin filament associated protein 1-like 2; NM_001001936)	-3.7661	3.34x10 ⁻⁹
SEPP1 (selenoprotein P, plasma, 1; NM_001085486)	-3.6776	0.000157
GANAB (glucosidase, α ; neutral AB; NM_001278192)	-3.4326	0.00015
CPE (carboxypeptidase E; NM_001873)	-3.2373	9.90x10 ⁻⁸

PAQR5 (progestin and adipoQ receptor family member V; NM_001104554)	-3.2328	2.91x10 ⁻⁷
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The top 10 genes, upregulated or downregulated, are shown. P<0.05 was considered to indicate a statistically significant difference. shRNA, short hairpin RNA; RefSeq, Reference Sequence database; BLID, BH-3 like motif containing inducer of cell death; +, upregulated; -, downregulated.

Table SIV. RNA array analysis-based identification of top-ranked genes modulated in BLID shRNA- vs. scrambled control shRNA-transduced MDA-MB-231 cells.

A, Upregulated genes		
Gene symbol (gene name; RefSeq accession number)	Fold increase/decrease (BLID shRNA vs. scrambled shRNA MDA-MD-231 cells)	P-value
THBS1 (thrombospondin 1; NM_003246)	+6.9940	8.83x10 ⁻¹³
S100P (S100 calcium binding protein P; NM_005980)	+5.0140	3.33x10 ⁻¹¹
FLG (filaggrin; NM_002016)	+4.9439	1.65x10 ⁻¹⁵
ID2 (inhibitor of DNA binding 2, dominant negative helix-loop-helix protein; NM_002166)	+4.6224	3.78x10 ⁻¹⁰
CYP1B1 (cytochrome P450, family 1, subfamily B, polypeptide 1; NM_000104)	+4.3772	5.30x10 ⁻⁸
BIRC3 (cIAP2) (baculoviral IAP repeat containing 3; NM_001165)	+4.3664	3.46x10 ⁻¹⁰
TNFSF18 [tumor necrosis factor (ligand) superfamily, member 18; NM_005092]	+3.9508	2.64x10 ⁻¹⁰
SCG5 (secretogranin V; NM_001144757)	+3.8185	1.19x10 ⁻⁵
SOST (sclerostin; NM_025237)	+3.8057	3.85x10 ⁻¹¹
CSF1 (colony stimulating factor 1; NM_000757)	+3.6480	1.03x10 ⁻¹⁰
B, Downregulated genes		
Gene symbol (gene name; RefSeq accession number)	Fold increase/decrease (BLID shRNA vs. scrambled shRNA MDA-MD-231 cells)	P-value
AKAP12 [a kinase (PRKA) anchor protein 12; NM_005100]	-5.4342	2.79x10 ⁻⁸
PKIB [protein kinase (cAMP-dependent, catalytic) inhibitor β; NM_001270393]	-4.7122	7.75x10 ⁻⁸
DFNA5 (deafness, autosomal dominant 5; NM_001127453)	-3.8540	1.01x10 ⁻¹⁰
MPP4 (membrane protein, palmitoylated 4; NM_033066)	-3.8385	4.06x10 ⁻¹¹
PTN (pleiotrophin; NM_002825)	-3.7402	4.81x10 ⁻¹³
CLGN (calmegin; NM_001130675)	-3.7212	5.20x10 ⁻⁸
KISS1 (KiSS-1 metastasis-suppressor; NM_002256)	-3.5428	6.94x10 ⁻⁸
AOX1 (aldehyde oxidase 1; NM_001159)	-3.4550	3.26x10 ⁻⁸
CHRDL1 (chordin-like 1; NM_001143981)	-3.4327	8.40x10 ⁻¹³

LRRC8C (leucine rich repeat containing 8; NM_032270)	-3.3912	2.90x10 ⁻¹¹
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The top 10 genes, upregulated or downregulated, are listed. P<0.05 was considered to indicate a statistically significant difference. shRNA, short hairpin RNA; RefSeq, Reference Sequence database; BLID, BH-3 like motif containing inducer of cell death; +, upregulated; -, downregulated.

Table SV. Antibody array analysis-based identification of top-ranked proteins modulated in BLID shRNA- vs. scrambled control shRNA-transduced MCF-7 cells.

Encoding gene symbol (encoding gene name)	Swiss-Prot ID	Fold increase or decrease
TAF6 [TAF6 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 80 kDa]	P49848	+2.9±0.1
PIK3CA (phosphoinositide-3-kinase, catalytic, α polypeptide)	P42336	+2.7±0.5
CDH3 [cadherin 3, type 1, P-cadherin (placental)]	P22223	+2.5±0.4
TP63/p73L (tumor protein p73-like)	Q9UBV9	+2.4±0.5
CLTC [clathrin, heavy polypeptide (Hc)]	Q00610	+2.4±0.2
APEX1 [APEX nuclease (multifunctional DNA repair enzyme) 1]	P27695	+2.3±0.2
ITPR3 (inositol 1,4,5-triphosphate receptor, type 3)	Q14573	+2.3±0.0
HSPE1 [heat shock 10 kDa protein 1 (chaperonin 10)]	Q04984	+2.2±0.4
DEK [DEK oncogene (DNA binding)]	P35659	+2.2±0.1
TUBB2A (tubulin, β polypeptide)	Q13885	+2.2±0.2
ARHGAP1 (Rho GTPase activating protein 1)	Q07960	+2.2±0.1
NME1 [non-metastatic cells 1, protein (NM23A) expressed in]	P15531	+2.2±0.2
STK4 (serine/threonine kinase 4)	Q13043	+2.1±0.2
GTF2I (general transcription factor II, i)	P78347	+2.1±0.1
RBP4 (retinol binding protein 4, plasma)	P02753	+2.1±0.2
GLUL [glutamate-ammonia ligase (glutamine synthase)]	P15104	+2.0±0.2
MAPK1 (mitogen-activated protein kinase 1)	P28482	-3.0±0.5
CDK2 (cyclin-dependent kinase 2)	P24941	-2.5±0.3
CYBB/NOX2 (cytochrome b-245, β polypeptide)	P04839	-2.4±0.1
IL-3 [interleukin 3 (colony-stimulating factor, multiple)]	P08700	-2.4±0.3
ARHGDI1 [Rho GDP dissociation inhibitor (GDI) β]	P52566	-2.3±0.3
GEMIN2 (survival of motor neuron protein interacting protein 1)	O14893	-2.3±0.3
LCK (lymphocyte-specific protein tyrosine kinase)	P06239	-2.2±0.2
AIMP1 [small inducible cytokine subfamily E, member 1 (endothelial monocyte-activating)]	Q12904	-2.1±0.1
G3BP1 (Ras-GTPase-activating protein SH3-domain-binding protein)	Q13283	-2.1±0.3
BCAT1 (branched chain aminotransferase 1, cytosolic)	P54687	-2.1±0.2
DHX16 [DEAH (Asp-Glu-Ala-His) box polypeptide 16]	O60231	-2.1±0.2
ROCK2 (Rho-associated, coiled-coil containing protein kinase2)	Q62868	-2.0±0.1
PLCB1 [phospholipase C, β 1 (phosphoinositide-specific)]	Q9NQ66	-2.0±0.3
XRCC6 [thyroid autoantigen 70 kDa (Ku antigen)]	P12956	-2.0±0.1

Proteins showing fold change +2.0 and higher or -2.0 or lower are listed. shRNA, short hairpin RNA; Swiss-Prot ID, Swiss-Prot protein database identification; BLID, BH-3 like motif containing inducer of cell death; +, increase; -, decrease.

Table SVI. Antibody array analysis-based identification of top-ranked proteins modulated in BLID shRNA- vs. scrambled control shRNA-transduced MDA-MB-231 cells.

Encoding gene symbol (encoding gene name)	Swiss-Prot ID	Fold increase or decrease
SYT1 (synaptotagmin I)	P21579	+2.8±0.3
CASP4 (caspase 4, apoptosis-related cysteine protease)	P49662	+2.3±0.1
JUP (junction plakoglobin)	P14923	+2.2±0.0
NUP62 (nucleoporin 62 kDa)	P37198	+2.1±0.2
CDKN1C [cyclin-dependent kinase inhibitor 1C (p57, Kip2)]	P49918	+2.1±0.0
MCL1 [myeloid cell leukemia sequence 1 (BCL2-related)]	Q07820	+2.1±0.2
IL-3 [interleukin 3 (colony-stimulating factor, multiple)]	P08700	-2.8±0.5
PSIP1 (PC4 and SFRS1 interacting protein 1)	O95368	-2.6±0.3
PLK3 (cytokine-inducible kinase)	Q9H4B4	-2.6±0.1
TP73 (tumor protein p73)	O15350	-2.5±0.3
JAK1 [Janus kinase 1 (a protein tyrosine kinase)]	P23458	-2.5±0.1
E1A_ADE05 (adenovirus 5E1A)	P03255	-2.3±0.2
STRN (striatin, calmodulin binding protein)	O43815	-2.0±0.3

Proteins showing fold change +2.0 and higher or -2.0 or lower are listed. . shRNA, short hairpin RNA; Swiss-Prot ID, Swiss-Prot protein database identification; BLID, BH-3 like motif containing inducer of cell death; +, increase; -, decrease.

Table SVII. Antibody array analysis-based identification of top-ranked proteins modulated in BLID shRNA- vs. scrambled control shRNA-transduced MDA-MB-468 cells.

Encoding gene symbol (encoding gene name)	Swiss-Prot ID	Fold increase or decrease
PIK3CA (phosphoinositide-3-kinase, catalytic, α polypeptide)	P42336	+5.8 \pm 0.4
GTF2I (general transcription factor II, I)	O15359	+5.0 \pm 0.2
E2F1 (E2F transcription factor 1)	Q01094	+3.4 \pm 0.1
GOLGA4 (golgi autoantigen, golgin subfamily a, 4)	Q13439	+3.3 \pm 0.1
PRKAR2B (protein kinase, cAMP-dependent, regulatory, type II, β)	P31323	+3.1 \pm 0.2
TAF6 [TAF6 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 80 kDa]	P49848	+3.1 \pm 0.5
NME1 [non-metastatic cells 1, protein (NM23A) expressed in]	P15531	+2.9 \pm 0.1
MKK4/MAP2K4 (mitogen-activated protein kinase kinase 4)	P45985	+2.9 \pm 0.0
ATRN (attractin)	O75882	+2.8 \pm 0.0
XPO1 [exportin 1 (CRM1 homolog, yeast)]	O14980	+2.7 \pm 0.1
DUSP4 (dual specificity phosphatase 4)	Q13115	+2.7 \pm 0.1
ACM1 (cholinergic receptor, muscarinic 1)	P11229	+2.7 \pm 0.1
AKAP1 [a kinase (PRKA) anchor protein 1]	Q92667	+2.7 \pm 0.0
CCNDBP1 [cyclin D-type binding-protein 1 (Cyclin D1 binding protein 1)]	Q9NYH3	+2.6 \pm 0.2
RPL22 (ribosomal protein L22)	P35268	+2.6 \pm 0.2
PCYOX (prenylcysteine lyase)	Q9UHG3	+2.6 \pm 0.0
UB2L3 (ubiquitin-conjugating enzyme E2L 3)	P68036	+2.6 \pm 0.2
SLC9A3R1 [solute carrier family 9 (sodium/hydrogen exchanger), isoform 3 regulatory factor 1]	Q9JJ19	+2.5 \pm 0.1
SYMPK (symplekin)	Q92797	+2.5 \pm 0.1
CASP9 (caspase 9, apoptosis-related cysteine protease)	P55211	+2.4 \pm 0.3
MPDZ (multiple PDZ domain protein)	O75970	+2.4 \pm 0.3
MAPK8IP1 (mitogen-activated protein kinase 8 interacting protein 1)	Q9UQF2	+2.4 \pm 0.3
CTSL (cathepsin L)	P07711	+2.3 \pm 0.2
NPAT (nuclear protein, ataxia-telangiectasia locus)	Q14207	+2.3 \pm 0.3
RASA1/RasGAP [RAS p21 protein activator (GTPase activating protein) 1]	P20936	+2.3 \pm 0.3
RPS6KA1 (ribosomal protein S6 kinase, 90 kDa, polypeptide 1)	Q15418	+2.3 \pm 0.3
CDH5 [cadherin 5, type 2, VE-cadherin (vascular epithelium)]	P33151	+2.3 \pm 0.1
TUBB2 (tubulin, β polypeptide)	Q13885	+2.3 \pm 0.3

MK167 (antigen identified by monoclonal antibody Ki-67)	P46013	+2.3±0.2
CHAF1A [chromatin assembly factor 1, subunit A (p150)]	Q13111	+2.3±0.2
STX11 (syntaxin 11)	O75558	+2.2±0.2
KLK10 (kallikrein 10)	O43240	+2.1±0.3
CRMA (CrmA)	P07385	+2.1±0.1
TSNAX (translin-associated factor X)	Q99598	+2.1±0.2
TCF3 [transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47)]	P15923	+2.1±0.3
IRS1 (insulin receptor substrate 1)	P35568	+2.1±0.1
AMACR (α -methylacyl-CoA racemase)	Q9UHK6	+2.1±0.3
CDC40 [cell division cycle 40 homolog (yeast)]	O75471	-2.4±0.1

Proteins showing fold change +2.0 and higher or -2.0 or lower are listed. . shRNA, short hairpin RNA; Swiss-Prot ID, Swiss-Prot protein database identification; BLID, BH-3 like motif containing inducer of cell death; +, increase; -, decrease.

Table SVIII. Transcriptome effects of BLID knockdown consistent in MCF-7 and MDA-MB-231 cells.

Gene symbol (gene name; RefSeq accession number)	Fold change (BLID shRNA vs. scrambled shRNA MCF-7 cells); P-value	Fold change (BLID shRNA vs. scrambled shRNA MDA-MB-231 cells); P-value
THBS1 (thrombospondin 1; NM_003246)	+2.3381; 6.46x10 ⁻⁵	+6.9940; 8.83x10 ⁻¹³
CXCL2 [chemokine (C-X-C motif) ligand 2; NM_002089]	+2.7447; 0.000282	+2.9942; 0.0001209
WIF1 (WNT inhibitory factor 1; NM_007191)	-2.1543; 0.002409	-3.1283; 5.53x10 ⁻⁵
TMEM64 (transmembrane protein 64; NM_001008495)	-2.2738; 5.48x10 ⁻¹¹	-2.6845; 2.52x10 ⁻¹²
JDP2 (Jun dimerization protein 2; NM_001135047)	-2.1826; 6.18x10 ⁻⁹	-2.3741; 1.24x10 ⁻⁹
PRKX (protein kinase, X-linked; NM_005044)	-2.1366; 6.92x10 ⁻⁹	-2.2756; 1.99x10 ⁻⁹

P<0.05 was considered to indicate a statistically significant difference. shRNA, short hairpin RNA; RefSeq, Reference Sequence database; BLID, BH-3 like motif containing inducer of cell death; +, upregulated; -, downregulated.

Table SIX. Transcriptome effects of BLID knockdown consistent in BLID knockdown MCF-7 and LCC9 cells.

Gene symbol (gene name; RefSeq accession number)	Fold change (BLID shRNA vs. scrambled shRNA MCF-7 cells); P-value	Fold change (BLID shRNA vs. scrambled shRNA LCC9 cells); P-value
IFIT2 (interferon-induced protein with tetratricopeptide repeats 2; NM_001547)	+17.063; 1.70x10 ⁻⁹	+7.2135; 3.88x10 ⁻⁷
IFIT3 (interferon-induced protein with tetratricopeptide repeats 3; NM_001031683)	+16.6726; 2.05x10 ⁻⁹	+20.4356; 6.76x10 ⁻¹⁰
CMPK2 [cytidine monophosphate (UMP-CMP) kinase 2; NM_001256477]	+14.5695; 4.39x10 ⁻⁹	+6.9444; 5.30x10 ⁻⁷
IFIT1 (interferon-induced protein with tetratricopeptide repeats 1; NM_001270927)	+7.3012; 3.32x10 ⁻⁵	+29.4236; 2.60x10 ⁻⁸
SAMD9 (sterile α motif domain containing 9; NM_001193307)	+6.3386; 3.78x10 ⁻⁶	+2.4833; 0.004721
OAS1 (2'-5'-oligoadenylate synthetase 1; NM_001032409)	+5.8863; 2.15x10 ⁻⁸	+6.2472; 1.30x10 ⁻⁸
XAF1 (XIAP associated factor 1; NM_017523)	+5.8702; 4.50x10 ⁻⁹	+5.9303; 4.11x10 ⁻⁹
DDX60 [DEAD (Asp-Glu-Ala-Asp) box polypeptide 60; NM_017631]	+5.7172; 7.95x10 ⁻⁶	+6.4024; 3.57x10 ⁻⁶
IFI6 (interferon, α -inducible protein 6; NM_002038)	+2.6636; 0.000302	+7.4249; 3.57x10 ⁻⁸
AFAP1L2 (actin filament associated protein 1-like 2; NM_001001936)	-3.7661; 3.34x10 ⁻⁹	-3.6520; 4.82x10 ⁻⁹
GANAB (glucosidase, α ; neutral AB; NM_001278192)	-3.4326; 0.00015	-3.7182; 7.64x10 ⁻⁵
PDZK1 (DZ domain containing 1; NM_001201325)	-3.1047; 0.000609	-4.4397; 3.52x10 ⁻⁵
GJA1 (gap junction protein, α 1; NM_000165)	-2.8930; 8.13x10 ⁻⁵	-5.1430; 3.49x10 ⁻⁷
SPANXA1 (sperm protein associated with the nucleus, X-linked; NM_013453)	-2.6123; 0.001506	-4.7876; 9.26x10 ⁻⁶
KLF12 (Kruppel-like factor 12; NM_007249)	-2.3156; 1.47x10 ⁻⁷	-2.5897; 2.31x10 ⁻⁸

RALGDS (Ral guanine nucleotide dissociation stimulator; NM_001042368)	-2.2944; 0.000492	-2.6274; 0.000108
SESN3 (sestrin 3; NM_001271594)	-2.1031; 3.47x10 ⁻⁶	-2.5052; 1.92x10 ⁻⁷
PRKX (protein kinase, X-linked; NM_005044)	-2.1364; 6.92x10 ⁻⁹	-2.6864; 1.73x10 ⁻¹¹

P<0.05 was considered to indicate a statistically significant difference. shRNA, short hairpin RNA; RefSeq, Reference Sequence database; BLID, BH-3 like motif containing inducer of cell death; +, upregulated; -, downregulated.

Table SX. Transcriptome effects of BLID knockdown consistent in BLID knockdown MDA-MB-231 and LCC9 cells.

Gene symbol (gene name; RefSeq accession number)	Fold change (BLID shRNA vs. scrambled shRNA MDA-MB-231 cells); P-value	Fold change (BLID shRNA vs. scrambled shRNA LCC9 cells); P-value
CYP1B1 (cytochrome P450, family 1, subfamily B, polypeptide 1; NM_000104)	+4.3772; 5.30x10 ⁻⁸	+2.1536; 0.000213
NEGR1 (neuronal growth regulator 1; NM_173808)	-3.0517; 1.65x10 ⁻⁶	-2.1352; 0.000164
NEURL1B (neuralized homolog 1B; NM_001142651)	-2.7064; 5.82x10 ⁻¹⁰	-2.5932; 1.17x10 ⁻⁹
GAD1 (glutamate decarboxylase 1; NM_000817)	-2.3636; 5.33x10 ⁻⁷	-3.2671; 4.73x10 ⁻⁹
PRKX (protein kinase, X-linked; NM_005044)	-2.2756; 1.99x10 ⁻⁹	-2.6864; 1.73x10 ⁻¹¹
GPR161 (G protein-coupled receptor 161; NM_001267609)	-2.2197; 2.60x10 ⁻⁶	-1.9485; 2.41x10 ⁻⁵
SLITRK5 (SLIT and NTRK-like family, member 5; NM_015567)	-2.1966; 6.32x10 ⁻⁸	-2.0081; 3.62x10 ⁻⁷
UBE2D3 (ubiquitin-conjugating enzyme E2D 3; NM_003340)	-2.1601; 2.40x10 ⁻⁵	-2.2086; 1.71x10 ⁻⁵
PABPC4L [poly(A) binding protein, cytoplasmic 4-like; NM_001114734]	-2.0070; 0.00021	-2.2722; 3.54x10 ⁻⁵

P<0.05 was considered to indicate a statistically significant difference. shRNA, short hairpin RNA; RefSeq, Reference Sequence database; BLID, BH-3 like motif containing inducer of cell death; +, upregulated; -, downregulated.

Table SXI. Proteome effects of BH-3 like motif containing inducer of cell death (BLID) knockdown consistent in MCF-7 and MDA-MB-231 cells.

Encoding gene symbol (encoding gene name)	Swiss-Prot ID	MCF-7 cells (fold decrease)	MDA-MB-231 cells (fold decrease)
IL-3 [interleukin 3 (colony-stimulating factor, multiple)]	P08700	-2.4±0.3	-2.8±0.5

Swiss-Prot ID, Swiss-Prot protein database identification; -, downregulated.

Table SXII. Proteome effects of BH-3 like motif containing inducer of cell death (BLID) knockdown consistent in MCF-7 and MDA-MB-468 cell lines.

Encoding gene symbol (encoding gene name)	Swiss-Prot ID	MCF-7 cells (fold increase)	MDA-MB-468 cells (fold increase)
PIK3CA (phosphoinositide-3-kinase, catalytic, α polypeptide)	P42336	+2.7 \pm 0.5	+5.8 \pm 0.4
TAF6 [TAF6 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 80 kDa]	P49848	+2.9 \pm 0.1	+3.1 \pm 0.5
NME1 [non-metastatic cells 1, protein (NM23A) expressed in]	P15531	+2.2 \pm 0.2	+2.9 \pm 0.1

Swiss-Prot ID, Swiss-Prot protein database identification; +, upregulated.

Table SXIII. Summary of miRNA array analysis: A subset of top-ranked human miRs showing changes in expression in BLID knockdown MDA-MB-231 and LCC9 breast cancer cells.

A, MDA-MB-231 cells		
Human microRNA	Fold change in miR level in BLID shRNA vs. Scr shRNA cells	P-value
hsa-miR-27a-star	+3.37	2.60x10 ⁻⁵
hsa-miR-933	+4.31	0.0025
hsa-miR-4486	+3.62	0.0046
hsa-miR-3180-3p	+3.30	0.0075
hsa-miR-4649-5p ^a	+3.28	0.0092
hsa-miR-1909	+3.24	0.0006
hsa-miR-3180	+3.16	0.0071
hsa-miR-4417	+3.10	0.0008
hsa-miR-1225-5p	+3.08	0.0087
hsa-miR-3197	+3.05	0.0017
hsa-miR-3187-3p _{st} ^a	+2.63	0.0118
hsa-miR-3141 _{st} ^a	+2.57	0.0136
hsa-miR-3196 _{st} ^a	+2.24	0.0065
hsa-miR-4466 _{st} ^a	+2.22	0.0008
hsa-miR-4497 _{st} ^a	+2.12	0.0025
hsa-miR-4529-3p	-4.11	0.0472
hsa-miR-181c	-2.78	0.0227
hsa-miR-152	-2.74	0.0005
hsa-miR-7	-2.63	0.0122
hsa-miR-518f-star	-2.62	0.0001
hsa-miR-330-3p	-2.41	0.0041
hsa-miR-422a	-2.23	0.0006
B, LCC9 cells		
Human microRNA	Fold change in miR level in BLID shRNA vs. Scr shRNA cells	P-value
hsa-miR-3141 _{st} ^a	+2.86	0.0074
hsa-miR-4649-5p _{st} ^a	+2.80	0.0196
hsa-miR-4758-5p _{st}	+2.34	0.0190
hsa-miR-4281 _{st}	+2.29	0.0069
hsa-miR-4725-3p _{st}	+2.20	0.0039
hsa-miR-2861 _{st}	+2.20	0.0038
hsa-miR-4741 _{st}	+2.17	0.0101
hsa-miR-4516 _{st}	+2.14	0.0029
has-miR-4466 _{st} ^a	+2.09	0.0015
hsa-miR-3187-3p _{st} ^a	+2.07	0.0460

hsa-miR-4739_st	+2.06	0.0025
hsa-miR-3940-5p_st	+2.05	0.0080
hsa-miR-4497_st ^a	+2.02	0.0039
hsa-miR-3196_st ^a	+2.01	0.0146
hsa-miR-584_st	-2.43	0.0253
hsa-let-7g_st	-2.24	0.0318

^aUpregulation of these miRs was seen in both MDA-MB-231 and LCC9 cells. Upregulation of hsa-miR-27a-star was also seen in BLID knockdown LCC9 cells (+1.53; P=0.0396) and BLID knockdown MCF-7 cells (+2.46; P=0.0003). Downregulation of hsa-let-7g was also seen in BLID knockdown MCF-7 cells (-2.38; P=0.0418). Three Affymetrix GeneChip miRNA 3.0 arrays (part #902018) were used per treatment group. Fold change (BLID shRNA knockdown vs. scrambled shRNA control) >2 was used as a cut-off, P<0.05 (n=3). shRNA, short hairpin RNA; Scr, scrambled; BLID, BH-3 like motif containing inducer of cell death; miRNA/miR, microRNA; +, high in the BLID shRNA group; -, low in the BLID shRNA group.

Table SXIV. RNA array analysis-based identification of top canonical pathways, diseases and biofunctions in which BH-3 like motif containing inducer of cell death-centric mRNAs are implicated in breast cancer cells.

A, Canonical pathway		
Pathway/disease/biofunction	P-value (MCF-7 cells)	P-value (MDA-MB-231 cells)
Interferon signaling ^a	2.60x10 ⁻¹³	N.L.
Antigen presentation pathway	1.49x10 ⁻⁷	0.0138
Communication between innate and adaptive immune cells	1.55x10 ⁻⁶	N.L.
Role of pattern recognition receptors in recognition of bacteria and viruses ^b	1.65x10 ⁻⁶	N.S.
Activation of IRF by cytosolic pattern recognition receptors ^c	6.46x10 ⁻⁶	N.L.
Role of osteoblasts, osteoclasts and chondrocytes in rheumatoid arthritis	N.S.	1.13x10 ⁻⁵
Molecular mechanisms of cancer	N.S.	1.72x10 ⁻⁵
Hepatic fibrosis/hepatic stellate cell activation ^d	0.0107	3.32x10 ⁻⁵
Mouse embryonic stem cell pluripotency	N.L.	7.68x10 ⁻⁵
TGF-β signaling	N.S.	1.54x10 ⁻⁴
B, Disease		
Pathway/disease/biofunction	P-value (MCF-7 cells)	P-value (MDA-MB-231 cells)
Antimicrobial response ^e	7.90x10 ⁻⁴ - 2.21x10 ⁻²⁹	N.L.
Inflammatory response ^f	4.70x10 ⁻³ - 2.21x10 ⁻²⁹	1.18x10 ⁻² -1.23x10 ⁻⁸
Infectious diseases ^g	4.62x10 ⁻³ - 7.61x10 ⁻¹⁷	3.49x10 ⁻³ -5.91x10 ⁻⁶
Dermatological diseases and conditions ^h	4.19x10 ⁻³ - 9.78x10 ⁻¹⁶	9.6 x10 ⁻³ -1.03x10 ⁻⁴
Organismal injury and abnormalities ⁱ	4.84x10 ⁻³ - 9.78x10 ⁻¹⁶	1.15x10 ⁻² -8.29x10 ⁻¹⁰
Connective tissue disorders	4.15x10 ⁻³ - 6.18x10 ⁻⁷	9.70x10 ⁻³ -8.29x10 ⁻¹⁰
Skeletal and muscular disorders	4.03x10 ⁻³ - 6.18x10 ⁻⁷	1.07x10 ⁻² -8.29x10 ⁻¹⁰
Cancer	4.84x10 ⁻³ - 1.51x10 ⁻¹³	1.15x10 ⁻² -4.18x10 ⁻⁹
Gastrointestinal disease	4.84x10 ⁻³ - 2.95x10 ⁻⁷	1.13x10 ⁻² -4.18x10 ⁻⁹
C, Biofunction		
Pathway/disease/biofunction	P-value (MCF-7 cells)	P-value (MDA-MB-231 cells)
Cell signaling ^j	3.82x10 ⁻³ - 2.94x10 ⁻¹⁴	1.14x10 ⁻² -2.32x10 ⁻³
Cell death and survival ^k	4.70x10 ⁻³ - 1.17x10 ⁻⁹	1.14x10 ⁻² -1.14x10 ⁻⁶
Cellular development	4.63x10 ⁻³ - 6.60x10 ⁻⁹	1.09x10 ⁻² -4.19x10 ⁻⁹

Cellular movement ^l	4.81x10 ⁻³ - 1.37x10 ⁻⁸	1.18x10 ⁻² -5.92x10 ⁻¹³
Drug metabolism	3.02x10 ⁻³ - 3.46x10 ⁻⁷	8.83x10 ⁻³ -8.83x10 ⁻³
Cellular growth and proliferation	4.63x10 ⁻³ - 2.34x10 ⁻⁶	1.09x10 ⁻² -4.19x10 ⁻⁹
Cellular function and maintenance	4.9x10 ⁻³ -4.3x10 ⁻⁵	1.05x10 ⁻² -9.69x10 ⁻⁷

Similar observations were made in RNA array analysis of LCC9 cells (P-values: ^a9.74x10⁻¹⁰; ^b1.98x10⁻⁴; ^c1.32x10⁻⁶; ^d1.45x10⁻³; ^e9.10x10⁻³-7.56x10⁻¹⁵; ^f9.10x10⁻³-7.56x10⁻¹⁵; ^g9.10x10⁻³-3.50x10⁻¹⁰; ^h9.10x10⁻³-1.29x10⁻¹¹; ⁱ9.10x10⁻³-1.29x10⁻¹¹; ^j8.43x10⁻³-1.31x10⁻⁸; 9.10x10⁻³-6.79x10⁻⁶; ^l9.10x10⁻³-6.89x10⁻⁸). N.L., not listed; N.S., not significant (>0.05).

Table SXV. Antibody array analysis-based identification of top canonical pathways, diseases and biofunctions in which BH-3 like motif containing inducer of cell death-centric proteins are implicated in breast cancer cells.

A, Canonical pathway		
Pathway/disease/biofunction	P-value (MCF-7 cells)	P-value (MDA-MB-231 cells)
Breast cancer regulation by stathmin 1	1.61x10 ⁻⁸	0.0021
fMLP signaling in neutrophils	9.39x10 ⁻⁷	0.0107
CCR3 signaling in eosinophils	1.10x10 ⁻⁶	N.S.
Gq signaling	3.47x10 ⁻⁶	N.L.
Glioblastoma multiforme signaling	3.69x10 ⁻⁶	N.S.
Glucocorticoid receptor signaling	0.0014	3.40x10 ⁻⁶
Production of nitric oxide and reactive oxygen species in macrophages	0.0001	4.12x10 ⁻⁶
ILK signaling	0.0331	1.01x10 ⁻⁴
MSP-RON signaling pathway	0.0051	1.05x10 ⁻⁴
Dopamine receptor signaling pathway	N.L.	1.24x10 ⁻⁴
B, Disease		
Pathway/disease/biofunction	P-value (MCF-7 cells)	P-value (MDA-MB-231 cells)
Cancer ^a	3.31x10 ⁻³ -6.03x10 ⁻¹⁶	3.85x10 ⁻³ -1.31x10 ⁻¹¹
Hematological disease ^b	3.26x10 ⁻³ -6.03x10 ⁻¹⁶	3.85x10 ⁻³ -1.31x10 ⁻¹¹
Immunological disease ^c	3.26x10 ⁻³ -6.03x10 ⁻¹⁶	3.85x10 ⁻³ -1.31x10 ⁻¹¹
Organismal injury and abnormalities ^d	3.31x10 ⁻³ -6.03x10 ⁻¹⁶	3.85x10 ⁻³ -1.31x10 ⁻¹¹
Infectious diseases	2.98x10 ⁻³ -7.36x10 ⁻⁷	2.57x10 ⁻³ -3.48x10 ⁻⁵
Renal and urological disease	2.12x10 ⁻³ -2.73x10 ⁻⁴	2.57x10 ⁻³ -1.04x10 ⁻⁶
C, Biofunction		
Pathway/disease/biofunction	P-value (MCF-7 cells)	P-value (MDA-MB-231 cells)
Cell death and survival ^e	2.98x10 ⁻³ -3.32x10 ⁻¹⁰	3.85x10 ⁻³ -1.77x10 ⁻¹⁰
Cell cycle ^f	2.98x10 ⁻³ -2.97x10 ⁻⁸	3.85x10 ⁻³ -1.49x10 ⁻⁶
Cellular movement	2.98x10 ⁻³ -4.40x10 ⁻⁸	3.85x10 ⁻³ -3.31x10 ⁻⁵
Gene expression ^g	2.72x10 ⁻³ -4.68x10 ⁻⁷	3.85x10 ⁻³ -9.47x10 ⁻⁷
Cellular growth and proliferation ^h	3.03x10 ⁻³ -3.78x10 ⁻⁶	3.85x10 ⁻³ -9.28x10 ⁻⁶
Cellular development ⁱ	3.03x10 ⁻³ -3.74x10 ⁻⁵	3.85x10 ⁻³ -5.67x10 ⁻⁸
Free radical scavenging	1.49x10 ⁻³ -1.49x10 ⁻³	1.52x10 ⁻³ -1.36x10 ⁻⁷
Cell-to-cell signaling and interaction	3.14x10 ⁻³ -5.77x10 ⁻⁵	3.85x10 ⁻³ -8.07x10 ⁻⁷

Similar observations were made in antibody array analysis of MDA-MB-468 cells (P-values: ^a1.47x10⁻²-5.99x10⁻¹⁸; ^b1.26x10⁻²-5.99x10⁻¹⁸; ^c1.26x10⁻²-5.99x10⁻¹⁸; ^d1.47x10⁻²-5.99x10⁻¹⁸; ^e1.31x10⁻²-1.50x10⁻⁷; ^f1.37x10⁻²-3.23x10⁻⁶; ^g1.21x10⁻⁴-4.68x10⁻⁶; ^h1.47x10⁻²-1.32x10⁻⁷; ⁱ1.29x10⁻²-1.32x10⁻⁷). N.L., not listed; N.S., not significant (>0.05).